FULL/LONG TITLE OF THE STUDY

Safe inhalation pipe provision (SIPP): A mixed method evaluation of an intervention to reduce health harms and enhance service engagement among people who use crack cocaine in England.

SHORT STUDY TITLE / ACRONYM

SIPP (Safe inhalation pipe provision)

PROTOCOL VERSION NUMBER AND DATE: V7 21st December 2023

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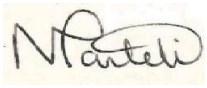
SIGNATURE PAGE

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 publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: 

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Contents

1. Summary of Research

Evidence of need: Escalating crack cocaine use is a public health concern [1]. 180,848 people used crack in England 2016/17; an 8.5% rise over 5 years [2]. While many also inject drugs or access services for opiate substitution treatment (OST), over 50,000 people who use crack (PWUC) do not use opiates and are less likely to access drug treatment services [2]. Provision of safe inhalation equipment for crack cocaine is prohibited under UK law. Pipes used for crack cocaine smoking are often homemade and/or in short supply, leading to pipe sharing and acute injuries from use of unsafe materials [3]. This increases risk of viral infection (hepatitis C, SARS-COV2) and respiratory harm (chronic obstructive pulmonary disease) among a marginalised underserved population.

Legislative review of crack pipe prohibition in the UK is needed but must be evidence informed. Police chief constables and police crime commissioners (PCCs) in the study sites support the SIPP intervention and have provided letters confirming that they will allow local SIPP implementation, providing a legal protection against prosecution. International evaluations of crack pipe supply suggest sustained reductions in pipe sharing and use of homemade equipment; increased health risk awareness; improved access to services; transitions from injecting to smoking and significant reductions in crack-related health problems [4-10].

Intervention overview: SIPP comprises: 1) The SIPP kit: A hard plastic case containing a straight stem borosilicate glass pipe; steel gauze filters/meshes; plastic mouth pieces harm reduction information and an ethics card stating the time-limited nature of distribution; 2) Provider training: an online crack harm reduction training module delivered to service providers prior to SIPP kit distribution; 3) Peer-to-peer (P2P) training: a brief face-to-face risk reduction intervention developed by peers.

Aim: To evaluate a safe crack inhalation intervention distributed to PWUC via drug treatment services and peer networks in order to reduce crack-related health harms and inform legislative review.

Research question: To what extent and how does SIPP reduce health risks and enhance service engagement among people who use crack cocaine?

Objectives:

1. Measure the effect and cost-effectiveness of SIPP on harms and risks associated with crack use (pipe sharing, presentation at drug services, using home-made pipes, cuts/burns, crack injecting).
2. Evaluate SIPP fidelity, reach and acceptability in diverse drug treatment and peer-network settings.
3. Explore the barriers and facilitators to SIPP uptake and service engagement among PWUC.
4. Explore the mechanisms through which SIPP facilitates changes in health risks and access to services, to inform implementation at scale.
5. Build peer-network research capacity and explore whether the quality and impact of their SIPP engagement with PWUC differs in comparison with SIPP engagement through drug treatment services.
6. Co-develop a scalable SIPP toolkit and harm reduction resources to enhance PWUC engagement with drug treatment services and to facilitate crack-related risk reduction practices.
7. Translate evidence to policy and advocacy outputs, including to inform legislative review.

Outcome measures:

Primary: crack pipe sharing in the past 28 days.

Secondary: drug treatment service engagement; reduced injecting; acute injuries (cuts, burns); use of homemade pipes; use of ash, respiratory risk markers (difficulty breathing, chest pain, coughing blood).

Design: Quasi-experimental design comprising a pre-post comparison study with a non-equivalent control group and a nested qualitative study to identify impacts and predictors of SIPP use to inform intervention scale up and an assessment of its cost-effectiveness.

Population: People who use crack cocaine (PWUC): self-identified crack use in the past 28 days.

Sites: We are collaborating with two peer network (CoAct/Mat Southwell, Bristol; and the Hepatitis C Trust Peer to Peer, Birmingham) and four drug treatment and linked outreach services: (CGL, Nottinghamshire South and Nottinghamshire West; Bristol Drugs Project; Health Shop and POW sex worker outreach, Nottingham). We have the support of Avon & Somerset and Nottinghamshire Police Forces for SIPP implementation. Control sites (n=4) are comparable areas (in relation to crack use) in England (services provided by CGL).

Delivery plan:

Phase 1 [months 1-6]: **Optimise**: Evidence review; Peer-researcher training; Co-production workshops with the peer networks to optimise and finalise SIPP components; P2 survey set up

Phase 2: [months 7-12]: **Generate baseline data:** Baseline cross-sectional survey to assess population characteristics across intervention and control sites and measure primary and secondary outcomes pre-intervention; Stakeholder interviews and focus groups with drug treatment staff to introduce SIPP, explore local context, potential implementation challenges and perceived mechanisms of change.

Phase 3 [months 13-21]: **Implement:** Implementation sites and peer networks will deliver SIPP for 6 months, with staggered set up for project manageability. Each person receiving SIPP will complete a brief survey, linked by minimum identifiers, to assess the dose-response effects of the intervention. In-depth interviews with PWUC receiving SIPP will explore: crack use practices, risks and service engagement; experience and acceptability of SIPP; barriers and facilitators to risk reduction and unmet need. Observations of SIPP provision and (where possible) the contexts of use will clarify causal mechanisms and identify contextual factors impacting SIPP fidelity, reach, uptake, acceptability and impact on practice.

Phase 4: [months 22-27] **Evaluate:** Follow-up cross-sectional survey at intervention and control sites to assess SIPP coverage and impact on primary and secondary outcomes. We will use the survey results and site monitoring data to perform an economic evaluation of SIPP informed by consultations with commissioners and providers. Follow-up interviews with staff and stakeholders at intervention sites will explore experiences and acceptability of SIPP, mechanisms of impact and adaptations required for better contextual fit.

Phase 5: [months 28-33] **Disseminate**: Coproduction workshops with PWUC and peer networks to develop harm reduction resources for PWUC, optimise SIPP kit for scale up; finalised SIPP implementation toolkit for dissemination through drug treatment services; a policy report and presentations to inform legislative review.

Patient and Public Involvement (PPI): Formative work with PWUC in London and with national networks of people who use drugs, drug treatment providers, local authority commissioners, policing teams and the hepatitis C trust have informed this proposal. This project is a community-academic partnership, addressing community-identified unmet need and building peer researcher capacity, with meaningful peer and community stakeholder involvement throughout ensuring project accountability and output relevance.

Impact: Led by a team of multidisciplinary researchers (combining clinical, social science, epidemiological, economic and substance dependence health expertise), drug treatment providers and peer-led drug user networks, this research will deliver value for money by reducing acute health harms and improving pathways to care for PWUC. Our qualitative component will provide insight

into the characteristics and unmet needs of PWUC. This is crucial for improving care for and reducing health inequalities among a highly marginalised and underserved population.

2. Background and Rationale

Use of crack cocaine, either via inhalation or injection, is and associated with serious health and social harms, such as infectious disease, premature mortality and high levels of acquisitive crime [1, 9-13]. England has the highest prevalence of people who use crack (PWUC) in the European region [14]. This is growing population, with an 8.5% rise in PWUC from an estimated 166,640 in 2012 to 180,748 in 2017 [2]. An official inquiry into this increase highlights it as a serious public health concern, calling for "research to explore the characteristics of 'hidden' crack users who are not currently in treatment" [1]. Most reported crack use is among people who inject drugs (PWID) and use opioids, or access services for opioid substitution therapy (OST), yet samples from drug treatment and criminal justice services are subject to bias [15]. Modelling data for 2017 estimate 29% of PWUC (52,677) do not use opiates and thus are less likely to be in touch with drug treatment services [2].

Provision of opiate substitution therapy (OST) and sterile injecting equipment is evidenced to have saved countless lives – not only through directly averting hepatitis and HIV transmission [16] – but indirectly, though providing links to ancillary health and social care services. While OST offers protection against heroin withdrawal, there is no commensurate pharmaceutical treatment available for crack use. Psychological treatment for cocaine dependence is advocated [17], yet PWUC have limited motivation to engage with services [1, 3]. Crack pipes are a valued commodity among PWUC and can provide a point of engagement with which to assess health risks and facilitate pathways to addiction treatment, health and social care.

UK drug services are prohibited from supplying crack smoking equipment under the Misuse of Drugs Act, 1971, although injecting equipment provision is allowed [4]. This means that pipes for smoking crack are often made from unsafe materials and shared [5-8]. Resultant acute and long-term health harms include: lip cuts and burns from unsafe pipes (metal cans, glass bottles); respiratory damage from fume and filter inhalation (plastic bottles, asthma inhalers, pot scrubbers, ash); infectious disease transmission (COVID-19, hepatitis C, HIV)) from sharing pipes and transitions to injecting [5, 7-10, 18-21].

This project is supported by police force partners in Nottinghamshire and Avon & Somerset Police who have provided permissions for pilot implementation of the SIPP intervention. These 'letters of comfort' are crucial to provide reassurance to services that they can take part without fear of prosecution. Local drug treatment providers and police and crime commissioners (PCCs) support SIPP as offering potential for a pragmatic and meaningful point of engagement with a high-risk population. Drug treatment services currently have little to offer PWUC. This is crucial to address, given that drug treatment service engagement is associated with marked reductions in offending, recidivism, morbidity and drug related death [1, 13, 20].

Our peer-network team members provide unprecedented access to PWUC not in touch with services. Peers are instrumental in transferring crack risk reduction knowledge [22] and providing support in the context of drug use, homelessness and exclusion [23, 24]. This project will add value by seeking to understand the barriers and facilitators to working with peer networks as research partners in order to inform future community-participatory research with marginalised populations. In addition, we will explore if the mode of SIPP delivery (peer network vs drug treatment service) influences SIPP acceptability and reduction in risk practices. This knowledge has transferable value to inform scale up of other harm reduction and public health interventions for marginalised populations (needle and syringe provision, vaccine rollout etc).

Formative work

We undertook a scoping review to inform our proposal and choice of primary outcome (pipe sharing), searching MEDLINE and EMBASE on 31/02/2020. We used search terms relating to crack cocaine; health outcomes and prevention measures. As reported in a resulting publication [3], we found a limited literature on safe crack pipe interventions, primarily from Canada where crack smoking equipment and information provision are widespread [21]. Study designs were observational without comparison groups but indicated positive public health impact. These included: reductions in the sharing and/or use of homemade crack paraphernalia; increased awareness of crack-related health risks; improved access to services offering crack paraphernalia and reduced injecting [6, 7, 18-20, 25, 26]. Reported decreases in pipe sharing appear incremental but sustained [12], with pipe acquisition through health services significantly and negatively associated with crack-related health problems [20]. These findings are not necessarily transferable to the UK, given different drug treatment and crack use contexts, and require local and robust evidencing.

Safe inhalation kits typically include heat-resistant Pyrex and/or borosilicate glass pipes, metal filters, rubber mouthpieces and push sticks for cleaning pipes and collecting crack residue [8, 12, 19, 27]. Pipe sharing has been chosen as our primary outcome measure due to evidenced risk evidence of HCV transmission from shared crack pipes [9, 10, 28] and concerns regarding COVID-19 transmission [3, 14]. The risk of blood borne virus transmission is exacerbated when the pipes shared are made from homemade materials.

Given prohibitions on crack pipe supply, there is a dearth of evidence on associated interventions in the UK context. There are indications of 'underground' distribution in some UK locations, including through secondary supply. It is crucial to learn from this work – key actors have input into proposal development. The UK PIPES study which measured risks associated with crack smoking devices found that risk awareness among PWUC was low, but information provision without equipment supply was inadequate to change practice [27]. Our SIPP provider training draws on this and the Royal College of General Practice Guidance for working with people who use crack in primary care [17], co-developed with the peer-led 'Crack Squad'. Our team includes the original lead of the 'Crack Squad' (MS) and PIPES (JS). We build on this learning to develop protocols with PWUC to improve service delivery and reduce crack-related risk.

3. Evidence explaining why this research is needed now

The SIPP intervention is crucial to implement now, given the multiple health and social harms associated with crack use, including high crime engagement [13, 29]. Crack pipe provision can reduce risk practices and provide a 'hook' to engage people in services [3, 7, 9, 18, 20, 22, 25]. This holds potential for long term public health benefits: 1) reduced viral transmission (HCV, SARS-COV2); 2) reduced respiratory problems (e.g. COPD); 3) increased treatment engagement providing an opportunity to address broader mental health and social harms associated with crack use through multi-agency referral and holistic intervention.

Recent surveillance data for England and Wales report high levels of crack injection, at 57% among PWID in 2019 [30]. Crack injection is associated with elevated blood borne virus (HCV, HIV) and bacterial infection risk, given increased injection frequency compared to opiate use [31]. The UK is a signatory to the 2016 Global Health Sector Strategy on viral hepatitis, with the 2030 goal of reducing hepatitis infections by 90% and deaths by 65% [32], yet new and repeat HCV infections remain high [31]. It is crucial for the HCV elimination strategy to engage with marginalised populations, less likely to engage with services or identify themselves as at risk of HCV, such as PWUC. Provision of materials to support transitions from injecting (crack pipes, foil for heroin smoking [33]) are crucial to reduce injecting-related health harms, such as HCV.

The importance of enhancing PWUC engagement and risk reduction practices is increasingly recognised by drug treatment services and police networks in the UK. The COVID-19 pandemic has generated support for the SIPP project, given that pipe sharing poses a high COVID-19 transmission risk [9, 34]. Smoking crack is associated with pulmonary and respiratory problems such as pulmonary oedema and COPD (chronic obstructive pulmonary disease) [11, 35]. Use of homemade pipes increases respiratory harms [27] – placing people at heightened risk of COVID-19 related morbidity if they contract the virus. High prevalence of COPD among this population [36, 37] is a continuing concern even as COVID-19 risk diminishes with vaccine rollout.

The 2021 Carol Black report stresses the importance of reinvigorating drug treatment service provision to engage with "very vulnerable groups, such as crack cocaine users … [who] do not receive adequate or any service but are at great risk" [29]. PWUC experience high levels of stigma, which can prevent them from help-seeking and contribute to health inequities [38, 39]. Pipes, a highly valued commodity among PWUC, can provide an engagement hook to assess unmet need, including in relation to respiratory health. Smoking risk is rarely prioritised in harm reduction interventions, which predominantly orientate around injecting practices. Injection cessation is a drug treatment goal and transitioning from injecting can be a step toward abstinence. There are, however, no supports provided to enable transitions from crack injecting to smoking.

Legislative review of crack pipe provision is broadly supported among PCC and drug treatment service providers, however any amendment to the Misuse of Drugs Act must be evidence informed. The 2014 amendment to allow foil provision for heroin smoking was informed by a small pilot evaluation, which found that foil provision supported transitions from heroin injection to smoking [33]. Our research is imperative to innovate service provision to increase its relevance to PWUC [40], inform legislative review and reduce crack-related, injecting and respiratory harms among this highly disenfranchised and growing population.

Legal precedent

There is legal precedent for public health interventions of this nature in the United Kingdom. Pizzey and Hunt [33] conducted an intervention titled "Distributing foil from needle and syringe programmes (NSPs) to promote transmissions from heroin injecting to chasing: An evaluation" between 2006 and 2007. Similarly to crack pipes, distributing foil for heroin smoking was prohibited at the time of the study. Pizzey and Hunt [33] aimed to evaluate the impact of smoking equipment supply on reducing injection frequency and other drug use harms. To conduct their intervention and evaluation, they were issued police letters of comfort from Avon and Somerset Police which stated that providing foil for smoking heroin through drug treatment services and NSPs would not lead to prosecution, and that no files would be prepared for the crown prosecution service. This intervention demonstrated a reduction in injection frequency and was influential in achieving legislative change that allowed the widespread supply of foil through NSPs [41].

Further precedent can be found in evidence generated by Garden et al. [42] to support the provision of acidifier for injection preparation. Prior to 2003, providing citric acid and vitamin C for injection preparation was in contravention of UK law. Garden's research received support from Strathclyde Police to be carried out in 2001-2002 in Glasgow, and allowed pharmacy needle exchanges to offer 100mg single use sachets of citric acid to people who inject drugs. Amendments were made to section 9A of the Misuse of Drugs Act to legalise their supply through medical and harm reduction providers in 2003 for citric acid and 2005 for vitamin C. They are now considered core items in injection equipment packs through pharmacy and drug treatment NSP [3]

The department of Health, Social Services and Public Health recognises the use of 'letters of comfort' in research, such as those issued by police services to allow foil distribution by Pizzey and Hunt [33]. In a DHSC circular announcing the changes made to the Misuse of Drugs Act in 1971 under the Misuse of Drugs Regulations 2001 to permit foil provision, it was stated that:

> *17. Following implementation of the legislative changes, drug treatment providers who have previously supplied foil as a result of 'letters of comfort' issued by some police forces will be expected to comply with the new legislative provisions. This means that the further provision of foil after the legislative changes comes into force must be in accordance with the conditions set out in the legislation. Police forces will be informed of the expectation to comply with the conditions as set out in the legislation* [43]

We are therefore confident that our letters of comfort meet criteria deemed acceptable by local police forces and the relevant public service bodies.

Formative work

We have conducted a small pilot with Community Driven Feedback, the original peer network in Bristol, to assess recruitment feasibility among people not in touch with services and to test the acceptability of our survey instrument with the target population as well as with the peer-researchers. Over three weeks two peers recruited 33 PWUC through peer networks and homeless hostels. Of the 33 respondents (25 male, 8 female), only five had accessed a drug treatment or harm reduction service in the past 28 days, but 23 said that they would, if pipes were available there. The average age of the sample was 41 years, with an average crack use duration of 16 years. Only 42% were stably housed. On average, they spent £108 on crack per day (range £20-£300). 17 (51%) respondents reported sharing pipes in the past 28 days, with 22 (67%) using a homemade pipe. Most respondents indicated health problems, with 19 (58%) reporting acute crack-smoking related issues (difficulty breathing, burns and cuts) in the past 28 days. Qualitative responses indicated unmet health and treatment care needs:

> *"Drug workers don't know about crack or what advice to give me. I want to reduce, but they only give me methadone or bupe"; "There's no one I can speak to. I want to stop."*

Given the complex health and social challenges PWUC face, we have worked with service users and providers to ensure that the SIPP intervention is relevant and comprehensive. Safe smoking equipment provision is just one component. We will co-produce an online training module for drug treatment and allied health providers on crack-related risks and harm reduction and, with peer networks, a brief risk reduction intervention to sit alongside SIPP provision. SIPP is, therefore, a pipe and engagement intervention.

We have consulted widely with drug treatment service and police providers and presented this proposal at policy and practice meetings (Scottish Injection Equipment Guidelines webinar, CGL National Harm Reduction Network webinar, Westminster Drugs Project seminar, etc). Providers speak of poor crack-specific knowledge and a lack of dedicated training, exacerbating problems of poor service engagement with PWUC. Our training component is informed by this feedback and will seek to address these needs. This study would not be possible without the support of local police and PCCs, who we will continue to engage throughout to ensure meaningful translation of project findings into policy and practice outcomes. We have also consulted with international experts, such as Ernst Wisse, Medecins du Monde, who leads a crack pipe program in Paris (distributing on average 2000 pipes per month) and who has agreed to be an advisory board member.

4. Aims and objectives

Aim: To evaluate a safe crack inhalation intervention distributed to PWUC via drug treatment services and peer networks in order to reduce crack-related health harms and inform legislative review.

Research Question: To what extent and how does SIPP reduce health risks and enhance service engagement among people who use crack cocaine?

Objectives

1. Measure the effect and cost-effectiveness of SIPP on harms and risks associated with crack use (pipe sharing, presentation at drug services, using home-made pipes, cuts/burns, crack injecting).
2. Evaluate SIPP fidelity, reach and acceptability in diverse drug treatment and peer-network settings.
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7. Translate evidence to policy and advocacy outputs, including to inform legislative review.

5. Research Plan

Design

We employ a mixed-methods quasi-experimental design to be delivered over five phases: 1) Optimisation; 2) Baseline data generation and set up; 3) Implementation; 4) Evaluation; 5) Protocol development and dissemination. (Figure 1).

Our evaluation comprises two work-packages A) qualitative process evaluation of the SIPP intervention (lead MH & JB); B) a pre and post intervention study with a non-equivalent control group (leads VH & LP).This pre-post intervention study with a non-equivalent control group [44-46] will enable us to measure differences in primary and secondary outcomes among PWUC following SIPP introduction intervention. The inclusion of the control group will strengthen the internal validity of our findings, the ability to attribute changes in outcomes to the intervention, through assessing seasonal and temporal/secular changes in crack use (maturation bias) or events occurring at the same time that might influence results (historic bias) [47]. The collection of repeated data from our intervention group will facilitate subgroup analyses of people known to have received multiple SIPPs compared to fewer, to investigate a dose-response effect of the intervention.

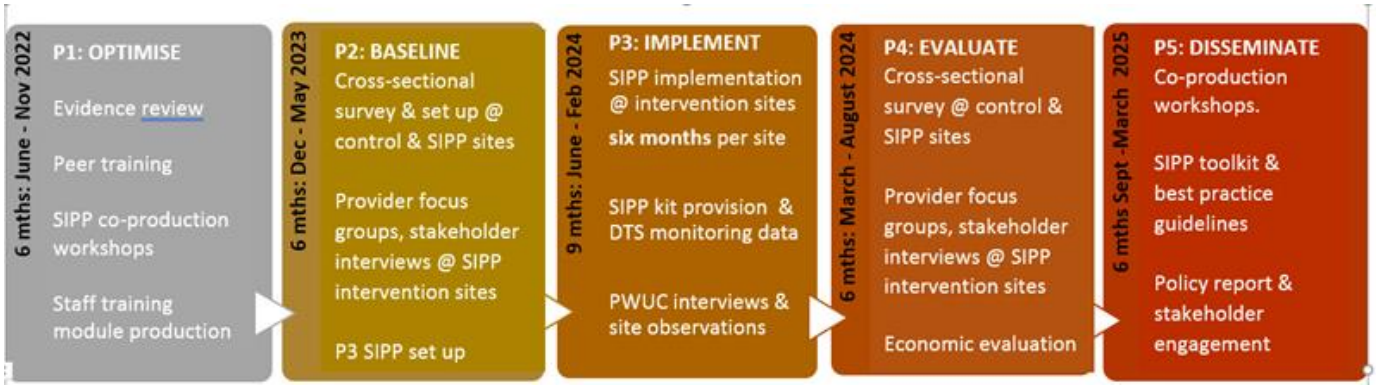


Figure 1: SIPP timeline

Classical experimental designs are not appropriate; peer networks refuse to support randomisation of SIPP provision given perceived community need. We are limited to delivering SIPP in areas where we have police approval (Avon & Somerset, Nottinghamshire) and anticipate that pipes will be diffused widely within communities, with potential contamination precluding recruitment of control sites within these areas. Participating service providers are also non-generic, they deliver services to

address specific needs of their local populations, including diversity in crack use, and are adapted to the local context and availability of supporting services, making randomisation problematic. Logistical difficulties (e.g. need for police support and the inconsistent presence of peer networks) further complicates the randomisation of SIPP by drug treatment site. We therefore propose a pragmatic quasi-experimental design that allows purposive selection of comparison sites, value for money and more immediate estimates of effectiveness of SIPP provision across diverse contexts [45]. Other quasi experimental approaches were considered, and advice sought from RDS on methodologies, however the various methods proposed such as stepped-wedge or interrupted time-series analyses were not considered practical by peers and/or service partners during consultation due to their reliance on repeated surveys among a population that can be hard to engage.

Intervention theory

Realist approaches to intervention theory [48] stress the vital importance of context in understanding mechanisms of change; what "works" in one time and place may be ineffective, or even harmful, elsewhere. The Consolidated Framework for Implementation Research (CFIR) provides a comprehensive taxonomy of constructs related to the intervention characteristics, inner and outer setting, individuals, and implementation process [49] These approaches are not incommensurate. We apply a pragmatic adaptation of CFIR (cf [50]) to structure our process evaluation with attention to the way in which the contexts of SIPP provision (inner setting: implementation climate/leadership dynamics; outer setting: PWUC/staff needs and resources, policy climate etc) interplay to impact mechanisms of change.

CI Busza will mentor PI Harris through the key stages of refining the intervention's hypothesised change pathway (i.e. theory of change) to inform subsequent design of a process evaluation framework that will (i) document and assess delivery of each component of the SIPP intervention, (ii) explore experiences, perceptions and interactions with the programme by both providers and participants and (iii) examine local contextual factors that may influence the effectiveness of the intervention as designed.

The aim of a comprehensive process evaluation framework is to ensure data are collected on progress along the hypothesised pathway from provision of the intervention activities to their intended outcomes. Most intervention studies assume a trajectory from the activities to be implemented to the behavioural or health outcomes of interest but not all explicitly identify the intermediate steps to allow exploration of the key process evaluation domaints, namely: fidelity to intervention design (were activities conducted as planned?), coverage (who was reached and were they from intended target groups? and how much of the intended delivery did they receive?,) feasibility of delivery (what challenges were faced and were they overcome?), acceptability to participants and staff (how were activities perceived by those directly involved?), and quality (did activities and services meet expected standards?). See figure 3, Phase 3, for working process evaluation framework.

Population

PWUC (people who use crack): self-reported crack cocaine inhalation or injection within the past 28 days; aged ≥18; capacity to consent. We include people who inject crack as a SIPP target population, given the potential for pipe provision to support transitions from injection and reduce injection frequency as well as to reduce risk practices among people who primarily smoke crack cocaine.
Exclusion criteria: under 18; in secure services; lacking capacity for informed consent; significant mental health problems; no history of crack cocaine use.

Outcome measures

Primary outcome: decrease in proportion of participants self-reporting sharing of crack pipes in the past 28 days (yes/no).

Secondary outcomes include: i) increased presentations at drug treatment services defined as number of new attendances at drug treatment service sites to obtain SIPP; ii) reduction in injecting frequency defined as number of times injected in the last 28 days; iii) decrease in proportion of those reporting current acute injuries defined as cuts/burns to mouth or lips verified by interviewer observer (yes/no); iv) reduction in the proportion of participants who use homemade pipes in the last 28 days (yes/no); v) reduction in proportion of participants using ash as a crack suspension device; vi) reduction in proportion of participants reporting respiratory risk markers defined as difficulty breathing, chest pain, coughing blood in the last 28 days.

Our primary outcome measure (crack pipe sharing) and many of our secondary outcomes are self-reported. Service presentations will be assessed through the collection of minimum identifiers for participants in pre and post surveys and each person obtaining SIPP to cross check against drug treatment service routine monitoring systems (such as NEO). Current acute health injuries will be self-reported but also verified via observation by the researchers collecting the survey data.

Studies have shown that self-report measures of risk behaviours among people who inject drugs are reliable, particularly when used with computer assisted survey instruments [51, 52]. The use of self-reported measures in evaluating the impact of harm reduction interventions such as needle/syringe programmes is widespread [53]. Self-reported crack pipe sharing has been used as an outcome measure for Canadian studies [5, 7, 8]. aiding comparability. In consultation with peer networks we have confidence that stigma associated with our primary outcome measure is low (pipe sharing is relatively common and rarely features in harm reduction risk messaging), and unlikely to be misreported. Use of homemade materials is likewise common and rarely stigmatised, given the dearth of available options.

There is a growing body of evidence showing associations between crack smoking and HIV and HCV acquisition, attributed to sharing of pipes [9, 10, 28, 54]. Reductions in viral transmission is a long-term outcome goal for which measurement of pipe sharing is a pragmatic proxy measure. This is necessary, given the time frame of our project (33 months) renders the detection of changes in biological markers for HCV infection untenable and would require a large sample of HCV negative participants for long term follow-up. Measures of respiratory damage (such as spirometry tests) are also unlikely to provide robust results in the study timeframe. Indications of COPD, for example, will be confounded by tobacco smoking practice and improvements may be difficult to ascertain (damage plateauing rather than progressing, for example).

Public and peer involvement

We have established a community-academic partnership to develop this proposal with peers contributing to the study design, data collection and dissemination. Peer network leads are project partners and all peers involved with the project will receive training in research methods. Through a dynamic process of peer researcher development and practice we will capacitate and evaluate peer-led provision of SIPP alongside SIPP provision through more traditional harm reduction services. In addition, each drug treatment service will employ a peer volunteer identified by the service (such as a ‘recovery champion’) who will be employed for 15 hrs per week for two blocks of 10 weeks to administer the before and after survey. This reduces drug treatment staff burden and capacitates a local peer volunteer in research methods. Peer researchers will be remunerated for their time and expenses, including for training participation. Peers will be actively involved in dissemination strategy, with outputs co-created and tailored to reach diverse audience. Our advisory group comprises service users, police, commissioners, and policy makers – they have input into the proposal, will oversee project delivery and aid translation of evidence into policy and practice.

We have worked closely with the peer leads throughout the development of this proposal to arrive at an implementation and evaluation design that is feasible and acceptable to the peer networks, including in regard to modes of recruitment, data collection devices, training needs, reimbursements

provided and control measures. The SIPP concept has been developed in consultation with PWUC and community drug treatment providers, including the type of pipe to be provided and inclusion of a brief risk reduction education component for delivery with each pipe. This will be developed by the peer networks and disseminated to drug treatment services. We are adopting a multi-pronged recruitment approach, working with community drug treatment services but also well-developed networks of people who use drugs, who are experienced in delivering harm reduction interventions to their communities. The peer leads we are partnering with were instrumental in providing safe injecting equipment to people who inject drugs in Bristol, Bath and Nottingham during the height of the COVID-19 pandemic when pharmacy and drug treatment service provision was limited. Mat Southwell, PPI lead, facilitated peer development of a COVID-19 risk reduction leaflet specifically for people who use illegal drugs. This has been widely disseminated, including to drug user networks internationally. We are in a unique position to capitalise on and support the capacity of peer leads and networks to increase their harm reduction engagement. They have unique access to populations of PWUC who don't engage with drug treatment services and are highly motivated to be involved for the benefit of their communities.

The intervention

We regard SIPP as a structural intervention. That is, an intervention that promotes the availability, accessibility or acceptability of specific resources needed for specific health outcomes [55]. SIPP is purposefully designed to be pragmatic and practical for implementation to busy/preoccupied PWUC in a variety of contexts, such as drug treatment services, outreach and through interaction with peers. SIPP development is informed by principles of harm reduction and models of peer support evidenced to have impact in diverse contexts [22, 24]. For hypothesised pathways to effect, see attached logic model.

SIPP consists of three components:

1.SIPP KIT: The SIPP kit adheres to best practice guidance for provision of safe crack inhalation equipment [21]. It comprises a straight stem borosilicate glass pipe; 2 x steel gauze filters/meshes; 2x plastic mouth pieces; a push-stick and harm reduction information provided in a hard plastic case (see figure 1). SIPP kits will be provided by Exchange Supplies at no cost and distributed to PWUC via participating drug treatment services and peer networks for the duration of the intervention (6 months). We will work with providers and peer researchers in P1 to agree and standardise procedures for SIPP kit distribution (for example, how many kits can be provided per person per visit). A short monitoring survey will be administered by providers/peer researchers to each person receiving a SIPP kit using ODK software. Survey data will be linked by minimum identifiers (initials, date of birth), stored on a secure LSHTM server and enable assessment of intervention impact on individual risk practice over time.

2. SIPP PROVIDER TRAINING: This will be an online module developed by Exchange Supplies in collaboration with the research team, and with specialist input from CI JS. It will follow the format of their prior training (see figure 2) but of shorter duration (less than 30 minutes to complete). The training is aimed at drug treatment and harm reduction providers and it will be made available at SIPP intervention sites prior to SIPP provision. Training evaluation will be embedded within the platform. Content will be informed by P2 service provider focus groups and consultations, potentially comprising: 1) International and UK crack use context, 2) Crack-related health risks, including from shared and makeshift pipes; 3) Evidence for pipe kit supply, legal status and local level approvals; 4) Harm reduction information provision for PWUC; 5) How to use SIPP kits – including a demo infographic 6) Respiratory health red flags - when and where to seek help.

3. SIPP PEER-TO-PEER (P2P) HARM REDUCTION: We will support the peer networks to develop a brief (5 minute) harm reduction intervention to be provided alongside SIPP kit provision. This can be tailored to suit an individual's specific information requirements and time available. It will be

shared with all SIPP providers to enhance their knowledge and confidence in providing crack-specific harm reduction information, including with the provision of each SIPP kit. Content, informed by the peer-networks, could include: 1) best practice crack pipe use; 2) benefits of using glass pipes over homemade pipes (less health risks etc); 3) benefits of not sharing pipes and tactics to avoid risk; 4) health issues to look out for and how to access help. We will observe and assess the acceptability of this and the provider training component (Phase 3 & 4) to inform the development of comprehensive harm reduction resources as a project output (Phase 5).

Figure 2: SIPP kit pipe, mouthpiece and mesh.

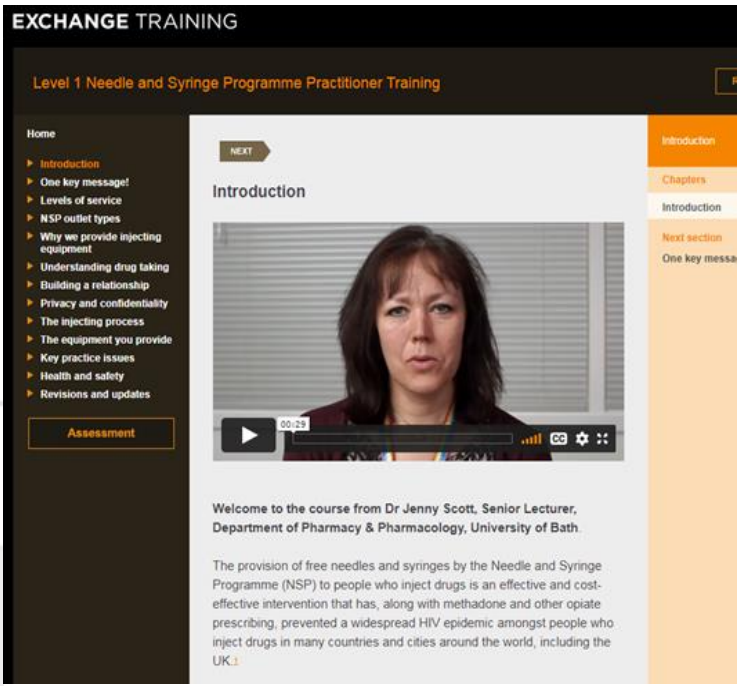


Figure 3: Example format of online training

Sites

Two peer networks and four drug treatment service providers will deliver the SIPP intervention in three geographical areas: Bristol; Nottingham; and Nottinghamshire (Nottinghamshire West based in Mansfield and Nottinghamshire South based in Hucknall). We have worked with local Dug Strategy Policing leads and PCCs in proposal development and have written support from Avon & Somerset Police and Nottinghamshire Police for crack pipe distribution at these sites for SIPP duration. This collaboration provides a unique opportunity to reach diverse and high need PWUC.

Each peer network has a well-established and reputable record of harm reduction equipment and information provision to their local communities (such as secondary needle exchange, naloxone training and provision, COVID-19 prevention information). Peer networks comprise of the Hepatitis C Trust peer-to-peer outreach, Birmingham, SIPP lead Philippe Bonnet; and CI Mat Southwell will establish a peer network in Bristol in collaboration with Bristol Drugs Project and the research team.

The Drug treatment services represent diversity in service provision (specialist drugs agencies/community health services), reach (rural/urban), crack using culture and demographics (smoking vs injecting; older/newer cohorts; ethnic diversity; housing status). They are: 1) Bristol Drugs Project, Bristol, SIPP lead Catherine Lord; 2) The Health Shop & POW sex worker outreach, Nottingham, SIPP lead Louise Wilkins; 3) Change, Grow Live, Nottinghamshire, SIPP lead Peter Furlong.

Our control sites are Change Grow Live (CGL) drug treatment services, determined according to comparability in service user demographics and crack use culture with the intervention sites. CGL

have confirmed control site participation and provided data on the number of clients reporting crack cocaine as their primary or secondary drug, with a total of 27,205 recorded across CGL services in England. We have identified Birmingham ROR Area 2 (1207 PWUC) as a control for Bristol Drugs Project (n=569 PWUC); Coventry Adult (n=693 PWUC) as control for Nottingham Health Shop, outreach and drug service (n=591 PWUC); Warwickshire Adult CGL based in Nuneaton and Leamington Spa (n=569 PWUC) as control sites for Nottinghamshire West CGL (n=237) and Nottinghamshire South CGL (n=207) based in Mansfield and Hucknall.

The inclusion of multiple and diverse sites strengthens the external validity of findings. Bristol has the highest proportion of crack users in the UK, including among the Somali population. POW will work to access street-based sex workers and, as with the other peer networks, will have privileged access to crack-houses, public injecting locations and homeless encampments rarely reached by service providers or researchers. Sites in Nottinghamshire (intervention) and Warwickshire (control) provide a unique rural perspective.

6. Delivery plan

Phase 1 (months 1-6): SIPP Optimisation & Set Up

Phase 1 comprises an evidence review, SIPP optimisation co-production workshops with peers, peer researcher training and set up for Phase 2 survey implementation. Staff recruitment, ethical approvals, data generation tools, control sites and participant information/ consent forms will be finalised in this period.

Specific phase objectives and associated research costs are as follows:

Objective 1: Evidence review (lead: LP, MH)

We have undertaken a scoping review of the available evidence for safe crack inhalation interventions, published as part of a commentary to support the SIPP project remit [3]. The small number of published studies, their methodological heterogeneity and limited quality (observational, uncontrolled) preclude a systematic review meta-analysis. We will, therefore, conduct a rapid review of the grey and published evidence for safe crack inhalation interventions with synthesis informed by the principles of realist theory [48]. We will employ a narrative approach, developing thematic summaries of the literature around a realist framework of exploring interventions, their mechanisms, outcomes and how they are shaped by contexts. This will inform phase 1 amendments to our logic model, to be iteratively developed throughout the project, and inform phase 5 transferability recommendations and protocol development. We will aim to publish this, also a protocol paper, in year 1.

Objective 2: Peer researcher training (lead MH, JS)

We will conduct two training workshops with the peer researchers in each site. Each peer network will support 2 trusted members as primary researchers, with 2 others receiving training in order to provide back up as needed. The peer identified by the drug treatment service (DTS) will receive 1-on-1 training, as appropriate to their circumstances. We will adapt materials used by Co-I JS in undergraduate teaching (basic research principles, conducting quantitative surveys) and those developed by PI MH (prior peer researcher training). Prior to workshops we will maintain contact with peer network leads to assess training needs and obtain feedback on draft project materials (survey instrument, participant information and consent forms).

- Training Workshops (each 3-4 hrs duration): We will run two workshops, on consecutive days. Workshop 1: work with the peers to: refamiliarize them with the study design and remit; revisit the participant information sheets, consent forms and the survey instrument to check for clarity and relevance. We will discuss the practicalities and any concerns regarding recruitment, data generation and reimbursements. Workshop 2: Role play taking consent and generating survey

data with a specific focus on familiarisation and practice with ODK software. Recap day 1. Additional training need will be assessed with provision made for remote sessions.

Support will be ongoing, led by PI MH & CI JS. We will provide virtual individual and group training recaps as needed and after the first day of data collection provide a debrief session by phone with weekly check-ins thereafter. Peers will have access to the PI and research fellow by phone during working hours. All peers will receive certificates to evidence research training and be reimbursed £40 per workshop and £40 for review of and feedback on study forms and protocols (network lead). Workshops: 8, Peers per site: 5 (4 peer network, 1 DTS).

Objective 3: SIPP optimisation co-production (Lead MH, JS)

Co-production Workshop: Peer researchers and 1 additional member (5 per network + DTS peer) will be invited to a third workshop to assess each SIPP component for acceptability; explore perceptions of local PWUC population characteristics and unmet needs; and to workshop the content of the brief P2P harm reduction component. We will then facilitate a series of virtual meetings where the networks will meet to share, optimise and standardise (or tailor) the P2P intervention as appropriate. Once finalised this will be disseminated to drug treatment service providers, including through presentation by the peers at a staff meeting or through virtual methods (including video) - as appropriate. Workshops: 4, Peers per site: 6.

Phase 2 (months 7-12): Pre-intervention data generation

We will implement a cross-sectional survey at each of the intervention and comparison sites to run for 10 weeks. This will be administered by peer researchers and providers at the drug treatment services and through peer networks using ODK software on handheld tablets. Contextual baseline data will be generated through focus groups with service providers and interviews with other local key stakeholders at intervention sites to inform P3 qualitative process evaluation. During this time, we will work with service providers and peer networks at implementation sites to set up for P3 implementation: introducing the staff training module; assisting SIPP kit delivery and familiarisation; finalising processes for monitoring data collection.

Objective 1: Baseline survey (Lead LP & VH)

Our survey instrument will comprise questions pertaining to PWUC demographics, crack use practices and risks (pipe sharing, use of homemade materials, use of ash, injecting); crack related health issues (difficulty breathing, coughing blood etc); as well as key confounders (recent imprisonment, confiscation of pipes by police, housing status, use of OST). This will be based on our provisional survey, piloted by CDF peers in 2020, and incorporate measures used in comparable surveys with PWUC in Canada [5, 7, 8, 10, 19].

We will employ a peer researcher for 15 hours per week at each intervention and control drug treatment service to administer the survey to PWUC. They will cover the busiest 3-hour periods each day, enabling service providers to cover survey administration in quieter periods. For drug treatment services, recruitment will consist of random sampling and open recruitment. For peer networks, recruitment will be via personal networks. A random sample of participants will be created from drug treatment service records of potentially eligible clients aged 18 years or older, with crack listed as drug of use, and having had contact with the service in the past 3 months. Drug treatment services will begin recruitment of individuals on the list. Should recruitment targets not be met at week 8, drug treatment services will open up recruitment to any eligible clients. Findings from the survey will be used to characterise baseline prevalence of primary and secondary outcomes including: crack sharing, injecting frequency and engagement in services of PWUC pre-delivery of SIPPS. Initials and date of birth will be collected to permit linking of surveys and matching to drug treatment records. The survey will be uploaded to ODK software, encrypted enabling secure storage of participant identifiers and minimising risk of data loss should the tablet be lost or stolen. The

encrypted form is sent to a central server hosted at LSHTM. All participants will receive £10 reimbursement on completion of the questionnaire. (See sample size justification and recruitment, p.13).

Objective 2: Baseline contextual data (lead MH)

The qualitative research team (MH & Research Fellow) will conduct focus groups with service providers and in-depth interviews with key stakeholders (including PWUC) in each intervention site. Our objective, drawing on the principles of CFIR, is to map the characteristics, internal and external setting and resources available to each organisation (drug treatment service and peer network) prior to SIPP implementation. This, with an understanding of key SIPP intervention uncertainties, will inform the selection of the most important questions to address in P3 qualitative process evaluation and provide a baseline context to aid understanding of post-intervention impact (including through follow up focus groups and interviews in P4).

- In-depth interviews with 3 key stakeholders per site (police/PCCs, commissioners, PWUC representatives, network leads) to explore external influences on SIPP implementation and sustainability (such as community/policy support; commissioning priorities and constraints); perception of local PWUC population characteristics and unmet need; potential SIPP implementation challenges, perceived mechanisms of change (n=12)
- Focus groups (FG, 4: 1 per service) with drug treatment and outreach staff (n=~6 per group) to explore: inner setting (team culture, leadership engagement; service provision for PWUC; barriers and facilitators to PWUC engagement); outer setting (organisational networks with other services; impact of external policies, constraints and incentives on service provision/priority setting; perception of local PWUC population characteristics and unmet need); characteristics of individuals (harm reduction knowledge; SIPP intervention expectations; perceived self-efficacy to implement SIPP; training needs). (n=~24).

Phase 3 (months 13-21): Implementation

Each site will deliver SIPP for 6 months, with staggered set up for project manageability. We will conduct a process evaluation, informed by MRC guidance [53], to 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 the implementation of repeated brief questionnaires among people receiving SIPP, in-depth interviews to understand local need and context and observations to explore how SIPP 'works' (or does not work) from the perspective of PWUC and drug treatment providers and to gain contextual insights to assess transferability and inform recommendations for implementation at scale.

Objective 1: Quantitative evaluation (Lead LP, VH)

During the implementation phase peer researchers and service providers will administer a brief monitoring questionnaire to those offered SIPP at each point of contact in intervention sites. We have cost for lead service provider time and will work with them in P1&2 to ensure monitoring data collection requirements are feasible within resources available. Questionnaires will measure exposure to SIPP (accepted/refused), and key outcomes (sharing of pipes in the last 28 days; use of unsafe pipes; assessment of cuts/burns; frequency of injecting).

We will assess the acceptability, reach and perceived impact of staff training activities through an embedded evaluation form in the training platform (monthly data provided by Exchange Supplies) and draw on routine service data (number of SIPP kits provided, minimal characteristics of recipients) to inform the process evaluation.

During the implementation phase, we will also collect primary cost data to estimate the incremental costs of the intervention. Cost data will be collected from study sites and per providers using an

ingredients approach, where the value of inputs is based on quantities and unit prices, including staff salaries, building space, training, supplies, equipment and overheads.

Objective 2: Qualitative process evaluation (Lead MH)

We will build on findings from Phase 2 stakeholder interviews and FG to assess SIPP acceptability, fidelity and contextual mechanisms of impact, with a focus on understanding SIPP implementation experiences and impact on practice from the perspective of PWUC, and the processes of implementation in context through structured and qualitative observations. We will employ a comprehensive process evaluation framework, to allow exploration of the key process evaluation domains. Our working document, to be modified in line with Phase two findings, provides example questions as below:

Research Domain		Research Questions
Implementation *What is implemented and how?*	**Fidelity & Quality**	How did implementation of SIPP intervention vary from what was planned i.e. (a) recruitment of PWUC at all sites, (b) training and protocols delivered, (c) provision of SIPP kits, (d) active engagement of peer networks, (e) SIPP harm reduction materials developed and used. What were the barriers and facilitators to implementation fidelity? What adaptations were made?
	Coverage (Reach & Dose)	How many: (a) PWUC were approached across all sites, (b) PWUC took up SIPP kits and/or peer-led harm reduction training (c) PWUC were referred or linked to drug treatment services, and (d) local law enforcement and/or government authorities maintained support. What were the barriers and facilitators to each of the above?
Mechanism of Impact *How does intervention lead to change?*	**Acceptability and Feasibility**	Which components of the intervention were best accepted and adopted by PWUC, peer network members, providers, and health system/policy stakeholders? What were the experiences and perceptions of PWUC who were actively, somewhat or not at all engaged with harm reduction and SIPP uptake? What were the challenges and barriers faced?
	Interactions and Consequences	How did various components of the intervention interact (i.e., SIPP kit provision, peer network harm reduction outreach, uptake of drug treatment services)? Were there any unanticipated pathways or consequences?
Context *How context affects implementation and shape outcomes?"*	**Proximal and Distal**	What social, cultural, political, and logistical factors impede or facilitate (or were affected by) how the intervention was implemented across the different sites. What were contextual reasons for adaptations to the intervention and its delivery?

Figure 4. Working Process Evaluation Framework

The qualitative research team (MH & Qualitative research fellow) will conduct PWUC interviews and observations, with peer researchers capacitated to conduct observations (and potentially, some interviews). Methods comprise:

1. In-depth interviews with a purposive sample of PWUC who receive SIPP: 4 at each drug treatment site, and 4 through each peer network (8 x 4 sites, n=32). Interviewees will be issued demographic form once consent has been taken, to enable systematic generation of demographic data not consistently recorded in qualitative work. Interviews will be informed by a topic guide and explore: crack use history and practices; perceived personal impacts of crack use

and crack use stigma (on health, daily life, social functioning); crack use environment and social networks; risk practices & risk mitigation strategies; barriers & facilitators to service engagement; perceptions and experiences of SIPP (acceptability, impact on practice/service engagement/health); unmet needs.

2. Structured observations conducted at least 1x per day by each researcher during their routine field work (recruitment, interview engagement), with additional time spent at the drug treatment services as required to capture observations of SIPP service provision. Observations will be notated on a form with domains informed by P2 data analysis and CFIR principles [49]. For example, CIFR processes of implementation: harm reduction domain. First level: is verbal HR advice provided alongside the SIPP kit? [yes/no]. If not, is this observed as staff-led: not offered [lack of time/confidence]; client-led: not desired [lack of time/interest]; setting-led: [minimal resources; inappropriate environment etc].
3. Unstructured observations: all researchers will be trained in taking ethnographic field notes and encouraged to do so during and at the end of each session in the field. These will attend to the contexts and social relations of SIPP implementation and - where possible - SIPP use. Peer researchers are well placed to observe use of the SIPP kits, given they will often be providing them in the environments where they are used. This will provide a valuable opportunity to observe how the SIPP kit is used in practice and the contexts in which safe practice is constrained and/or capacitated.

Phase 4 (months 22-27) Impact evaluation

We will implement a follow-up cross-sectional survey at the intervention and control sites to measure the impact of SIPP on our primary and secondary outcomes and to assess SIPP community awareness and reach. The qualitative team will conduct follow-up interviews and focus groups with provider and key stakeholder participants from P2 to aid contextualisation of impact evaluation findings.

Objective 1: Follow-up survey and analyses (Lead VH, LP)

Our follow-up survey will be conducted in the same way and at the same sites (both control and intervention) as in P2. The same peer researchers (as much as possible) will be employed to collect survey data on handheld tablets using ODK software. The survey will run for 10 weeks at each site, with recruitment open to all PWUC attending the drug treatment service sites during this time. Peer researchers will recruit all contacts via their peer networks irrespective of whether they engaged in SIPP or not during the implementation phase. The same structured questionnaire tool will be used with the addition of questions relating to extent of SIPP uptake and awareness. We estimate that in both intervention and control sites there will be approximately 75% overlap of people completing baseline and follow-up surveys. We will use data linkage to estimate a) coverage of SIPP in sites; and b) impact of SIPP on primary and secondary outcomes (see analysis below).

Objective 2: Follow-up stakeholder interviews (lead MH)

Qualitative focus groups with service providers and interviews with local key stakeholders in each intervention site will follow the methods of Phase 2, Objective 2. Where practicable we will aim to include the same participants (n=12 Stakeholders, n=30 service providers) with topic guides orientated toward following up topics explored in P2, as well as: SIPP implementation process challenges and enablers (external/internal); perceived SIPP acceptability (target audience/providers/wider community) and consequences (including unintended); adaptation suggestions (for contextual fit/scalability); identification of additional need (respiratory screening, linked mental health services etc); organisational climate for change, including through legislative review process.

Objective 3: Economic evaluation (Lead SS)

To inform design of the economic evaluation, we will undertake a scoping review of the literature to identify evidence that links reported changes in behaviour, health engagement, or safe drug taking practices to longer term outcomes, including blood-borne virus transmission, respiratory illness, mental health, and referral to social services. The purpose of this exercise is to fully explore and reflect on the potential relationships between determinant aspects of condition / disease and associated identifiable and measurable outcomes. We will also host discussion with service providers, project team members, and commissioners to identify relevant outcomes for the decision-making context. This process, along with expertise within the project team, will be sued to fine tune the 'decision problem' and an appropriate conceptual model structure.

We will estimate the incremental, economic costs of the SIPP kits from the provider perspective following economic best practice [56]. Primary cost data will be collected form study sites and peer providers using an ingredients approach, where the value of inputs is based on quantities and unit prices, including staff salaries, building space, training, supplies, equipment and overheads. Our cost-effectiveness analysis will estimate the likelihood that the intervention is cost-effective as implemented in study sites, using estimates of treatment effects from the impact evaluation. We will explore potential future changes in key drivers of costs (including the costs of pipes and mode of delivery) in sensitivity analysis.

Phase 5: (months 28-33) Dissemination

Our dissemination and final co-production phase will be conducted at each site in collaboration with peer researchers, key PWUC representatives and service providers.

Objective 1: Finalise SIPP toolkit (Lead MH, JS, AP)

- Co-production workshops (n=4) will be held at each site with the peer researchers and additional PWUC representatives (n=~10 per group) to disseminate and discuss findings, with a focus on workshopping SIPP adaptations (if required) and planning content for a comprehensive harm reduction resource to be collectively developed and published as a project output. We will schedule follow up virtual meetings and feedback, to refine the harm reduction resource content and draft with core peers (2 per network).
- Produce SIPP toolkit for dissemination in collaboration with Exchange Supplies: discuss project findings/share co-production workshop outputs; finalise core SIPP components.

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

- Develop and deliver online live webinar training and slide-sets to accompany the toolkit targeted at drug treatment providers and commissioners; police & crime commissioners; community peer networks.
- Work with Release to assess the case for legislative review and (if warranted) to prepare a policy advocacy strategy to be presented through multiple channels, including a drug-policy webinar with high profile speakers, also targeted meetings with policy makers and politicians (Public Health England, The All Party Parliamentary Group on Drug Policy Reform, Advisory Council on the Misuse of Drugs).
- Prepare NIHR report, ensure diversity of community publications and presentations (Drug and Drink News; Black Poppy Publication; National Needle Exchange Forum; CGL National Harm Reduction Forum etc), alongside dissemination through traditional academic channels (International Harm Reduction conference; Lisbon's Addictions conference, public health and social science peer review publications)

Objective 3: Best-practice engagement guidelines (Lead MH, JS, NE)

- Guidelines for service providers and commissioners will be informed by qualitative process evaluation and health economic evaluation findings, and comprise recommendations for cost effective SIPP implementation and commissioning, including staff training and resourcing requirements, but also comprise recommendations for engagement with and care of PWUC more broadly. This might include, for example, an increased focus on respiratory health, joined up pathways for mental health and housing support, including through outreach and in-reach specialist services. Draft guidelines will be iteratively developed through a process of consultation with stakeholders including PWUC, drug treatment service provider, commissioner and policing representatives.

7. Sampling, Recruitment and Analysis

COVID-19 CONTINGENCIES: All 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 qualitative interviews with PWUC participants (via phone) and we have procedures in place for ensuring informed consent is thorough and ethical when conducted via remote means. Of note, during COVID-19 restrictions the peer-networks remained active: supplying injecting equipment and COVID-prevention education to compensate for service closures/restricted hours. With PPE, they can incorporate SIPP provision and data collection into their secondary supply structures. The risk of drug treatment service closure due to COVID-19 is assessed as very low. Survey data collection can be supported remotely, if necessary, given this is to be primarily conducted by peers and providers already in situ at the services.

Quantitative Workpackage (lead LP, VH)

While our primary analyses focus on samples recruited via drug treatment services, that can be subject to bias; in that they do not reflect the diverse population of people who are 'hidden' from service data capture [15]. This is particularly an issue in relation to PWUC in England, for whom drug treatment services have little to offer. Recruitment of a sub-sample via our peer networks who have been carefully selected for their long-standing history and trusted reputation among PWUC will facilitate recruitment of PWUC who are disengaged from services and therefore a more diverse sample of PWUC. We will compare indicators of social exclusion and health harms and drug use risk behaviours between those recruited via peer networks and drug treatment services to assess levels of service need (see Analysis below) At pre and post intervention surveys, participants will complete structured questionnaires administered by peer researchers (on tablets using ODK). These will cover: demographics; drug use practices; indicators of social exclusion; primary and secondary outcomes. We will collect minimal identifiers (date of birth, initials) needed to link people over time to allow assessment of primary and secondary outcomes and new drug treatment service presentations.

Sample size

We will recruit a total of 600 PWUC recruited at a rate of 100 per month at pre and post intervention survey at participating drug treatment sites (Objective 1): a sample of 306 (204 SIPP, 102 control) is sufficient to compare proportional differences in pipe sharing at 90% power with significance of p=0.05. We assume 52% will share pipes, and that there will be a difference of 20% (52% to 32%) between intervention and control; substantiating previous evidence suggesting pipe provision reduces prevalence of sharing from 37% to 12% over a 6 month period [7] (Hypothesis 1). We expect 67% to have used home-made pipes and 43% to have respiratory difficulties, burns or cuts. Pilot findings suggested that 16% visited a needle/syringe programme or drug service and 71% would if pipes were available. A sample of 306 (204 SIPP, 102 control) and 281 (187 SIPP; 94 control) is sufficient to observe a reduction in use of home-made pipes in the last 28 days from 67% to 47% and from 43% to 23% for respiratory difficulties, burns or cuts at 90% power, differences that have been

suggested elsewhere [18, 20]. A sample size of 153 (102 SIPP, 51 control) is sufficient to measure injecting reductions from 51% to 21% over a 6 month period substantiating other emerging evidence [7]. A sample of 108 (72 SIPP, 36 control) is sufficient to observe an increased presentation at drug services from 16% to 48%, conservatively building on estimates from the pilot study to account for the small sample size (n=32). An inflated sample of 600 (400 SIPP, 200 control) allows for only 50% of the SIPP group to have ≥2 contacts with SIPP providers over 6 months, of which 51% may inject as well. It also accounts for being able to link 75% of participants between baseline and follow-up surveys and for multivariable analyses to adjust for any baseline differences in characteristics between intervention and control sites. In addition, we will employ targeted sampling methods to recruit 140 participants representing diverse crack user sub-populations via peer networks to widen the evidence base on health needs and service access among PWUC not currently engaging in services. Total n=740.

Recruitment

For the surveys we will recruit individuals via drug treatment services and through peer networks recruiting a total of 500 via sites engaging in SIPP and 240 not engaging in SIPP in pre and post intervention surveys (Phases 2 and 4). This equates to a total of 50 participants per week across seven services (less than 8 people per week per service) and 14 participants per week across 3 peer networks (5 participants per week per network). Services in the three intervention sites include the Bristol Drugs Project, and Health Shop Nottingham. Four CGL service in Birmingham. Three CGL control sites will be chosen to maximise compatibility with intervention sites. These are: Birmingham for Bristol, Coventry for Nottingham, and Warwickshire (Leamington Spa and Nuneaton) for Nottinghamshire (Ashfield and Hucknall). A review of drug treatment service data indicate a range in the number of PWUC seen over a 12 month period (374-1287) and recruitment targets have been set proportionally (see figures 5 and 6).

Recruitment Service	Annual recorded number of PWUC service users	Target sample size	Recruitment target per week
Bristol Drugs Project	569	175	18
Nottingham Health Shop / DTS & POW outreach	~591 (POW=85)	175	18
Nottinghamshire CGL (Mansfield and Hucknall)	444	50	5
3 peer networks & POW outreach	~485 (POW=85)	140	14
CGL Birmingham ROR (control)	1207	88	8
CGL Warwickshire (Leamington Spa and Nuneaton) (control)	569	25	3
CGL Coventry (control)	693	87	8
Total		740	74

Figure 5. Recruitment targets

We will review recruitment rates on a weekly basis, identifying potential under-recruitment in sites early and acting to mitigate risk in accordance with the stop/go criteria below. Each project partner site is working with us to identify and confirm additional sites, operating under the same police authority remit, that can be brought on board to aid recruitment if required.

- Week 2: if 10% of recruitment target has not been met at a site we will bring another site in the area on board.

- Week 4: If 20% of recruitment target has not been met at a site we will bring another site in the area on board.
- Week 6: If 30% of the total recruitment target has not been met across all sites, we will discuss with NIHR reconfiguring the project design from an impact evaluation to a health needs assessment of PWUC. This would involve completion of the baseline survey, given lack of survey data on PWUC health needs and risks in the UK, but removal of the follow-up survey. Associated costs for the follow-up survey would be returned to NIHR.
- Week 8: If 75% of the total recruitment target has not been met across all sites, we will extend the survey duration to 14 weeks.

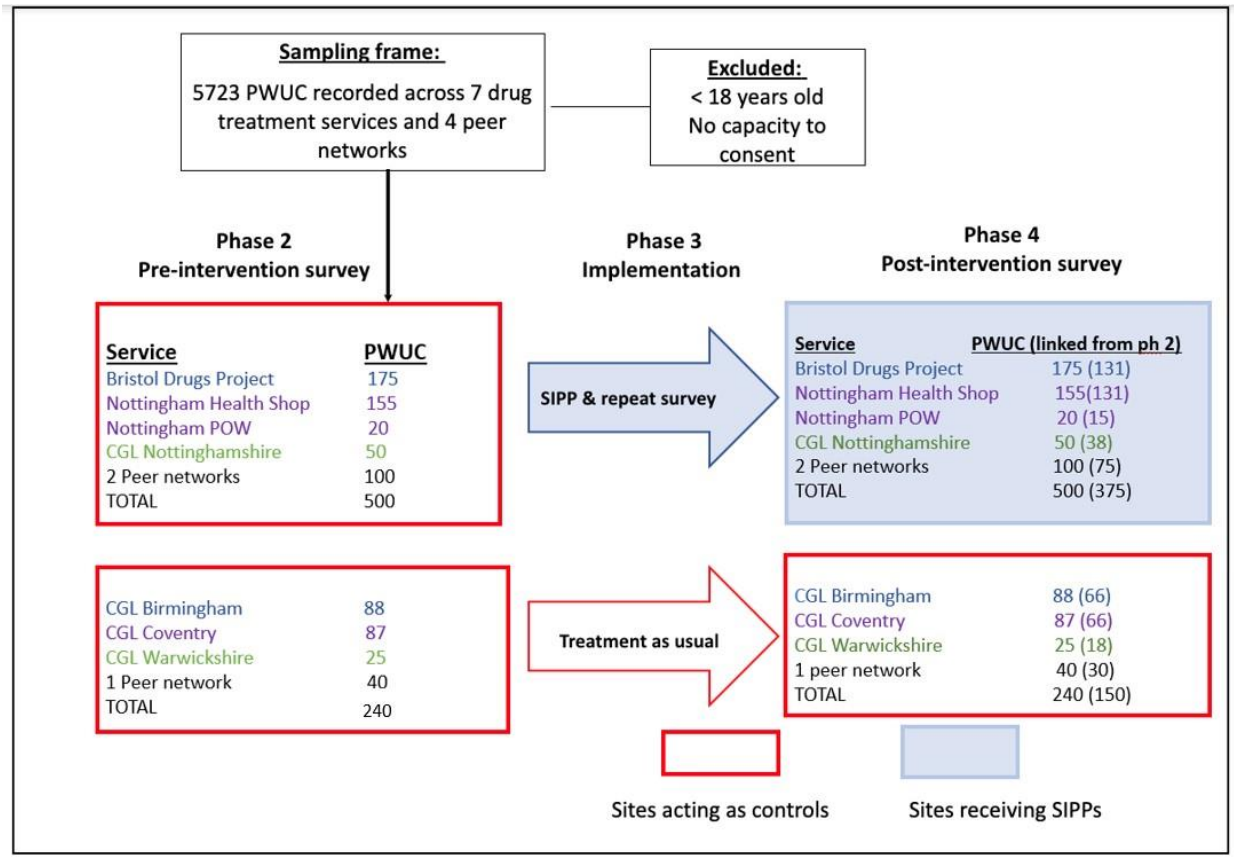


Figure 6: Participant flow into pre & post surveys at intervention & non-equivalent control sites

Each site is supportive of and invested in the SIPP project, with the study Co-Investigator for each site highly motivated to help us achieve planned recruitment targets. Project partner CGL is the largest provider of drug treatment services in England with an estimated 27205 services users reporting crack use. We will work with CGL to identify alternative control sites should planned recruitment sites prove unproductive. The Hepatitis C Trust oversees an extensive network of trained peer volunteers throughout England, including at all study sites. They have provided confirmation that they will assist and/or replace peer volunteers at each site if the peer networks have difficulty recruiting. We will advertise the survey extensively, and in discussion with services and peer collaborators, are reassured that the £10 cash reimbursement, run up advertising at each service and prior relationships with between participants and drug treatment services as well as through the peer networks will facilitate cross-sectional survey engagement.

Analyses

We will test six hypotheses.
H.1. There will be a 20% difference in sharing of pipes between participants engaging in SIPPs and those not using SIPPS across drug treatment services.
H.2 There will be a 20% difference in prevalence of cuts and burns between participants engaging in SIPPs and those not using SIPPs across drug treatment services.
H.3 There will be a 20% difference in the use of home-made pipes between participants engaging in SIPPs and those not using SIPPs across drug treatment services
H.4 We will observe a 30% difference in repeat presentations at drug services among participants using SIPPs compared to those not using SIPPs.
H.5 We will observe a 30% difference in prevalence of injecting between participants engaging in SIPPs compared to those who do not use SIPPs at drug treatment services.
H.6 Increased exposure to SIPPS in drug treatment services and via peer networks will be associated with greater reduction in sharing of pipes.

First, we will describe the demographic characteristics, drug use behaviours and indicators of social exclusion for participants stratified by exposure group at baseline and follow-up. We will consider excluding participants from analyses if there is extreme imbalance across groups. Second, we will estimate the change in primary outcome (sharing of pipe in last 28 days) for participants in intervention sites compared to control sites. Logistic regression will be used to compare baseline prevalence of sharing pipes in the last 28 days and estimate the odds of sharing pipes, use of home-made pipes, cuts/ burns and engagement in services, between intervention and control sites post-intervention. (H. 1-4) Linear regression models will be used to compare baseline frequency of injecting between intervention and control and estimate relative changes in mean frequency of injecting (as a continuous variable) (H.5). Primary analyses will use an adjusted, individual-level intention-to-treat approach, including all participant data (irrespective of participation at baseline and follow-up and assuming missing observations are missing at random). We will measure changes in outcomes between baseline and follow-up and compare between intervention and NEC sites. We will adjust for a priori confounders including sex, age, duration of crack use known to be associated with engagement in services and primary outcomes, along with any variables with evidence of imbalance (i.e ethnicity, sex work, homelessness) described above. Survey time will be treated as a categorical variable in all models. As a sensitivity analysis we will focus on participants for which we have baseline and follow-up (through data linkage) to assess changes in outcomes over time and between intervention and NEC. Both these analyses take an intention-to treat approach including all participants irrespective of their engagement with SIPPs. A third analysis will take a per-protocol approach focussing on participants with both baseline and follow-up data and exposure to the intervention.

Appropriate statistical models will be selected based on evidence of clustering observed. The model will include fixed effects for time and treatment and we will explore the appropriateness of including a random effect to account for heterogeneity of participants within sites or a fixed effect to account for heterogeneity across sites. We will explore the need to adjust for clustering within treatment sites and by sites using intra-class correlation coefficients.

We will measure changes in outcomes at baseline and follow-up among participants recruited via peer network and drug treatment services using mixed effect models adjusting for confounders to assess changes in primary and secondary outcomes pre and post intervention. Descriptive analyses (chi-squared tests for binary variables and t-tests for continuous variables) will also compare health harms, drug use risk behaviours and indicators of social exclusion (homelessness, prison, sex work) between those recruited via drug treatment services and peer networks to assess level of need among those not engaged in services. We will examine evidence of a dose-response relationship between intensity of exposure to SIPP and primary and secondary outcomes using logistic regression

models and categorising exposure to SIPPS as a continuous or categorical variable (1, 2-3, 4-5,6+ exposures) depending on the distribution of contacts with SIPPS in the intervention sites and adjusting for key confounders. (H.6). Analysis of the evaluation forms completed by the service providers will assess training reach and acceptability.

Qualitative workpackage (lead MH, JB)

Sample

The qualitative sample will be purposively sampled for variation in gender, ethnicity, age, accommodation status and duration of crack use. To enable this process we will, in P1 assess the demographic of PWUC for each site and develop a qualitative sampling quota based on this information. Our sample will primarily be stratified by site, with the aim of recruiting an equal number (4) PWUC from each drug treatment service provider (n=16) and through each peer network (n=16). Our quota will ensure *at least* one woman and, where possible, one person of non-white ethnicity is recruited from each group of 4, with attention to demographic variation across the sample. Our sample size aligns with the aims of a nested qualitative process evaluation - interviews conducted will be of sufficient depth to enable comprehensive thematic analysis not only of SIPP acceptability and perceived impact but in relation to the experiences and engagement requirements of PWUC more broadly. The service provider and stakeholder participants (P2&4) will be purposively sampled to reflect variation in relevant occupational roles. Total PWUC n=32.

Recruitment

We will primarily recruit through 'arms-length' means. The short monitoring questionnaire provided to each SIPP kit recipient will inform of the option of a qualitative interview. Participants can indicate interest on the form and leave contact details. We will sample from these responses, in accordance with the purposive sample quota as noted above. Given the small number of participants to be recruited through each site, we envisage this will be sufficient, but will allow for recruitment through flyers (distributed through peer networks and in drug treatment waiting rooms) and through direct contact by providers/peer researchers if necessary. Stakeholders will be recruited through professional networks, and providers through the engagement of the research team at each site. At P2 interviews and focus groups, providers and stakeholders will be asked if they consent to a follow-up P4 interview, with the aim of retaining a subsample of participants across both baseline and follow up data generation points.

Participant information materials and consent process: Recruitment flyers and participant information sheets will be designed with PWUC members of our advisory group and taken to the first Peer researcher workshop (P1) 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. All survey participants will receive a £10 cash. This is in line with current procedures at LSHTM, including for reimbursing participants who use drugs in related studies.

Analysis

All interviews and focus groups will be recorded (with participant consent) and transcribed verbatim. Observation field notes will be generated throughout and integrated alongside transcripts in analyses. Qualitative data will be managed in NVIVO12. We will conduct a thematic analysis comprising 6 stages: data familiarisation (including through field notes and analytic memos); coding framework development; first level coding (primarily deductive, informed by research

questions/CFIR and analytic memos); second level inductive coding; category mapping; thematisation and write up. This process is a modification of Braun & Clarkes six stage guidelines for thematic analysis [57] and will be led by the PI, MH.

Our qualitative data will be analysed through triangulation [58] using: (a) multiple forms of qualitative data (interviews, focus groups, observations); (b) multiple forms of participant perspective (service providers, PWUC from diverse communities/treatment engaged/disengaged); (c) multiple intervention sites; and (e) multiple time points (pre/post intervention). The primary focus of triangulation will be to identify congruence and divergence, as well as to maximise the confidence with which judgements are made regarding potential relative intervention effects. Where possible, quantitative and qualitative analyses will build upon one another, qualitative to explore baseline survey data findings and also inform impact evaluation – by providing insight into local secular changes at intervention sites, not captured by comparison site data. We will present our data thematically with input from PWUC and providers.

8. Dissemination, impact and future work

We will disseminate findings through community, policy, police and academic networks, including through initiatives led by PWUC. Our advisory board comprises service users and providers, police, international experts and policy makers who have input into the proposal, will oversee project delivery and aid translation of evidence into policy and practice. Additional specialised input will be sought as appropriate. We will target Local Authorities, Clinical Commissioning Groups, Drug Treatment Service providers, The Association of Police & Crime Commissioners and key stakeholders for research updates, tailored policy briefings and presentations, including through our teams existing memberships (e.g. Addiction Professionals).

We will coordinate communications teams within LSHTM, University of Bath, Liverpool St John Moores University and collaborators such as Release, to foster effective findings dissemination. Peers will be actively involved throughout (including in the Advisory Board), with outputs co-created and tailored to reach diverse audiences. 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 findings and outputs.

We have long-standing collaborative working relationships with key drug treatment service providers, CGL; Turning Point and Humankind. Key learning will be shared across all applicable services nationally via established governance and service user forum structures. We will publicise and disseminate findings though key policing and drug treatment provider forums, such as Collective Voice, NHS Alliance and the Association of Police & Crime Commissioners. The project PI has presented the SIPP concept at The Annual Society for the Study of Addiction Conference, the CGL National Harm Reduction forum and in webinars lead by Hepatitis Scotland and the Westminster Drugs Project and would update at all fora on project findings.

Peer-review publication will prioritise multi-disciplinary dissemination, targeting high impact public health and social science journals (Addiction, PLOS One etc). We will present at conferences attended by a range of professionals (Society for the Study of Addiction, RCGP & SMMGP Managing Drug & Alcohol Problems in Primary Care Conference; National Needle Exchange Forum) and disseminate in partnership with international experts (such as Medecins du Monde). 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 present findings through community

forums and at conferences attended by PWUC and providers such as DDN National Service User Involvement Conference and the International Harm Reduction Conference.

Outputs

- Adapted SIPP kit and training package.
- Crack harm reduction resource for PWUC.
- Guidelines for providers and commissioners to optimise PWUC engagement and health outcomes.
- Policy brief to inform legislative review, action to submit to ACMD.
- Peer-reviewed publications (systematic review, protocol, policy review paper, > 3 findings papers)
- Articles in periodicals aimed at: addiction specialists; healthcare providers; policy makers and PWUC.
- International and national conference presentations.
- Full study report detailing the research, findings and its policy, managerial and practice implications.
- Project website and Twitter account to disseminate lay information about the study.

We will work with our advisory committee to develop innovative knowledge translation strategies and have cost for development of a PWUC-orientated resource at the dissemination phase. We will host a launch Webinar using the Exchange Supplies platform, inviting a range of presenters, including police force partners to share their perspectives on the SIPP intervention. 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. 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 findings into policy and practice.

Anticipated impact

Should SIPP be proven to be acceptable and effective, we anticipate downstream effects to include:

- Roll-out of simple low-cost interventions on a national scale to improve engagement among PWUC with drug treatment and harm reduction services.
- Potential benefits from roll-out at scale including reduced sharing and the consequential health benefits.
- Improvements in engagement with care for health problems seen in PWUC, including co-ordinated respiratory and mental health care, facilitated through engagement with drugs services.
- Increased engagement in community drug treatment among treatment naive or disconnected PWUC, who also use opiates. This includes both substitution therapy and psychosocial interventions.

These impacts will directly benefit both PWUC and drug treatment service providers. Our aim is that SIPP promotes a culture change in which PWUC feel services have something to offer them, feel more confident to access the care they need and better supported to protect their health.

Future work

Depending on study findings and future funding acquisition, the team wish to build on this work in at least two ways.

1. **Further innovating harm reduction provision for PWUC.**

This would likely include developing (through laboratory studies, led by JS) effective filtration devices for crack pipes that reduce particulate inhalation and (though improved pipe design) the temperature of smoke inhaled. It is anticipated that product development would be in partnership

with Exchange Supplies, a social enterprise, as in previous projects focussing on heroin injection equipment [59, 60].

2. Follow-up of the survey cohort to assess health conditions and service access over time.

This research is likely to engage a unique cohort of individuals, including people who use crack but do not inject drugs. Other surveillance studies in the UK, such as the Unlinked Anonymous Survey, only sample people who inject drugs and/or do not focus on respiratory health harms. The SIPP study duration means that an assessment of the intervention on long term health outcomes is not possible. For this reason, we propose to include a consent to follow-up in the second arm of the survey. This would enable the team, dependent on future funding, to follow up this cohort either in person and/or through linkage to NHS health records and/or drug treatment service data. The focus of follow up would be on understanding long term health outcomes among this cohort, with a focus on respiratory harms and service access.

We will ask participants of the SIPP post-intervention survey whether they are willing to consent to future follow up. At the end of undertaking the SIPP survey, they will be informed about the potential for a follow-up study and that this is dependent on funding acquisition. They will be provided with a participant information sheet and the opportunity to ask questions. If they agree to take part, they can then choose to opt in to one or more of three options: 1) direct contact for a follow-up questionnaire; 2. linkage to NHS health records; 3. linkage to drug treatment service records. The procedure for each will be outlined in the participant information sheet, including the contact details required to enable follow-up. The participant contact details will be recorded on the tablet administered, ODK facilitated SIPP survey and they will be asked to sign a separate paper consent form which will be stored security in a locked filing cabinet in a limited access room at LSHTM. These contact details would not be made available to anyone outside the team, and future follow up would not take place without protocol development, associated funding acquisition and ethical approvals.

Procedures for follow-up:

Depending on funding acquisition and the specific outcomes of focus in the follow-up study, follow-up would likely happen at 12 months and at five years post SIPP completion, given that given that the respiratory and broader health consequences of the intervention are long-term.

Participants who consent would be asked to opt in to one, two or all the following options

1. **In-person follow-up**

This would be for completion of a questionnaire and/or interview like that employed in the SIPP study. This will require in-person contact. The participant will be asked to nominate at least two methods of contact, such as providing their address, email, phone number, details of a friend or relative, or providing permission to contact them via their drug treatment service. The team would use one of these methods to let the participant know about the option for a follow-up questionnaire or interview. They could then choose to take part or not. If agreeing to participate, a member of the research team would agree a time and place for them to meet, like SIPP recruitment procedures. Follow-up study specific consent and participant information procedures would take place prior to data generation.

2. Linkage to NHS health records:

This does not require in-person contact. The participant would be informed that this allows the team to look at their health outcomes over time as they are monitored by their GP and other health care services. If they agree they will be asked to provide: 1) their permission to access their NHS Health Records and 2) their full name and date of birth so we can identify their records. The participant will be informed that NHS health records are held by NHS Digital, NHS Central Register, NHS Personal

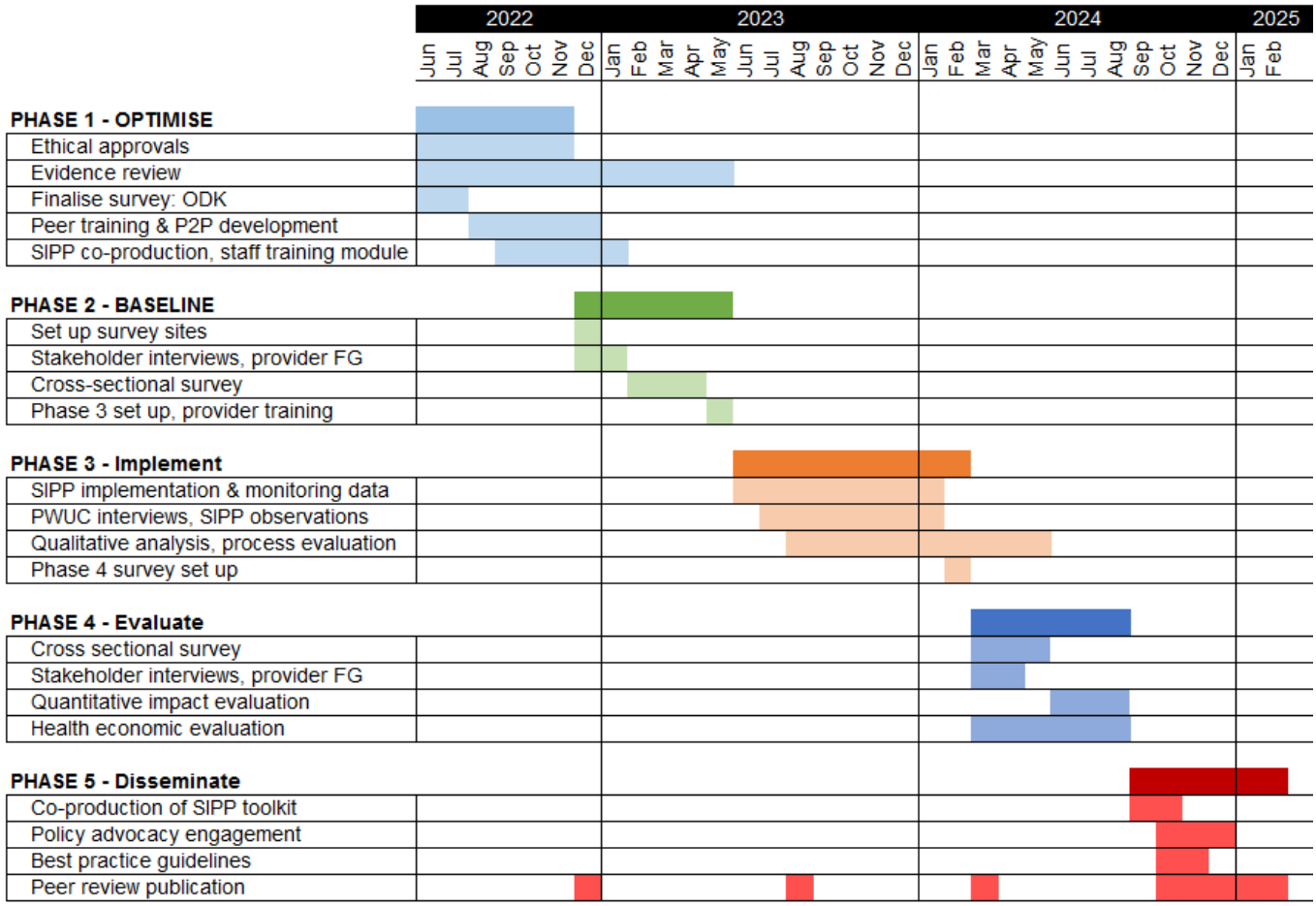
Demographics Service and the Department of Health and Social Care. In order to access these records, the team would provide the Personal Demographics Service at NHS Digital with the participant name and dob so they could find their NHS number. NHS Digital will then use patient identifiers (not personal information) to provide the team with information about health service use and health status.

3. **Linking to drug treatment specialist service records:**

This does not require in-person contact. The participant would be informed that this allows the team to look at their drug treatment service access. Also, that this information in combination with health records is valuable as it can help the team understand if there is a relationship between service access and health outcomes over time. If they agree they will be asked to provide 1) their permission to access their drug treatment records and 2) their full name and date of birth to access your records.

We will provide updates of progress regarding this future study on the SIPP website https://www.lshtm.ac.uk/research/centres-projects-groups/sipp and notify community provider project partners and peers so that they can keep participants informed.

9. Project / research timetable



10. Project management

A project manager will 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, 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.

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 with evaluation expertise, drug treatment and harm reduction providers also international experts in PWUC engagement initiatives and PWUC representatives.

The PI, will 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, Local Authority and Third Sector R&D Offices who provide research management support and advice. The applicants, and those involved in project management and oversight will collectively ensure the quality, integrity, and timeliness of the project activities and deliverables.

Ethics / Regulatory Approvals

Ethical approval will be sought from LSHTM ethics committee and local governance bodies as soon as funding is confirmed. R&D approvals will be sought from study sites. Data collection will not start until ethical approval for the project has been obtained. Preparation of protocols for ethics, participant information sheets and consent forms, and other supporting documentation for consideration during 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 PWUC in the development of participant information sheets and consent forms to ensure clarity and relevance. All project staff involved in primary data collection, data management, and analysis will be required to update their research ethics training as required by LSHTM and ensure compliance with the GDPR requirements and the UK Data Protection Act 2018. The project team will develop a data management plan, as required by LSHTM, with support from LSHTM Library & Archives Service.

Consultation has taken place with drug treatment providers, service users/PWUC 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 is cognisant of ethical issues concerning work with vulnerable populations and is familiar with signs of drug withdrawal and/or intoxication which could impact consent. 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. The transcription agency will sign a data sharing agreement, all transcripts will be anonymised and stored separately from consent forms (kept in locked LSHTM file).

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. All questionnaire data will be collected via the Open Data Kit software (ODK collect) on handheld password-protected tablet devices. Once an interview is completed the participant 'finalises' the questionnaire. Once the questionnaire is finalised, ODK Connect applies an asymmetric public key encryption using 256-bit encryption, which is irreversible and ensures that the finalized questionnaire data are not readable and are not tampered with. The encrypted form is sent to a central server hosted at LSHTM. From the server, the encrypted form will be downloaded to a secure server at LSHTM by the data manager (LP or VH). The data can only be decrypted by using the ODK briefcase by the data manager. Data will be sent to the secure server only when the device is within wifi range and so the information will be captured and stored on the device until that time. The datasets are stored within the designated project folder on the secure server. Access to each project folder is restricted to the members of LSHTM who have been nominated by the PI.

Project / research expertise

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

MH leads a mixed-method programme of research on health intervention for people who use drugs (PWUD), including through NIHR projects. She has 18 years' experience in qualitative and participatory research with PWUD and holds the 2020 Society for the Study of Addiction (SSA) Award for Impact on Policy and Practice.

VH, Professor of Public Health, has over 20 years' experience of public health research and practice with PWUD. He has extensive statistical & survey expertise. As Principal Scientist at Public Health England, he led the Unlinked Anonymous Monitoring Survey of infections and risk among PWID from 1996-2017.

LP, Professor of Public Health Epidemiology has extensive expertise in mixed-methods evaluations of complex interventions among marginalised populations. With VH, she will lead the quant work-package.

SS, Assistant Professor in Health Economics, has expertise in health economic evaluation.

JS, Senior Lecturer in Pharmacy Practice, has expertise in intervention development in community services for PWUD, laboratory-based harm reduction equipment testing and development and delivery of online training including with Exchange Supplies (current L1 NICE accredited NSP training).

JB, Associate Professor and Director Centre for Evaluation, LSHTM, has extensive experience leading process evaluations of interventions for vulnerable and marginalised populations

NE, Executive Director of Release, has extensive legal, advocacy and drug policy experience.

AP has worked as a harm reduction clinician and activist for over 20 years. Since founding Exchange Supplies in 2002 he has developed, and brought to market, many innovative harm reduction products and resources.

LW, SR, NS, PK are provider leads in the SIPP sites with extensive experience in providing care to PWUD.

MS has developed peer-networks in Bath, the West Midlands and internationally. He is a technical advisor in harm reduction & community mobilisation & co-author of specialist guidelines for stimulant use (UNODC, RCGP).

PB is Hepatitis C Trust peer-network lead for West Midlands. He has extensive experience in peer training and harm reduction intervention delivery, including as Chair of the National Needle Exchange Forum.

Success criteria and barriers to proposed work

Project activities: We will monitor our progress against a set of activity indicators which will reflect the activities as defined in Section 8 (above) and the planned timelines indicated in Section 9 (e.g. protocol publication submission in month 2-4). 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: publishing in high-impact journals, nurturing our social media presence, leveraging our collective experience of adult learning and teaching to inform training, and committing to best practice when engaging with PPI and PWUC. 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	Mitigation
Worsening situation around COVID-19 necessitates drug treatment service closures and/or enhanced social distancing requirements.	The peer networks were active during the previous COVID lockdowns and will continue to operate with appropriate PPE in the eventuality of another lockdown. Each service has COVID risk mitigation strategies, such as facilitating outreach teams, through which we can continue to generate data. We are experienced in generating data remotely, supported by LSHTM guidance.
Dissolution of partnerships or recommissioning of services limiting access to PWUC and intervention sites	We have included multiple partners, including as co-applicants. We have sought express commitment to support the study from partners. We have discussed recommissioning risk with service provider partners and are liaising with local commissioners to ensure that SIPP project participation is a requirement in retendering applications to participating services.
Peer network disruption (whether through incarceration, ill health, internal conflict, competing priorities) precludes or compromises their research involvement.	We will ensure regular and frequent liaison with peer-networks to receive early notification of any risks and provide support as appropriate. The Hepatitis C Trust is a study partner. They operate an extensive peer network, with over 200 trained peer volunteers - including in our project sites. All peers receive regular support and training. We have been assured that the Hepatitis C peer volunteers can support the study in all sites, if required.

We are unable to recruit to the cross-sectional survey as planned.	We have set recruitment targets in accordance with PWUC footfall at each site. We will assess site recruitment against targets on a weekly basis. If at week 2 and 4, 10% and 20% of the target has not been met, we bring other identified sites in each area on board. At week 6, if 30% of the total recruitment target has not been met across all sites, we will discuss with NIHR reconfiguring the project design from an impact evaluation to a health needs assessment of PWUC. This would involve completion of the baseline survey, given lack of survey data on PWUC health needs and risks in the UK, but removal of the follow-up survey. At week 8, if 75% of the total recruitment target has not been met across all sites, we will extend the survey duration to 14 weeks.
Difficulty retaining service provider and service user representatives.	We have sought explicit commitments from community groups. We will stay in regular contact and give special care to how we carry out PPI so that participation is not tokenistic and there is regular and meaningful engagement.

Diversity

Our key patient group - PWUC– are a highly marginal group in society. We will ensure diverse representation in PPI and purposively sample for diversity in the qualitative components. We have a strong track record of engaging diverse and highly marginal people who use drugs 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 PWUC. Our research will strengthen and increase the body of research evidence available to policy makers regarding this population group. We are specifically targeting different groups of PWUC through our recruitment strategy and partnerships, including outreach teams working with sex workers for example. Improving health among PWUC will reduce health inequalities.

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