Preventing blood borne virus infection in people who inject drugs in the UK: the development and feasibility of psychosocial interventions

Summary of Research

In the UK, around 33%-56% of people who inject drugs (PWID) have Hepatitis C. Rates of HIV (0-1%) and Hepatitis B (6-18%) are much lower. PWID are at risk of these blood borne viruses (BBV) as a result of sharing injecting equipment (needles and syringes, water, spoons, cotton etc) and unsafe sex. New injectors, those who are homeless, male and female PWID involved in prostitution and women are more at risk and report higher rates of these viruses. Preventing PWID from getting or passing on these viruses is an important health issue. Opiate substitution therapy (methadone or buprenorphine) and needle exchanges have reduced BBV but behavioural interventions such as individual or group brief or multi-session interventions led by peers or staff that teach PWID how to reduce risk behaviours could further prevent the spread of BBV. Most studies of behavioural interventions to reduce sexual and injecting risk behaviours have been carried out in the US, where the treatment system is different. Interventions need to be developed and tested that are relevant to UK PWID and the UK drug treatment system. There remains a need to find out what kind of behavioural intervention PWID would find useful, whether they would attend the intervention and whether it would reduce BBV transmission risk behaviours. The project has 6 phases. In Phase 1, a systematic review of the international and UK literature on what type of intervention works in which setting will be assessed. In Phase 2, the views of 60 PWID attending needle exchanges, homeless hostels, drug treatment and harm reduction centres in England (London, Yorkshire), Scotland (Glasgow) and North Wales will be sought on what type of psychosocial interventions they would find useful and acceptable (e.g. content, number of sessions, who should deliver the intervention, information they would find helpful). In Phase 3, the views of 40 UK (from England, Scotland, Northern Ireland and Wales) drug treatment NHS and third sector service providers and policy makers (including but not limited to: the Scottish Executive, Department of Health, Welsh Government, UK Government, Public Health Agency Northern Ireland) will be gathered using telephone interviews on the delivery and effectiveness of psychosocial interventions. Findings from Phases 1-3 will be used to develop a psychosocial intervention in Phase 4, incorporating existing and new evidence and what PWID and service providers and commissioners want and think is needed. In Phase 5, a trial will be conducted among 128 PWID in 4 different UK regions to assess the feasibility and acceptability of the psychosocial intervention developed in Phase 4. Findings will inform the parameters of a future multisite efficacy RCT including the number of eligible participants, the willingness of participants to consent and be randomised, adherence and compliance rates, confirmation of the suitability of 'reduction of risk behaviours' and 'increase of BBV transmission knowledge' as appropriate outcome measures, expected variability of these outcome measures, follow-up rates and response rates to questionnaires. In total, 128 (64 men) PWID attending NHS and third sector drug treatment (64 PWID) or needle exchanges (64 PWID) in London, York, Yorkshire, Glasgow and North Wales will be allocated at random to the group psychosocial intervention or to receive an information leaflet about the risks of BBV. All participants will continue to receive their usual care. Differences in number of risk events (e.g. sharing needles, cotton, water etc) in past month will be assessed pre, end and 1 month post intervention using intention-to-treat analysis. Focus groups with PWID who attended and staff who delivered the intervention will be conducted at the conclusion of the intervention to elicit their experience and help to identify any problems the intervention. In Phase 6, discussions with another 4-6 UK regions will take place to identify any challenges with conducting the research/ introducing the psychosocial intervention to their treatment settings in the future. This phase will facilitate the development of a future multisite RCT of the intervention including these additional 4-6 regions involved in this phase. Recommendations for specific intervention/s that could be tested in future studies will then be made to the HTA. The intervention has the potential to reduce BBV among PWID and their partners/social networks. The project findings will be disseminated at conferences and in publication. There will also be 2 dissemination events (one

for key stakeholders and one for service users) in each of the 4 participating regions in the project. The research team has clinical and research experience in addiction and BBV. Service users will be members of the intervention development (3 meetings) and project steering groups (6 meetings).

Background and Rationale

Prevalence

Preventing the transmission of blood borne viruses (BBV) among PWID is a major public health issue. Hepatitis C (HCV) is the most prevalent BBV among PWID: with 56% in Scotland (61% among needle exchange attenders[1], 49% in England, 33% in Wales and 34% in Northern Ireland being HCV positive[2]. The rate of HIV and hepatitis B (HBV) among PWID in the UK is low ranging from 0% in Wales and Northern Ireland to 1.4% in England for HIV and from 6% in Northern Ireland to 18% in England for HBV[2].

Risk factors

HBV and HIV are transmitted via blood or body fluids. Sharing injecting equipment/ paraphernalia pose the greatest risk of HCV transmission among PWID [3]. While there is no increased risk of HCV transmission in a long term, heterosexual relationship, the risk of transmission increases with multiple sexual partners and among women who are infected with HIV or other sexually transmitted diseases [4]. Sex trading, younger age, cocaine injecting, depression, requiring help injecting, having unsafe sex with a regular partner and having an HIV positive sexual partner were associated with HIV among PWID[5-9]. A higher prevalence of sharing and increased rates of HCV have been reported among new injectors, crack cocaine users, the homeless and those recently released from prison[10,11]. Research suggests a gap in PWID HCV transmission knowledge contributing to the high prevalence[12,13]. Higher HIV and HCV infection rates have been reported among people with mental disorders[6,14]. PWID with mental disorders report greater sharing of injection equipment, lower rates of condom use, multiple partners, sex trading, and having sex with an PWID[5,6,15]. Depressive symptoms are also associated with drug[15-18] and sexual risk behaviours [19,20]. The prevalence of intimate partner violence (IPV) is high among PWID[7,21]. Women who are IPV victims are less likely to use condoms, more likely to share needles, to have multiple sexual partners and to trade sex[21,22], increasing BBV vulnerability[22]. BBV risk behaviours should be understood in the context of PWIDs sexual and drug using relationships [23]. Female PWID share with their partners for trust and intimacy, perceiving less risk in such relationships [24].

Current policy and practice

The UK drug policies highlight the need for a harm reduction approach. Such an approach recognises that there is a need to reduce the risks associated with drug misuse including injecting. This approach is facilitated in the UK by the provision of opioid substitution (e.g. methadone or buprenorphine), key worker support, needle and syringe programmes that offer PWID free injecting equipment (and paraphernalia) and information to reduce sharing behaviour and therefore the transmission of BBV, as well as support for stopping injecting. The use of psychosocial interventions to reduce risk behaviours among PWID is not current practice in the UK presently.

What works

While advances have been made in treatment and pre-exposure prophylaxis for HIV and a vaccine is available for HBV, there is currently no vaccine available to prevent HCV infection. There is evidence to suggest that opiate substitution therapy and needle exchanges[25, 26] are effective in reducing HIV and HCV among PWID. However, recent research stresses that while increasing the coverage of these interventions can reduce HCV prevalence among PWID, these reductions are modest and psychosocial interventions are required to further decrease HCV prevalence[26] by educating PWID about transmission risks and motivate them to reduce sexual and drug taking risk behaviours. Recent systematic reviews and meta-analysis of psychosocial interventions to reduce HIV and HCV risk behaviours among PWID have reported modest effects[27-29] and conclude that

"limited progress [has been made] in developing more effective interventions"[27] and that "multi-component interventions are required"[29]. A recent Cochrane review on "Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users" [30] reported minimal differences identified between multi-session psychosocial interventions and standard educational interventions for both injection and sexual risk behaviour. However, there were large pre-post changes for both groups suggesting both were effective in reducing risk behaviours. They also found evidence of benefit for multi-session psychosocial interventions when compared with minimal controls. Moreover, people in formal treatment were more likely to respond to multi-session psychosocial interventions, and single-gender groups were associated with greater benefit. The research team has recently completed a systematic review to determine the efficacy of psychosocial interventions to reduce sexual and risk taking behaviours and increase knowledge of HCV transmission among PWID for the REDUCE project http://www.thereduceproject.imim.es/ led by the Principal Investigator. This review included both randomised controlled trials and intervention studies; only one of the 11 studies included was conducted in the UK. It remains unclear how generalizable such interventions and findings are to PWIDs and harm reduction and treatment settings in the UK. In addition, this review highlighted the need to include risk factors for BBV risk behaviours previously neglected in psychosocial interventions such as those that improve coping skills and assertiveness, address negative mood and risks incurred in intimate relationships[22,30] and consider social network and dyad interventions especially among hard to reach groups. Co-investigator Strang has reviewed Route Transition Interventions to assist PWID move to smoking[31].

Evidence explaining why this research is needed now

Research suggests that while rates of HIV and HBV are low and stable among PWID in the UK, the incidence of HCV continues to grow especially among hard to reach groups such as new PWID, women, black and minority ethnic PWID, those who are homeless or involved in prostitution. Public Health England's, "*Shooting Up"* report [32] reported that while needle and syringe sharing is lower than a decade ago, **around one in seven PWID continue to share needles and syringes** and that there is an increased risk of infection for those who inject amphetamines and amphetamine-type drugs, such as, mephedrone. Therefore, the need to address the risks and increase knowledge to reduce infection and transmission among PWID remains priority.

Rationale

The proposed research has the capacity to generate new knowledge by developing and testing psychosocial interventions for hard to reach PWID and to examine the transferability of non UK interventions to another health care system; their efficacy in NHS and other addiction services; and the feasibility and acceptability to staff and service users of such psychosocial interventions. Before conducting a larger definitive trial of an intervention, a feasibility trial is required to estimate the sample size required, recruitment and the response rates and the design and testing of suitable outcome and costing measures. Effective psychosocial interventions could reduce the transmission of BBV among PWID and result in significant reductions in health and social care costs to the NHS. Major potential patient benefits from participating in the intervention include reduction and cessation of BBV transmission risk behaviours and an increase in BBV transmission knowledge, which may reduce transmission and re-infection and improve health and quality of life. If psychosocial interventions were found to be effective, the risk of BBV transmission/re-infection would be reduced among PWID and their sexual partners and drug networks.

Aims and objectives

The proposed project will develop an evidence based psychosocial intervention to reduce BBV and increase BBV transmission knowledge among PWID, and conduct a feasibility trial, comparing the psychosocial intervention to an information leaflet, to inform the future parameters of a large multisite RCT. The main objectives of the proposed project are:

1. to update recent systematic reviews of the efficacy of psychosocial interventions to reduce drug and sexual risk behaviours associated with HIV, Hepatitis C virus (HCV) and Hepatitis B virus (HBV) [BBV] transmission and/or re-infection
2. to conduct a brief scoping exercise of the UK grey literature to identify ongoing research, information about current services relevant to preventing the spread of BBV and reducing risk behaviours among PWID
3. to survey all UK commissioning drug partnerships (previously Drug Action Teams) for information on psychosocial interventions available and their effectiveness in reducing BBV risk behaviours among PWID
4. to source and review content of all effective psychosocial interventions to reduce BBV risk behaviours among PWID
5. to elicit why PWID engage in risk behaviours
6. to determine the type of psychosocial intervention acceptable and required by PWID to reduce BBV risk behaviours
7. to ascertain key local and national stakeholders' views on the delivery and effectiveness of psychosocial interventions
8. to develop a psychosocial intervention to reduce BBV risk behaviours among PWID
9. to conduct a feasibility RCT comparing the intervention to an information leaflet in NHS and third sector community drug treatment and needle exchanges
10. to assess the feasibility of conducting a future large scale effectiveness RCT
11. to recommend specific intervention/s which could be tested in future research
12. to develop the outline of a multisite RCT to test the efficacy of the psychosocial intervention

Research Plan

1. Design

This is a 20 month mixed methods project with 6 complementary phases to address the objectives outlined above. Phases 1-3 will gather the information required to develop an evidence based intervention in Phase 4. The feasibility and acceptability of this intervention will be assessed in Phase 5, and finally in Phase 6, the results will inform the preparation for a future multisite trial in the UK.

- Phase 1. Determining the evidence base (Objectives 1-4)
- Phase 2. Understanding PWIDs' influences on behaviour and views on psychosocial interventions (Objectives 5, 6)
- Phase 3. Key stakeholders' views on the delivery and effectiveness of psychosocial interventions (Objective 7)
- Phase 4. Intervention development (Objective 8)
- Phase 5. Feasibility RCT (Objectives 9, 10)
- Phase 6. Preparation for a future multisite RCT (Objectives 11, 12)

The project addresses two elements of the development and evaluation process (i.e. developing the evidence base and feasibility) of the MRC Framework for Developing and Evaluating Complex Interventions [33]. Using a mixture of qualitative and quantitative methods will update our understanding of the barriers, facilitators and feasibility of psychosocial interventions to reduce BBV and injecting risk behaviours among PWID. ***Ethical approval*** The Integrated Research Approval System will be used to gain ethical and R&D approval to conduct the study. This approval is not required for the project till month 5; therefore, we believe we have afforded sufficient time for ethical approval.

2. Phases of the project

2.1. Phase 1. Determining the evidence base

A systematic review of efficacy of psychosocial interventions to reduce Hepatitis C risk behaviours conducted in 2012 by Principal Investigator Gilchrist for the REDUCE project (Table 1) will be updated (to include studies from 2012-2014) to include HIV and Hepatitis B. Cochrane Library, CINAHL, MEDLINE, and PsycINFO database and Clinical trials databases will be searched for intervention studies and randomised control trials that address BBV and risk behaviours among PWID. Outcomes considered will be injecting risk behaviours, sexual risk behaviours, incidence of infection and re-infection. In addition, backward and forward searching of citations will be conducted. Citations will be included regardless of language and country of origin. Trials will be assessed using Cochrane risk of bias tool and reported using the PRISMA statement. A scoping review of UK grey literature will also be conducted. UK commissioning drug partnerships (previously Drug Action Teams) will be contacted using an online survey to source available interventions. All interventions will be sourced where possible from the authors and reviewed by the intervention development group of the project in Phase 4. This will ensure that the intervention is evidence based and that any issues regarding recruitment and retention, intervention content, acceptability etc. are considered in the development phase of the current project.

Table 1. Systematic review of efficacy of psychosocial interventions to reduce HCV incidence, risk behaviour and transmission knowledge (from the REDUCE project)

Reference	RCT	HCV incidence	HCV risk behaviour	HCV transmission knowledge
Tucker et al.[34]	Yes	-	No difference between intervention and control groups	-
Evans et al.[35]	No	-	-	Transmission knowledge increased
Garfein et al.[36] Purcell et al.[37]	Yes	No difference between intervention and control groups	Intervention group significantly reduced injecting risks compared to control group No difference between intervention and control groups for sexual risks	-
Abouh-Saleh et al. [38]	Yes	No difference between intervention and control groups	No difference between intervention and control groups	No difference between intervention and control groups
Kapadia et al.[39]; Lakta et al.[40]; Dumright et al.[41]	Yes	-	Intervention group significantly reduced injecting risks compared to control group	-
Stein et al.[42]	Yes	No difference between intervention and control groups in seroconversion rates Intervention group significantly reduced injecting initiation compared to control group	-	-
Zule et al.[43]	Yes	-	Intervention group used new syringe at last injection significantly increased compared to control group No difference between intervention and control	-

Reference	RCT	HCV incidence	HCV risk behaviour	HCV transmission knowledge
			groups for condom use at last sexual encounter	
Hagedorn et al. [44]	Yes	-	-	Transmission knowledge increased significantly in intervention group compared to control group
Nyamathi et al. [45]	Yes	-	-	No difference between intervention and control groups

In 2010, the Cochrane group published a review on "Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users" [46] and found minimal differences between multi-session psychosocial interventions and standard educational interventions for both injection and sexual risk behaviour. They did however find large pre-post changes for both groups suggesting both were effective in reducing risk behaviours. Multi-session psychosocial interventions were more effective when compared with minimal controls. Those receiving formal treatment were more likely to benefit from multi-session psychosocial interventions, and single-gender groups were associated with greater benefit.

2.2 Phase 2. Understanding PWIDs' influences on behaviour and views on psychosocial interventions

In-depth interviews with a convenience sample of 60 'current injectors' that have injected at least once in the past 4 weeks (15 from London, Yorkshire, Glasgow and North Wales) from GUM clinics, homeless hostels and drug treatment/harm reduction centres will elicit the influences on risk behaviours and determine the content and preferred mode of intervention delivery. We will purposively select 5 women and 10 men in each region based on factors of influence including sex, age, drug injected & length of time injecting. It is necessary to identify the influences on risk taking behaviour and understanding of transmission knowledge among the target population of PWID in the UK to inform the development of an evidence based intervention in Phase 4 that is relevant to their needs. While we will identify effective interventions that have been developed and tested during the systematic review in Phase 1, most of these have been conducted out with the UK. Therefore, Phase 2 is necessary to identify the "information, motivation, and behavioural skills factors that are important" [47] to PWID in the UK prior to designing an intervention to reduce BBV transmission risk behaviours among the target group in Phase 4.

2.3 Phase 3. Key stakeholders' views on the delivery and effectiveness of psychosocial interventions

40 national and local stakeholders including service providers, policy makers and commissioners with responsibility for BBV will be interviewed by telephone using structured interviews (10 from Scotland, England, Wales and Northern Ireland) to determine their views on whether psychosocial interventions are effective and how they should be delivered. Stakeholders in England and Wales will be selected and recruited by Public Health England and Wales respectively who have responsibility for overseeing the delivery of BBV action plans. In Scotland, key stakeholders will be identified by the co- applicants and will be selected from those people with responsibility for delivering the Sexual Health and Blood Borne Virus Framework. In Northern Ireland, key stakeholders will be invited from The Department of Health, Social Services and Public Safety who have responsibility for BBV. The telephone structured interviews will be conducted by the researchers in Glasgow and London. As well

as gathering the views of key stakeholders with responsibility for delivering and commissioning services in BBV prevention in the UK, this phase will identify the system barriers and facilitators necessary for successful implementation of the intervention in Phase 5, and beyond in Phase 6. All interviews in Phases 2 and 3 will be recorded and transcribed verbatim. To ensure the correct stakeholders are included from Northern Ireland, we will consult with the Public Health Agency Northern Ireland, Northern Ireland Drug and Alcohol Strategy Team (Department of Health, Social Services & Public Safety, & the 4 Drug & Alcohol Co-Ordination Teams in Northern Ireland. The Northern Ireland Clinical Research Networks(CRN), The CRN Cymru and the Scottish CRNs on how to engage with appropriate stakeholders to roll out the research and disseminate the findings.

Qualitative analysis

A qualitative research framework approach will be used for analysis[48]. In framework analysis, data are sifted, charted and sorted in accordance with key issues and themes using five steps: familiarization; identifying a thematic framework; indexing; charting; and mapping and interpretation. The main purpose of framework analysis is to describe and interpret what is happening among a pre-designed sample (e.g. PWID) with a set of a priori issues. Familiarization refers to the process during which the researcher becomes familiarized with the transcripts of the data collected. After familiarization the researcher identifies emerging themes or issues. Indexing refers to the researcher identifying portions or sections of the data that correspond to a particular theme. In the charting phase, data are arranged in charts of the themes, and finally in the mapping and interpretation phase, the analysis is used to provide a schematic diagram of the results assisting the researcher to interpret the data.

2.4. Phase 4. Intervention development

The target population for the intervention is PWID who are at risk of acquiring or transmitting a BBV (e.g. hepatitis B, C and HIV). In this phase, the intervention development group (consisting of academics, service users, treatment providers and other key stakeholders) will use the results gathered in phases 1-3 of the research to develop an evidence based psychosocial intervention to reduce BBV transmission risk behaviours among PWID. The intervention group will review the content of previous effective interventions, alongside the views of PWID and key stakeholders to determine what should be included in the brief psychosocial intervention and its method of delivery. The guidelines for training and assessing fidelity will be developed alongside intervention development. The intervention will be informed from previous effective interventions and the REDUCE intervention will be adapted where possible. **Cognitive behavioral theories** are commonly used to help understand risky injection behavior, accepting that how a person thinks (cognitive) plays a role in the development and maintenance of behavioural responses to life situations (behaviour). These theories describe the determinants of whether health behaviour (i.e. risky injecting or sexual practices) is performed or not. The target population for the intervention is IDU who are at risk of acquiring or transmitting a BBV (e.g. hepatitis B, C and HIV). Wagner et al. [49] argue that *"greater integration of Cognitive Behavioural Theories with a risk environment perspective may yield more conclusive findings and more effective interventions in the future".* The theoretical basis for the intervention will draw on the **information motivation and behaviour skills model** [47] of health behaviour change. The information motivation and behaviour skills model was developed as a model for promoting and evaluating AIDS-risk behaviour change in any population of interest. The model proposes that "AIDS-risk reduction is a function of people's information about AIDS transmission and prevention, their motivation to reduce risk and their behavioural skills for performing the specific acts involved in risk reduction. There are 3 "fundamental determinants" in the model to change or reduce AIDS-risk behaviours: AIDS-risk-reduction information, motivation and behavioural skills (see Figure 1). ***Information*** about how AIDS is transmitted and information about how infection can be prevented – this can facilitate behaviour change by improving the understanding of how behaviour change can be achieved. ***Motivation*** is required to change AIDS risk behaviour and act on the information/ knowledge regarding AIDS transmission and prevention (information). Motivation can be increased

by considering possible barriers to behaviour change and finding solutions to overcome those barriers. ***Behavioural skills*** are required to ensure that skills are learned that will allow the IDU to change their behaviour. Behavioural skills "affect whether even a knowledgeable, highly motivated person will be able to change his or her behaviour in an AIDS-preventive fashion". Information and motivation work largely through behavioural skills to results in behaviour change. While the model was originally developed for HIV risk behaviour change it can be adapted to include other BBV.

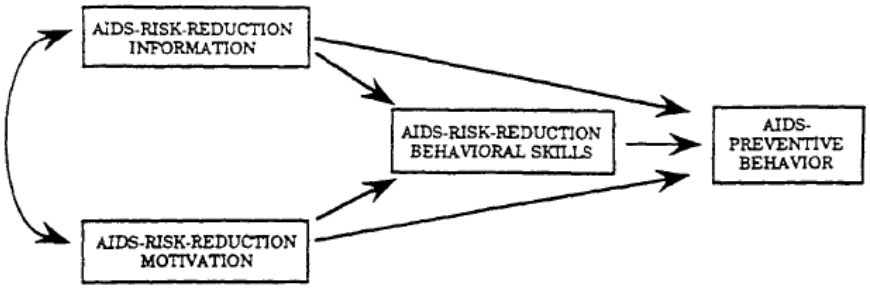


Figure 1. Three fundamental determinants of AIDS-risk reduction.

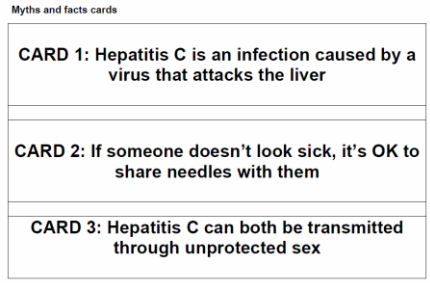
We will use the Behaviour Change Techniques (BCT)Taxonomy [50] to identify specific techniques included in a range of behaviour change interventions to clarify differences and similarities in intervention content (e.g. among those targeting similar behaviours in similar settings). This method has been used to inform intervention design, description & evidence synthesis. Such BCT are defined as "observable, replicable & irreducible component of an intervention designed to alter or redirect causal processes that regulate behaviour" that is, the taxonomy is used to identify "active ingredients" of interventions (e.g., feedback, self-monitoring, and reinforcement). Without standardised definitions of the "ingredients" included in behaviour change interventions, it is difficult to replicate effective interventions & to identify techniques that contribute to an intervention's effectiveness. Standard training on the use of the taxonomy will be completed by the intervention development group http://www.ucl.ac.uk/health-psychology/research/theories-techniques#1 who will then independently rate interventions using the BCT taxonomy & link these to the intervention's effectiveness [50]. Thereafter, the Delphi Method will be used to debate & reach consensus on the key components of each intervention & what needs to be adapted from existing interventions for the current study. All decisions will be reported to ensure transparency & a systematic approach to decision making. Similar methods have been undertaken by the PI in the REDUCE study & also in a study for perinatal drug users [51]. R6 suggested "some form of process management is required". We will adapt for the purpose of the study & use the Mixed Methods Appraisal Tool[52] to manage the findings across all studies.

While the content of the intervention will be informed by Phases 1-3 of the proposed project, we anticipate that the delivery methods of the psychosocial intervention will include: information/demonstration (video, leaflets or in person) [information], motivational enhancement (e.g. decisional balance about whether to change behaviour or not) [motivation], group discussion, game and role play exercises, problem solving, risk reduction planning and skills building [behavioural skills]. (see outline of session 1 from the REDUCE intervention manual below and examples from some of the games and exercises as examples in Figure 2 below) http://www.thereduceproject.imim.es/files/manual/FINAL_REDUCE_INTERVENTION_190313_ENGL.pdf, we anticipate the delivery methods of the psychosocial intervention will include: information/demonstration (video , leaflets or in person), group discussion, game and role play exercises, risk reduction planning and skills building. The use of social media will also be considered.

A manual for the psychosocial intervention will be designed that will facilitate the intervention delivery & replication. The intervention will be delivered by existing drug workers trained in its use. We are not able to determine the exact number of sessions or whether one

intervention will be used in all settings with all participants, e.g. there may be specific 'add-ons' to address sex/gender/BBV status issues.

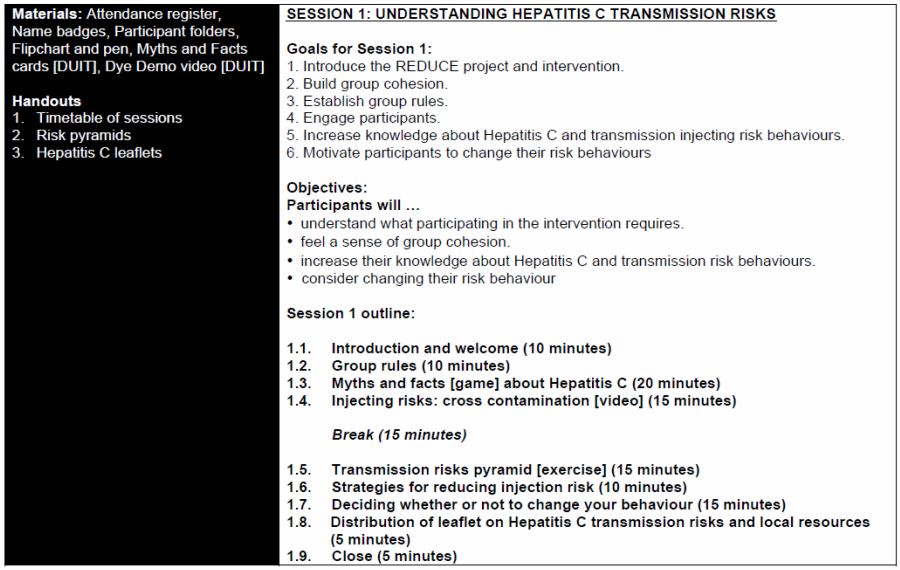
Figure 2. Examples of the methods used in the REDUCE intervention


Myths and facts cards

CARD 1: Hepatitis C is an infection caused by a virus that attacks the liver

CARD 2: If someone doesn't look sick, it's OK to share needles with them

CARD 3: Hepatitis C can both be transmitted through unprotected sex


Materials: Attendance register, Name badges, Participant folders, Flipchart and pen, Myths and Facts cards [DUIT], Dye Demo video [DUIT]

Handouts
1. Timetable of sessions
2. Risk pyramids
3. Hepatitis C leaflets

SESSION 1: UNDERSTANDING HEPATITIS C TRANSMISSION RISKS

Goals for Session 1:
1. Introduce the REDUCE project and intervention.
2. Build group cohesion.
3. Establish group rules.
4. Engage participants.
5. Increase knowledge about Hepatitis C and transmission injecting risk behaviours.
6. Motivate participants to change their risk behaviours

Objectives:
Participants will …
- understand what participating in the intervention requires.
- feel a sense of group cohesion.
- increase their knowledge about Hepatitis C and transmission risk behaviours.
- consider changing their risk behaviour

Session 1 outline:

1.1. Introduction and welcome (10 minutes)
1.2. Group rules (10 minutes)
1.3. Myths and facts [game] about Hepatitis C (20 minutes)
1.4. Injecting risks: cross contamination [video] (15 minutes)

Break (15 minutes)

1.5. Transmission risks pyramid [exercise] (15 minutes)
1.6. Strategies for reducing injection risk (10 minutes)
1.7. Deciding whether or not to change your behaviour (15 minutes)
1.8. Distribution of leaflet on Hepatitis C transmission risks and local resources (5 minutes)
1.9. Close (5 minutes)

2.5. Phase 5. Feasibility RCT

2.5.1. Design

A feasibility RCT will be conducted in 4 regions (London, Glasgow, Yorkshire, North Wales) among 128 PWID to assess the feasibility an acceptability of the intervention developed in Phase 4 and to inform parameters for a future multisite definitive RCT and economic evaluation.

2.5.2. Inclusion criteria

PWID 1) aged 18 and older attending NHS and third sector community addiction and harm reduction clinics and needle exchange programmes (static and mobile); 2) who have injected drugs at least once in the past 4 weeks; 3) who plan to stay in the area for the next 3 months and 4) who are able to complete the assessment (alone or with help of researcher) and communicate in a group intervention in English. PWID are not routinely screened for BBV at drug treatment services & therefore do not always know their BBV status. In a recent study, the discordance between PWID perceived versus actual HCV status was 20%[53] & was even higher in the NESI study.Thus it would not be possible to allocate PWID to different interventions based on BBV status. REDUCE included PWID who were HCV-ve, HCV+ve or did not know their status in the same group for similar reasons without issue. As the focus of the proposed psychosocial intervention will be to increase knowledge about transmission/ reinfection & promote motivation/skills for safer injecting & sex practices, the intervention content will be the same regardless of BBV status. When deciding intervention content, we will ensure it is relevant to all PWID regardless of BBV status.

2.5.3. Exclusion criteria
Exclusions include PWID who are too intoxicated or in withdrawal to give informed consent.

2.5.4. Sample
In each region 16 PWID from drug treatment services and 16 from needle and syringe exchanges will be randomly allocated to receive the psychosocial intervention or an information leaflet (Table 2). A mix of NHS and 3rd sector services will be recruited.

2.5.5. Settings
In all 4 regions, PWID will be recruited from Tier 3 **community drug services** (engaged with services) – provided by the NHS Trust (Glasgow, London and Wales) and provided by Compass, a third sector organisation in Selby. To ensure those not as engaged with treatment are reached, PWID will also be recruited from Tier 2 harm reduction **needle exchange services**. Further details on each region and the services where recruitment will take place are described below.

London, England
South London and the Maudsley NHS Foundation Trust (SLAM) provide substance misuse services in Lambeth, Southwark, Croydon, Greenwich and Bexley. The estimated number of opiate and/or crack (OCU) users in London is almost 52,000 and an estimated 13,056 of these are PWID[50]. PWID will be recruited from Lambeth and Southwark Drug and Alcohol Services that provide Tier 2 and 3 treatment and advice for people, aged over 18, who have substance misuse (drug and/or alcohol) related problems. PWID not engaged with services will be recruited from a large pharmacy needle exchange in Southwark (independently contracted by the NHS).

Glasgow and Clyde, Scotland
Glasgow is the largest city in Scotland and has a population of almost 600,000. It is situated within Greater Glasgow and Clyde (GG&C) health board which provides services for 1.2 million people. Glasgow contains the highest proportion of deprived areas in Scotland as measured by the Scottish Multiple Index of Deprivation (SIMD, 2012). It is estimated that GG&C has ~ 8862 PWID [50]: the vast majority of these are heroin users (over 90%, University West of Scotland, Health Protection Scotland and the West of Scotland Specialist Virology Centre, 2012). In Glasgow services for PWID are organised via Community Addiction Teams. These are based in North, South, East and West of GG&C Health Board and oversee community rehabilitation services. Most injecting equipment provision occurs via pharmacies although services such as Turning Point also provide such equipment. In GG&C, PWID who are not engaged in treatment will be recruited from Turning Point needle exchange.

York and Selby (Yorkshire), England
Selby is a market town in North Yorkshire with a population of around 13,000 is characterised by high deprivation and unemployment. The estimated number of opiate and/or crack (OCU) users in Yorkshire and the Humber is almost 37,620 and an estimated 13,387 of these are PWI [53]. The substance misuse services are provided by a 3rd sector organisation, Compass who provide Tier 1-3 addiction treatment. Compass Selby Drugs Project provides counselling and advice as well as offering free needles, syringes, condoms and specialist advice, assessment and referral to residential rehabilitation, specialist NHS drug units and other agencies providing treatment for addiction and BBV testing. In York, PWID will be recruited from a homeless hostel needle exchange (Arc Light).

North Wales, Wales
The North West Wales substance misuse service serves an adult (15 to 59) population of 384 000 and has an estimated population of PWID of between 1700 and 3400. Approximately 3000 referrals, not all of these PWID, were made to the community safety partnership across North Wales where the main problem was drug use; 41% for heroin, 8% for amphetamines. The service offers a wide range

of treatment options including opiate substitution treatment, needle and syringe exchange, psychosocial interventions and blood born viral testing and vaccination. Services are provided across the region via a number of clinics and through a mobile harm reduction service that reaches PWID who are not currently engaged in treatment. Hepatitis C prevalence amongst PWID tested by the North Wales substance misuse services, and reporting to the Welsh enhanced surveillance of BBV was 33% in 2012 (although the unlinked anonymous monitoring program of HIV and hepatitis in injecting drug users (Public Health England) suggests prevalence may be higher). The substance misuse services are managed by the Betsi Cadwaladr University Health Board, which covers the largest NHS area in the UK - from Holyhead in the West to Wrexham in the East of Wales. In North Wales, PWID will be recruited from the mobile harm reduction bus. The bus accesses PWID who are not currently in treatment but who attend the bus for needle exchange and harm reduction advice; currently the bus serves a wide range of locations, both rural and urban across North Wales. PWID who are in treatment will be recruited via the community drug teams that are managed by the North Wales substance misuse services (The Betsi Cadwaladr University Health Board); these teams serve both rural and urban populations.

2.5.6. Sample size calculation

As this is feasibility study, the main purpose is to assess the acceptability and feasibility and to obtain information that would inform the design of a larger full scale trial. Therefore, no formal sample size calculation has been conducted. Based on recruitment rates in the REDUCE study and consent rates in similar studies [36], we aim to recruit 16 participants within each location/setting (128 patients in total), half of which will be allocated to the treatment arm and half to the control arm (64 patients per arm). This sample size exceeds that recommended for feasibility studies of between 24 and 50 [54-57] and will allow feasibility assessments within both community clinics and needle exchanges. Based on previous studies, retention is estimated around 64%-83% at one month follow-up (82-106 participants).

Table 2. Sample and setting

	Intervention group	Control group
London	8 SLAM drug and alcohol services 8 Pharmacy Needle Exchange	8 SLAM drug and alcohol services 8 Pharmacy Needle Exchange
Yorkshire	8 Compass Selby drugs project 8 Compass Selby drugs project/Arc Light– needle exchange	8 Compass Selby drugs project 8 Compass Selby drugs project/ Arc Light – needle exchange
Glasgow	8 GG&C Community Addiction Teams 8 Glasgow Drug Crisis Centre Needle Exchange	8 GG&C Community Addiction Teams 8 Glasgow Drug Crisis Centre Needle Exchange
North Wales	8 Betsi Cadwaladr University Health Board substance misuse services 8 Mobile needle exchange van	8 Betsi Cadwaladr University Health Board substance misuse services 8 Mobile needle exchange van

2.5.7. Method of randomisation and blinding

Randomisation will be conducted using a secure remote randomisation service provided by York Trials Unit. This will be available as a web-based system (24 hours) and/or a telephone system (09:00 to 17:00, Monday to Friday, excluding Bank Holidays and statutory University closures). Participants will be randomised by block randomisation, ensuring balanced allocation within each location/setting and stratifying by gender. The system will automatically generate emails to confirm the randomisation, to be sent to pre-specified member of the study team. Given that this is a feasibility study and the finances available, the assessor will not be blind to the group allocation of participants,

as they will also be responsible for participant recruitment and reminder telephone calls to attend intervention sessions etc. The statistician will be blind to group allocation.

2.5.8. Recruitment and retention

Participants will be recruited for the study by researchers in waiting rooms of drug treatment and needle exchange programmes (including pharmacy and the mobile bus). Researchers will explain the study to potential participants before gaining informed consent to participate. This will allow the participant the opportunity to ask any questions about participating in the research. Participants will be reimbursed for the time taken to participate in each phase of the research (qualitative interviews, and the feasibility and acceptability study). Contingency management will be used to try to retain participants in the psychosocial intervention. **Contingency management**, recommended by NICE [58], is "highly efficacious in improving outcomes in substance misuse treatment". Contingency management offers incentives or rewards (usually vouchers or privileges such as take-home methadone doses) contingent on retention or positive engagement in treatment (e.g. drug-negative urine sample). Participants in the intervention arm will receive a £10 voucher to enhance retention in the intervention. Payment will also be given for each follow up research interview post intervention, which will also serve as an incentive for continuing to participate in the follow-up. In order to retain participants, consent will be asked from participants for their contact details (mobile, house phone, email) and those of a close friend to be recorded, as well as email and facebook accounts to enable the researcher to call to remind participants of their appointments and to arrange follow-up interviews. In addition, participants will be asked for their consent for researchers to liaise with the service from which they were recruited if it is not possible to contact them through the contact details they have provided. This method has been successfully used in the REDUCE (and many other) studies to improve engagement and retention in research studies. In cases where participants do not show >3 times for their follow up research appointment, telephone follow up interviews will be offered.

2.5.9. Care pathways in feasibility randomised trial

All participants in the feasibility trial will receive treatment as usual in addition to the trial interventions. In community addiction treatment, treatment as usual in NHS/ 3rd sector Community Addiction treatment in the UK is fortnightly tier 3 key work/care planning (based on the National Treatment Agency models of care, 2006) delivered by a drug worker. In needle and syringe exchange programmes, injecting equipment and paraphernalia is supplied free of charge, and service users can exchange/ return used syringes. Injecting and harm reduction advice and physical health care (treatment of wounds etc) is provided as required. The HTA assesses the value of a health technology (i.e. the evidence based psychosocial intervention) compared to the best alternative (currently an information leaflet). Psychosocial interventions to reduce BBV risk behaviours and transmission are not standard practice in NHS and third sector treatment in the UK. Previous studies have compared psychosocial interventions to video and leaflet information sessions [e.g. 36,38], therefore we consider the proposed approach to be ethical.

Intervention arm

A psychosocial intervention will be developed in Phase 4. Participants randomly allocated to the intervention arm will participate in a psychosocial group (brief) intervention (estimated 1-4 sessions) facilitated by a drugs worker. They will also receive treatment as usual from the service from which they are recruited. While the intervention to be used in the feasibility trial is not yet confirmed, we anticipate it will be brief (around 1-4 sessions) and will draw on the **information motivation and behaviour skills model** [47] of health behaviour change:

- Understanding BBV injecting and sexual transmission risks
- Motivation for change
- Skills building for safer injecting and sexual practices

- Negotiating safer injecting and sexual practices

Control arm
Participants randomly allocated to the control arm will be given an information leaflet on reducing the transmission of blood borne viruses by a drugs worker. They will also receive treatment as usual from the service from which they are recruited.

2.5.10. Outcomes and instruments
Differences in number of risk events in past month will be assessed pre, end and 1 month post intervention using intention-to-treat analysis. Table 3 describes the questions and instruments that will be self-completed by PWID (or where required/requested will be completed with assistance from the researcher). Good reliability and validity of self-reported behaviours by IDU have been reported when compared to biomarkers, criminal records and collateral interviews[59]. The Blood Borne Virus Transmission Risk Assessment Questionnaire(TRAQ)[60] will assess the frequency with which PWID have participated in specific injecting, sexual and other risk-practices in the previous month that may expose them to blood-borne viruses. TRAQ has 34 questions that make up three sub-scales measuring frequency of current injecting risk(20 items), sexual risk(8 items) and other skin penetration risk behaviours(6 items). TRAQ provides a total risk score and scores for each of the three sub-scales. The instrument consists of two item types, specific risk-practice items and protective practice items. The REDUCE questionnaire on HCV knowledge will also be completed(3) and asks PWID to respond 'true' or 'false' or 'don't know' to 53 statements about ways that HCV can be transmitted. A point is scored for each correct answer-producing a total score. The higher the score the greater the knowledge. The brief(18 items) HIV-Knowledge Questionnaire [61] will also be administered.

We will assess all outcomes in terms of missingness, consistency over time and sensitivity to change in order to determine the primary outcome for the main trial. This will be conducted on the number of risk events, individual risk events (a composite of which may be selected as future outcome), as well as the overall mean of both the sexual & drug risk scales from the TRAQ and the BBV knowledge questionnaires. In addition, the acceptability & relevance of outcomes to service users & providers will also be explored in the qualitative work, which would also contribute to selection for the full trial.

As described in the section on retention, researchers will call (and email where details provided) to remind the participant that they have an intervention session or research interview on a specified date and time. In addition, they will call/email/facebook them the day before and on the date agreed to remind them. We have found this assertive approach to be successful and necessary in other research among substance users including the REDUCE project. As we will have gained participants 'consent to liaise with their service provider, we will also be able to track participants that we are unable to reach through the contact details provided.

Table 3. Outcome instruments

Outcome assessed	**Instrument**
injecting, sexual & other risk-practices in past 30 days (34 items)	Blood Borne Virus Transmission Risk Assessment Questionnaire(TRAQ)
HCV transmission knowledge (53 items)	REDUCE questionnaire on HCV knowledge
HIV transmission knowledge (18 items)	Brief HIV-Knowledge Questionnaire

2.5.11. Contamination
To address contamination we will train only a limited number of drug workers in each site to provide the psychosocial intervention. Those staff who have not been trained in the psychosocial intervention will deliver TAU. There is expected to be some contamination between PWID in different arms who

may talk to each other (this could be picked up qualitatively), but as a feasibility study it is more important to try out both intervention and control in each setting. The proposed study will examine feasibility & is not powered to determine effect. The full scale trial would very likely be a cluster design, thereby eliminating any contamination.

2.5.12. Fidelity

A sample of the sessions to assess the feasibility of the quality assurance methods proposed for the main trial, including acceptability to drug worker & service users. On the basis of a gold standard approach at the feasibility stage, fidelity criteria could be developed. The audiotaped sessions will facilitate the development of a valid QA/competency checklist. This information could also inform development or refinement of the training manual and/or the intervention itself, & might suggest the level of supervision that was likely to be required. Therapist fidelity to manual guidelines will be assessed by the local MHRN using a standardised checklist in England, discussions will be undertaken with networks about how best to do this in Wales & Scotland. During the feasibility trial, drug workers will complete a brief checklist after every session (group or individual) to identify what aspects of the manual was implemented. Service users will also be asked to complete a brief checklist after each session.

2.5.13. Statistical analysis

Baseline characteristics of all participants will be tabulated by treatment arm. As a feasibility trial, this study is not powered to determine the effectiveness of the intervention, but will be used to estimate feasibility parameters for a future effectiveness trial. Such feasibility parameters will include the proportion of people who were found eligible after baseline assessment, the proportion that consented to participate in the trial and were randomised to treatments arms, as well as the treatment compliance and attrition rates over the course of the study. These will be summarised by location, setting and treatment arm. All outcome measures will also be summarised descriptively by location, setting and treatment arm. Continuous data will be described using means, standard deviations, medians and interquartile ranges, and categorical data will be described by counts and percentages as appropriate. Longitudinal methods will be used to model outcome measures across the two follow-up time points, predicted by treatment arm, the outcome at baseline as appropriate and relevant covariates, including the stratification factors. Distributional assumptions of the outcome measures will be assessed and outcomes transformed where required and/or analytic models selected accordingly (e.g. zero inflation for counts). While there is insufficient power to determine the effectiveness of the intervention, 95% confidence intervals around mean differences and odds ratios between treatment arms will be used as a first estimate of potential effect sizes and compared with those available in the literature. All analyses will be carried out in Stata[62] on an intention-to-treat (ITT) basis. We expect there to be clustering around locations, settings & intervention facilitators. Given the aims (and size) of the feasibility trial, we will not make any formal adjustments for this, but will comment on the variability within & between these groups descriptively. The sample size for the feasibility study will not be large enough to calculate ICCs, but estimates from the literature will be used for the full scale trial, which is likely to follow a cluster design. Clustering around 'therapists' will then be accounted for by adding them as a random effect in the analysis model.

2.5.14. Feasibility and acceptability of the intervention to staff and patients

Two focus groups in each region with participants who attended at least one session of the intervention will examine barriers to participation and what worked/worked less well within the intervention. Focus groups with staff will determine the acceptability of delivering the intervention and to identify and barriers and facilitators to its uptake and delivery.

2.5.15. Analysis of qualitative data

Focus groups will be digitally recorded and transcribed verbatim. Data will be organized and coded using NVivo[63]. Multiple coders will enhance the rigour of the analysis. A qualitative research

framework approach will be used for the analysis [48]. Framework analysis is better adapted to research that has specific questions, a limited time frame, a pre-designed sample and a priori issues. In the analysis, data are sifted, charted and sorted in accordance with key issues and themes using five steps: familiarization; identifying a thematic framework; indexing; charting; and mapping and interpretation.

2.5.16. Economic evaluation

The economic component of the study will assess the feasibility of conducting an economic evaluation of an adequately powered trial. The economic component will evaluate whether data can be obtained and the extent to which questionnaires are completed and return the required information, in order to inform the design and implementation of an economic evaluation of a full trial. The costs of providing the intervention will be collected from local data sources to establish the incremental cost of the psychosocial intervention over and above treatment as usual in each setting. Questionnaires will be designed to record service use by individuals in the intervention and control groups based on their use of health and social care and contacts with the criminal justice system. Quantities of resource use will be multiplied by unit costs to estimate a cost profile for each participant. The completeness of returned data, barriers to data collection and the acceptability of data collection methods to users and professionals will be presented. The study is not powered to perform a full economic evaluation at this stage since the perspective adopted includes criminal justice costs, which are high tariff low frequency events. In a feasibility trial the sample size is such that the distribution of these infrequent events between intervention and control will have a significant bearing on cost-effectiveness results which would be misleading in a small sample, results that are likely to be more a result of chance than a demonstration of cost effectiveness. The health economic component of the feasibility study would pilot service use questionnaires to measure the use of health care services including primary and secondary care contacts. Data returned from the feasibility phase will enable the revision of these instruments to improve the collection of data through further development, with further information used to identify the major services and hence cost that are associated with this population. A full future multisite trial would be powered to detect clinical differences; a full economic evaluation would be undertaken alongside a future trial which is only being assessed for feasibility in the current proposal. The feasibility trial will include EQ-5D[64] which will permit the calculation of quality-adjusted life year **(**QALY) changes. However, we would expect the major health benefits to occur over the longer term. The same applies for costs avoided in the longer term which again would be modelled beyond the follow up period proposed. Literature will provide guidance for the data requirement for modelling post-trial outcomes and costs. The early stages (Phase 1) will use resources to search the literature and determine the data required to guide future modelling.

2.5.17. Recommendations for a full scale RCT

Integrating findings from the qualitative and quantitative analyses, final reporting of the feasibility trial will provide recommendations to aid the design of a large adequately powered trial. However, we cannot make definitive recommendations or draw conclusions with regard to the effectiveness or cost effectiveness of the intervention.

2.6. Phase 6. Preparation for a future multisite RCT

Discussions with additional UK regions regarding a future multisite trial will ensure any challenges to implementation in other regions/communities are considered.

3. Dissemination and projected outputs

Results will be presented at national practitioner conferences & published in peer-reviewed journals (e.g. Addiction, Journal of Substance Abuse Treatment, Harm Reduction Journal) to reach a wide audience. The London Joint Working Group on Substance Misuse & Hepatitis C (LJWG), the Hepatitis C Trust & the National Viral Hepatitis National Patients in Scotland, work in collaboration with a wide group of stakeholders to improve the prevention, diagnosis, treatment & outcomes of

hepatitis C in people who use drugs. These organisations will assist with the dissemination of the findings from this project. The LJWG is an expert group whose mission is to eliminate HCV in drug users & those engaged in drug services in London. Their strategic objectives include influencing local policy makers, establishing a baseline level of need through comprehensive data collection, assessing the effectiveness of their recommendations through the setting & monitoring of clear measurable outcomes. The LJWG has recently commissioned a 'Public Health report on commissioning of HCV services for People who inject drugs'. It is envisaged that an academic paper & report of the systematic review & rapid evidence review will be prepared. Findings from the pilot & feasibility study will also be published. 8 dissemination events will be held-one for service users in Scotland, London, Yorkshire & North Wales & one for commissioners/practitioners in each region to present the findings of the research & develop ways to ensure the sustainability of the psychosocial intervention if it proves efficacious following a full trial in the UK. Practitioners, commissioners & policy makers with responsibility for preventing BBV will be invited to attend, including representatives from Public Health England, Health Protection Scotland, Public Health Wales, Departments of Health, & Drug (& Alcohol) Action Teams in England, Wales & Scotland. Invitations to attend these dissemination events will also be sent to appropriate organisations in Northern Ireland. In addition, we will liaise with the National NIHR Clinical Research Coordinated Centre in Leeds to determine how best to engage & disseminate with the devolved nations, including identifying strategic groups to target with policy briefings in all 4 countries in the UK. This Centre currently has a mechanism in place that brings together the English CRNs & the devolved nations networks regularly. Policy briefing papers will be submitted to Strategic groups responsible for the delivery of BBV services in each UK country summarising the findings & recommendations from the project. Service users involved in the project will develop feedback leaflets with the study findings & present the findings to service user groups. Training will be provided to support service users with these tasks.

The use of social media, such as facebook and twitter, will be considered to disseminate findings.

The results from Phases 1-3 will inform the development of an evidence based psychosocial intervention. The intervention will be free to download from the project webpage hosted by Kings College London. It is envisaged that two peer-reviewed papers will be submitted 1) on the systematic review of the effective interventions to reduce HIV, HBV & HCV risk behaviours among IDU & 2) on the findings from the pilot & feasibility study. In addition, these will also be summarised in the report to the HTA which will also include recommendations for specific intervention/s which could be tested in future research. A policy briefing will be prepared for distribution to relevant policy makers & commissioners. A service users' feedback summary will be developed by the service users involved in the projects working group. Podcasts of the dissemination events will also be available. It is hoped that the findings will be presented at relevant conferences on BBV, such as the international symposium on HCV in 2015/16.

If the intervention was feasible & effective it could be integrated into mainstream NHS & voluntary organisation service provision for attenders of harm reduction & drug treatment services. The intervention has the potential to reduce sexual & injecting risk behaviours among at risk IDU in the UK that could result in a reduction in transmission, acquiring & re-infection of Hepatitis C, B & HIV among IDU and their social & sexual networks. This in turn, could reduce the health and social care costs involved in caring for IDU with these viruses. The new evidence & local knowledge produced & widely disseminated from this project will assist service providers, commissioners and policy makers deliver and commission evidence based services in the prevention of BBV among IDU in the UK. The uptake of recommendations will be facilitated by CI Taylor & Strang's involvement with Government Strategy groups in this area. CI Strang is also Head of the Addictions Clinical Academic Group (CAG) at Kings Health Partners. Involving the CAG from the outset will enhance the likelihood of its impact in changing clinical practice. The involvement of the LJWG on Substance Misuse and HCV & the Viral Hepatitis National Patients Forum will provide feedback via established links with relevant stakeholders. Recommendations for specific intervention/s that could be tested in future research will be presented in the final report to the HTA.

4. Research timetable and milestones (Gantt chart Table 4)

IRAS ethical and Research and Development approval will be required. This process will begin as soon as we are notified of the award. Ethical approval is needed by month 5, allowing a minimum of 4 months for the IRAS approval. The systematic review of the literature and scoping exercise of UK ongoing research and treatment in the area of reducing BBV will take place during months 1-4 (Phase 1). During this time, potential interventions will be sourced and reviewed. 60 qualitative interviews with service users in 4 UK regions will be undertaken to understand their influences on behaviour and views on psychosocial interventions during months 5-7 (Phase 2). 40 telephone qualitative interviews with key stakeholders in the 4 UK countries will be undertaken during months 8-10 (Phase 3) to determine their views on the delivery and effectiveness of psychosocial interventions. The intervention will be developed/modified from the results of Phases 1-3 (months 4-11). The feasibility trial will be conducted during months 12-17, with analysis being undertaken during months 17-19 (Phase 5). Phase 6, preparation for a full multisite trial will take place at various stages across the project to ensure buy in to all project phases that will inform the future trial development in months 18-20. Dissemination events will take place in the final month of the project.

5. Project management

KCL will oversee the monitoring/financial management. Gilchrist will project manage/co-ordinate the project & supervise the research assistant at Kings College London. Adverse effects will be reported to Gilchrist & reported to the ethics committee within 48 hours. Keding will manage the statistical analysis of the intervention study & Watson will manage the trial in Phase 5. ***Supervision*** Gilchrist, Munro, Hughes & Craine will supervise the research assistant at KCL, University of the West of Scotland, University of York & NHS Wales respectively. Dr Parrot will supervise the junior health economist. ***Research team meetings*** Monthly team meetings throughout the duration of the project (chaired by Gilchrist). The project involves 4 regions in the UK (London, Yorkshire, Glasgow and North Wales). To reduce costs, monthly research team meetings will be undertaken using Skype/video conferencing to communicate & monitor progress. The research team have a demonstrated history of working together in this manner (e.g. Gilchrist, Taylor & Munro used Skype for research meetings for the REDUCE project but met quarterly in person; Gilchrist & Hughes hold journal editorial meetings successfully using Skype). ***Steering group*** 6 steering group meetings. The research team will attend the 6 steering groups in person. The steering group will be chaired by Emily Finch, Clinical Director for Addictions (South London & the Maudsley NHS Trust). As she is not a member of the research team, she is an independent Chair. Costs incurred by the steering group are included in the budget. ***Intervention development group*** 3 meetings to inform the development of the intervention, chaired by Gilchrist. ***Trial management*** Monthly trial management meetings during Phase 5 (chaired by Watson).

6. Patient and Public Involvement

8 service users (2 from Foundation 66, SDF, CARDUF & Hepatitis C Trust) will participate in 3 intervention development group & 6 steering group meetings. This will enable service users to influence development, delivery & evaluation of the research. Service users will contribute to developing the research safeguarding protocol, adapting/modifying the intervention, study materials (e.g. patient information leaflet, consent form, questionnaires, topic guide for qualitative interview) & in identifying emerging themes from the qualitative interviews. During the intervention development phase, service users will provide feedback on the intervention content/style/delivery. The intervention will be adapted according to their suggestions & experience. They will also assist with development of the study materials to ensure jargon is avoided & the research process is clear for potential participants. Service users will disseminate findings at service user events in each region. They will also assist with dissemination, including the development of a more user friendly "lay" version for peers & develop feedback leaflets to disseminate findings to study participants.

Table 4. Research timetable and milestones

	2014		2015												2016					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ethical approval																				
R & D approval																				
PHASE 1. DETERMINING THE EVIDENCE BASE																				
Systematic review of efficacy of psychosocial interventions																				
Scoping review of UK grey literature will also be conducted																				
Commissioning drug partnerships will be contacted to source available interventions																				
Reviewing of interventions																				
PHASE 2. UNDERSTANDING PWIDS' INFLUENCES ON BEHAVIOUR and VIEWS ON PSYCHOSOCIAL INTERVENTIONS																				
15 qualitative interviews with service users per region (60 in total)																				
Transcription of interviews																				
Coding framework development/ analysis																				
PHASE 3. KEY STAKEHOLDERS' VIEWS ON THE DELIVERY and EFFECTIVENESS OF PSYCHOSOCIAL INTERVENTIONS																				
40 telephone structured interviews with key stakeholders																				
Transcription																				
Coding framework development/ analysis																				
PHASE 4. INTERVENTION DEVELOPMENT																				
Development of intervention																				
PHASE 5. FEASIBILITY RCT																				
Recruitment of participants/baseline																				
Delivery of intervention																				
Post intervention follow up																				

	2014		2015												2016					
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
One month post intervention follow up																				
Analysis																				
PHASE 6. PREPARATION FOR MULTISITE TRIAL																				
Exploratory work with other regions																				
Development of HTA proposal																				
DISSEMINATION																				
Dissemination events																				
Draft papers																				