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The impact of drug consumption rooms on risk practices and access to care in people who inject drugs in France: the COSINUS prospective cohort study protocol.

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TITLE : The impact of drug consumption rooms on risk practices and access to care in people who inject drugs in France: the COSINUS prospective cohort study protocol.

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ABSTRACT

Introduction: The high prevalence of hepatitis C and the persistence of HIV and HCV risk practices in people who inject drugs (PWID) in France underlines the need for innovative prevention interventions. The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of drug consumption rooms (DCR) on PWID outcomes. Secondary objectives are to assess how DCR a) influence other drug-related practices, such as the transition from intravenous to less risky modes of use, b) reduce drug use frequency/quantity, c) increase access to treatment for addiction and comorbidities (infectious, psychiatric and other), d) improve social conditions, and e) reduce levels of violence experienced and drug-related offenses. COSINUS will also give us the opportunity to investigate the impact of other harm reduction tools in France and their combined effect with DCR on reducing HIV-HCV risk practices. Furthermore, we will be better able to identify PWID needs.

Methods and analysis: Enrolment in this prospective multisite cohort study started in June 2016. Overall, 680 PWID in 4 different cities (Bordeaux, Marseilles, Paris and Strasbourg) will be enrolled and followed up for 12 months through face-to-face structured interviews administered by trained staff to all eligible participants at baseline (M0), 3-month (M3), 6-month (M6) and 12-month (M12) follow-up visits. These interviews gather data on socio-demographic characteristics, past and current drug and alcohol consumption, drug-use related practices, access to care and social services, experience of violence (as victims), offenses, other psychosocial issues, and perception and needs about harm reduction interventions and services. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual and structural factors, including DCR attendance and exposure to other harm reduction services, on the main outcome (HIV-HCV risk practices).

Ethics and dissemination: This study was reviewed and approved by the institutional review

board of the French institute of medical research and health (opinion number: 14-166). The findings of this cohort study will help to assess the impact of DCR on HIV-HCV risk practices and other psychosocial outcomes and trajectories. Moreover, they will enable health authorities to shape health and harm reduction policies according to PWID needs. Finally, they will also help to improve current harm reduction and therapeutic interventions and to create novel ones.

Strengths and limitations of this study

- This is the first multisite cohort of PWID conducted in France.
- The study's findings will help to assess the impact of DCR and other harm reduction services on HIV-HCV risk practices in PWID.
- The findings will also assess the needs of PWID in France by providing a greater understanding of their social conditions, access to prevention and treatment services.

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INTRODUCTION

Rationale

In France, as elsewhere, people who inject drugs (PWID) faced a dramatic HIV epidemic in the 1990s. In response, the French government's harm reduction policy - which first developed programs for access to sterile injection material in 1987 - extended access in 1994 to include syringe vending machines and the sale of ready-to-use injection kits (Steribox®) in community pharmacies[1], as well as new state-funded needle exchange programs (NEP)[2]. These public health initiatives were concomitant with opiate maintenance treatment (OMT) programs with methadone (available since 1994) and buprenorphine (available since 1995)[3 4] and highly active antiretroviral therapy (HAART) for HIV-infected individuals.[5] HIV prevalence in PWID dramatically decreased from 40% to 20% in 14 years from 1988 to 2002,[2 6] with a prevalence in 2011 of 10%.[7] An estimated 77% to 85% of opioid-dependent individuals in France are currently treated with OMT.[7]

Despite this progress, and just as in many countries where OMT and NEP are available,[8] the impact of this harm reduction policy on the hepatitis C virus (HCV) epidemic in France has not been as great as that for HIV.[2 9-12] This is because this policy was adopted when HCV prevalence was already too high to be rapidly controlled. In 2011, HCV infection prevalence in the country was 64% among many PWID.[7] HCV incidence was also very high, between 11% and 22%,[13] compared with neighboring countries such as the Netherlands.[14] The delay in implementing an efficient harm reduction policy may explain the persistent high national prevalence of HCV in PWID today.[15] Besides HCV and HIV infections, numerous other physical problems can result from injecting drug use, including soft tissue infections,[16 17] cardiovascular and pulmonary complications,[18] and bacterial and fungal infections.[19]

In addition, PWID are more vulnerable to psychiatric comorbidities and precarious socio-economic conditions,[7] to stigma - which is associated with more risk practices - and to lower

use of NEP.[11] Because of the increasing amount of available data regarding these elements, a growing number of studies are exploring the role that social and political environments play in risk practices, not only for PWID who inject in public, is being increasingly studied, in order to inform future prevention intervention policies for PWID.[20]

Despite the French health authorities' reluctance to open DCR for many years, mostly because of the country's persistent repressive policy toward drug use and general negative public opinion,[21] their success in other countries encouraged the French government to reconsider DCR as a possible additional harm reduction (HR) tool. Two DCR, in Paris and Strasbourg, were opened in 2016 as part of a 6-year experiment granted on the condition that the health and social impact of the facilities would be rigorously evaluated. In this perspective, the COSINUS cohort (COhort to identify Structural and INdividual factors associated with drug Use) was set up in 2016 to prospectively evaluate the impact of DCR on the reduction of risk-taking behaviors in PWID.

The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of the DCR on PWID outcomes.

Research objectives and hypothesis

The main objective of COSINUS is to evaluate the impact of regular DCR use on HIV and HCV risk practices. The hypothesis is that PWID with regular access to DCR have fewer practices at risk of HCV and HIV transmission than PWID with no access. It will also investigate the impact of regular DCR use on access to care. Furthermore, data from COSINUS will be used to study the impact of other individual (e.g., age, gender, ethnicity, housing) and structural (e.g., exposure to social services, harm reduction services including education about safer injection)[22] factors on several outcomes (other risk practices, criminality, current drug use, negative life events, etc.). More specifically, it will help provide a greater understanding of the combined effect of different harm reduction services on PWID health

and risk practices.

METHODS AND ANALYSIS

Study design

This prospective, multicenter cohort study, which started in June 2016, will enroll a total of 680 PWID by October 2017 in 4 different French cities with different geographical and health characteristics (Bordeaux, Marseilles, Paris and Strasbourg). The study design and data collection tools were partly inspired by an evaluation of the Vancouver Downtown Eastside DCR (Insite)[23] and the Vancouver Injection Drug User Study.[24] Individual follow-up will last 12 months. PWID in the DCR in Paris and Strasbourg constitute the "treatment" group (hereafter "DCR-exposed"), while PWID already enrolled in harm reduction programs in Bordeaux and Marseilles constitute the "control" group (hereafter "DCR-unexposed"). Data collection consists in face-to-face interviews (each lasting approximately 20 to 35 minutes) administered by a trained interviewer at baseline, 3 months, 6 months and 12 months. Data collection is coordinated by the logistics department of methodology and management (CMG) of ORS PACA – INSERM-IRD UMR1252 (SESSTIM) in Marseilles, under the supervision of the cohort's four PIs (Marc Auriacombe for Bordeaux, Perrine Roux for Marseilles, Marie Jauffret-Roustide for Paris and Laurence Lalanne-Tongio for Strasbourg), and is managed by each site-investigator. Participants are compensated for their time with 10 euros worth of service vouchers after each of the 4 interviews. The study protocol was approved by the National scientific research ethics committee in Paris (CEEI/IRB).

Participants

Subjects are eligible if they are regular users of illegal drugs except cannabis (heroin, cocaine / crack, amphetamines, ecstasy), and/or prescription drugs (methylphenidate, buprenorphine,

benzodiazepines, morphine sulfate, oxycodone, methadone), and have injected drugs at least once during the previous month. Participants must be over 18 years old and French-speaking. They must also provide informed consent to participate in the study. To avoid duplicate enrollment, the month, year and place of birth are recorded for each participant.

Measures

The evaluation of DCR is based on the following main outcome: the proportion of participants reporting at least one HCV risk practice (sharing of syringes/needles, sharing of other injecting paraphernalia (filter, swab, water, cup, etc.)) in the previous month.

The other variables that will be collected are: sociodemographic characteristics (gender, age, housing, employment, living in a couple, ethnicity, parenthood, social allowances, country of birth); history of drug use (age at first drug use, first injection and related context); current drug and alcohol use (type, frequency, quantity of drugs used, context of drug use, use disorder diagnostic criteria, craving); overdoses and suicide risk; drug use-related HIV-HCV risk practices (injecting, snorting, smoking, sharing and reusing injecting equipment); addiction treatments; DCR attendance; health conditions and access to care and prevention (type and frequency of care, satisfaction with care, HIV, HCV and HBV screening, education in injection, other HR services); criminality (illegal activities and experience of prison); negative life events (violence, sexual assault, loss of a relative, etc.); psychosocial assessment (anxiety, ADHD, PTSD, etc.); injection initiation (experience and context); cognitive assessments (GONOGO, mnesic test); sexual health (sexual risk practices, contraception); discrimination and life course (parents, childhood).

This interview questionnaire includes the full version or some items from several already validated questionnaires as follows: i) the Blood-Borne Virus Transmission Risk Assessment (BBV-TRAQ)[25] to evaluate the risk practice; ii) a section of the Addiction Severity Index, which is a multi-dimensional questionnaire which measures drug use based on participants'

self-report;[26 27] iii) the Alcohol Use Disorders Identification Test (AUDIT-C) questionnaire to measure alcohol consumption;[28] iv) a set of questions from the PRIMER study to examine injection initiation;[29] v) three validated questionnaires to measure psychiatric outcomes: the 25-item Wender Utah Rating Scale (WURS) for attention-deficit/hyperactivity disorder screening,[30] the Beck Anxiety Inventory to measure anxiety[31] and the Post-traumatic stress event questionnaire;[32 33] vi) finally, two questionnaires measure participants' cognitive ability: the go-no go task[34] and the mnesic test.[35]

Table 1 displays the schedule for each assessment.

Table 1. Summary of data collection at each follow-up visit

	M0	M3	M6	M12
Socio-demographic characteristics	x	x	x	x
Socio-economic characteristics	x	x	x	x
History of substance use	x			
Current drug use	x	x	x	x
Alcohol and tobacco use	x	x	x	x
Overdoses and suicidal risk	x		x	x
Drug use-related HIV-HCV risk practices	x	x	x	x
Addiction treatment	x	x	x	x
Health conditions and access to care	x		x	x

Screening for HIV and HCV	x		x	x
Criminality	x	x	x	x
Prison experience	x		x	x
Negative life events	x			x
Initiation injection	x		x	x
HR services user satisfaction	x		x	x
Sexual health		x		
Other practices at risk of dermal contamination		x		
DCR attendance and other services	x	x	x	x
Life course		x		
Attention Deficit Hyperactivity Disorder – ADHD		x		
Anxiety: Beck anxiety inventory			x	
Post-traumatic stress disorder			x	
Discrimination		x		
GONOGO Task		x		x
Mnemonic Test		x		x

Sample size

The main outcome is the comparison of the percentage of PWID reporting at least one HCV risk practice during the previous month between the DCR-exposed and DCR-unexposed groups. The sample size needed was calculated according to this main outcome. Many studies

from different countries with DCR have shown that between 30%[36 37] and 60%[38] of users regularly attend them. In the French context, the proportion of PWID reporting at least one HCV risk practice varies according to the context and the characteristics of PWID recruited in different studies, from 25%[22] to 50%[39]. We hypothesize 33% in DCR-exposed participants. Supposing that one third of participants will regularly attend DCR, with an alpha=5 % and a power of 80 %, we need a total of 131 participants in each group. Given an expected attrition rate of 40% after 12 months of follow-up,[40] the sample size is therefore 680 (Paris=250, Marseilles=200, Bordeaux=150, Strasbourg=80).

Statistical methods

COSINUS was developed to show the impact of DCR on HIV-HCV risk practices. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual factors (sociodemographic, behavioral and cognitive data) and structural factors, including DCR attendance and exposure to other HR services (access to OMT, social services, education to safer injection, etc.), on the main outcome (reporting at least one HIV-HCV risk practice during the previous month). Data analysis will be carried out with logistic regression models for qualitative data in two ways, multinomial regression for qualitative data of more than two terms, or linear regression for continuous data. A Cox model-based approach (or duration models) will be used to study the impact of DCR attendance (or other HR services) for a certain event at a certain time (transition from injection to another mode of use, access to care). Analyses will be performed using several statistical software packages (SPSS v. 12.0, Intercooled Stata® v. 10.0 and SAS; statistical v 10.0).

DISCUSSION

The COSINUS cohort study is the first in France designed to assess the impact of DCR on

HIV-HCV risk practices. It is important to note that DCR in France are seen as an additional tool to existing NEP and OMT programs, as well as the recently approved education program for safer injecting practices.[22]

To date, most of the data published on the effects of DCR are from the Vancouver INSITE research team,[41] whose work greatly contributed to the preliminary design of our cohort study. However, the French and Vancouver contexts are very different in terms of substances available on the black market, access to OMT, sharing practices, sero-prevalence of HIV and HCV, and harm reduction policy. In France, an estimated 180 000 drug users are currently on OMT,[42] corresponding to an estimated coverage of 80% in urban areas.[7 22] Two thirds of individuals receiving OMT are treated with buprenorphine. This figure contrasts with other high-level income countries, where methadone is more accessible.[43] This high coverage of OMT may have played a role in decreasing long-term HCV prevalence over recent years.[2 9-11] The decrease in prevalence of HCV has been slower than that seen for HIV. This reflects the situation in other European countries such as the Netherlands and Switzerland.[44] Overall, despite high coverage of prevention and treatment services, HCV prevalence data suggest that PWID – including those receiving OMT[45] - still have a high risk of transmitting HCV.[15 46] DCR can therefore be an addition to existing HCV prevention tools by engaging difficult-to-rich PWID in OMT and safer injection practices.

Although there are differences between the French and Vancouver contexts in terms of black market substance abuse (see above), and despite some heterogeneity across and within the four different metropolitan areas where our study is being conducted,[7] similarities between the two contexts exist, specifically regarding reduced access to sterile syringes, low socioeconomic levels, and a high proportion of PWID injecting in public spaces.[7 39] COSINUS will help us understand the dynamic of HIV-HCV risk practices at a national level, both in already existing DCR and in sites providing other HR services.

Many prospective studies have tested, evaluated and validated DCR worldwide and have shown several benefits for public health.[47] Although public opinion on DCR is mixed and has seen shifting attitudes over time,[21 48] DCR acceptance by drug users and the drug-using community has been positive to date.[49-52] Any evaluation of DCR needs to take into account the social environment where DCR are implemented, especially social acceptability by the neighborhood.[53] DCR facilitate access to needles and provide safer places for users at high risk both to themselves and to their environment.[38 54 55] They provide hygienic and safe conditions for intravenous users and staff. They reduce morbidity and mortality associated with overdoses and with HIV and HCV infections, which is not only beneficial to PWID but increases healthcare cost-effectiveness.[56] They promote access to opioid dependence treatment[57] and to prevention interventions related to drug injecting practices.[58 59] However, few existing DCR provide education programs for safer injection[60] or have a space to inhale drugs. Moreover, data about the combined effect of DCR with other HR services are sparse. The Canadian experience has shown the importance of the evaluation process of such a controversial HR tool.[61 62] More specifically, evidence-based findings from an evaluation process of the DCR "Insite" helped to advocate against its closure, which was threatened by the Federal Government.[63] The COSINUS cohort study will not only study the impact of regularly attendance in DCR on HIV-HCV risk practices in PWID in France, but will also assess the combined effect of DCR together with other HR services (e.g., education about safer injection, access to OMT, social activities) on these practices.

In addition to evaluating DCR and other HR services, this cohort will be used for a more global assessment of the needs of the PWID population in terms of access to treatment for addictive disorders. It will also examine the reasons for not seeking treatment, while identifying users who may benefit from it. It will help to provide a greater understanding of users' social conditions, practices, their access to prevention and treatment services, and of

the role of incarceration and violence in this population often excluded from the health care system.

ETHICS AND DISSEMINATION

This study was approved by the Institutional Review Board (IRB00003888) of the French institute of medical research and health (opinion number: 14-166). All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. All participants in the survey gave their informed consent.

The results from this cohort will enable health authorities shape health and harm reduction policies according to PWID needs, as well as improve and create novel harm reduction and therapeutic interventions. All relevant results will be published in peer-reviewed international scientific journals and presented at conferences, nationally and internationally.

LIST OF ABBREVIATIONS

ADHD: Attention Deficit Hyperactivity Disorder

CEEI/IRB: Institutional Review Board

CMG: the logistics department of methodology and management

COSINUS: COhort to identify Structural and INdividual factors associated with drug Use

DCR: Drug Consumption Rooms

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

HR: Harm Reduction

INSERM: National Institute of Health and Medical Research

NEP: Needle Exchange Programs

OMT: Opiate Maintenance Treatment

PWID: People Who Inject Drugs

DECLARATIONS

Authors' contributions

Study conception and design: PC, CD, LL, MA, MJR, PR. Drafting of Manuscript: MA, MJR, LL, PR, CK, CD drafted the first version of the manuscript. MA, LL, MJR, and PR are the COSINUS cohort study PIs. SK, LBM, MG, CK, CC are the study-site interviewers and contributed to improving the design of the study. All authors significantly contributed to the manuscript and approved the final version.

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Competing interests

The authors declare that they have nothing to disclose regarding funding or conflict of interest with respect to this manuscript.

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The impact of drug consumption rooms on risk practices and access to care in people who inject drugs in France: the COSINUS prospective cohort study protocol.

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ABSTRACT

Introduction: The high prevalence of hepatitis C and the persistence of HIV and HCV risk practices in people who inject drugs (PWID) in France underlines the need for innovative prevention interventions. The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of drug consumption rooms (DCR) on PWID outcomes. Secondary objectives are to assess how DCR a) influence other drug-related practices, such as the transition from intravenous to less risky modes of use, b) reduce drug use frequency/quantity, c) increase access to treatment for addiction and comorbidities (infectious, psychiatric and other), d) improve social conditions, and e) reduce levels of violence experienced and drug-related offenses. COSINUS will also give us the opportunity to investigate the impact of other harm reduction tools in France and their combined effect with DCR on reducing HIV-HCV risk practices. Furthermore, we will be better able to identify PWID needs.

Methods and analysis: Enrolment in this prospective multisite cohort study started in June 2016. Overall, 680 PWID in 4 different cities (Bordeaux, Marseilles, Paris and Strasbourg) will be enrolled and followed up for 12 months through face-to-face structured interviews administered by trained staff to all eligible participants at baseline (M0), 3-month (M3), 6-month (M6) and 12-month (M12) follow-up visits. These interviews gather data on socio-demographic characteristics, past and current drug and alcohol consumption, drug-use related practices, access to care and social services, experience of violence (as victims), offenses, other psychosocial issues, and perception and needs about harm reduction interventions and services. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual and structural factors, including DCR attendance and exposure to other harm reduction services, on the main outcome (HIV-HCV risk practices).

Ethics and dissemination: This study was reviewed and approved by the institutional review

board of the French institute of medical research and health (opinion number: 14-166). The findings of this cohort study will help to assess the impact of DCR on HIV-HCV risk practices and other psychosocial outcomes and trajectories. Moreover, they will enable health authorities to shape health and harm reduction policies according to PWID needs. Finally, they will also help to improve current harm reduction and therapeutic interventions and to create novel ones.

Strengths and limitations of this study

- This is the first multisite cohort of PWID conducted in France.
- The study's findings will help to assess the impact of DCR and other harm reduction services on HIV-HCV risk practices in PWID.
- The findings will also assess the needs of PWID in France by providing a greater understanding of their social conditions, access to prevention and treatment services.

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INTRODUCTION

Rationale

In France, as elsewhere, people who inject drugs (PWID) faced a dramatic HIV epidemic in the 1990s. In response, the French government's harm reduction policy - which first developed programs for access to sterile injection material in 1987 - extended access in 1994 to include syringe vending machines and the sale of ready-to-use injection kits (Steribox®) in community pharmacies[1], as well as new state-funded needle exchange programs (NEP)[2]. These public health initiatives were concomitant with opiate maintenance treatment (OMT) programs with methadone (available since 1994) and buprenorphine (available since 1995)[3 4] and highly active antiretroviral therapy (HAART) for HIV-infected individuals.[5] HIV prevalence in PWID dramatically decreased from 40% to 20% in 14 years from 1988 to 2002,[2 6] with a prevalence in 2011 of 10%.[7] An estimated 77% to 85% of opioid-dependent individuals in France are currently treated with OMT.[7]

Despite this progress, and just as in many countries where OMT and NEP are available,[8] the impact of this harm reduction policy on the hepatitis C virus (HCV) epidemic in France has not been as great as that for HIV.[2 9-12] This is because this policy was adopted when HCV prevalence was already too high to be rapidly controlled. In 2011, HCV infection prevalence in the country was 64% among many PWID.[7] HCV incidence was also very high, between 11% and 22%,[13] compared with neighboring countries such as the Netherlands.[14] The delay in implementing an efficient harm reduction policy may explain the persistent high national prevalence of HCV in PWID today.[15] Besides HCV and HIV infections, numerous other physical problems can result from injecting drug use, including soft tissue infections,[16 17] cardiovascular and pulmonary complications,[18] and bacterial and fungal infections.[19] In addition, research on existing drug consumption rooms (DCR) showed that they improve access to primary health care and improve safer injection conditions.[20] By attracting the most

marginalized PWID,[21] they also reduce the level of public injection and so the number of used syringes has dropped in public spaces.[22] Finally, it has also been shown that DCR are effective in reducing fatal overdoses.[23]

Despite the French health authorities' reluctance to open DCR for many years, mostly because of the country's persistent repressive policy toward drug use and general negative public opinion,[24] their success in other countries encouraged the French government to reconsider DCR as a possible additional harm reduction (HR) tool. Two DCR, in Paris and Strasbourg, were opened in 2016 as part of a 6-year experiment granted on the condition that the health and social impact of the facilities would be rigorously evaluated. These two DCR accept all PWID 18 years or older and provide the following services: the possibility to administer drugs by injection (or inhalation in some cases, only for PWID), access to social, medical and psychiatric consultations, the provision of sterile equipment, the collection and disposal of used injection equipment, primary care, harm reduction counselling and HCV, HBV and HIV testing. In this perspective, the COSINUS cohort (COhort to identify Structural and INdividual factors associated with drug Use) was set up in 2016 to prospectively evaluate the impact of DCR on the reduction of risk-taking behaviors in PWID.

The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of the DCR on PWID outcomes.

Research objectives and hypothesis

The main objective of COSINUS is to evaluate the impact of regular DCR use on HIV and HCV risk practices. The hypothesis is that PWID with regular access to DCR have fewer practices at risk of HCV and HIV transmission than PWID with no access. It will also investigate the impact of regular DCR use on access to care. Furthermore, data from COSINUS will be used to study the impact of other individual (e.g., age, gender, ethnicity, housing) and structural (e.g., exposure to social services, harm reduction services including

education about safer injection)[25] factors on several outcomes (other risk practices, criminality, current drug use, negative life events, etc.). More specifically, it will help provide a greater understanding of the combined effect of different harm reduction services on PWID health and risk practices.

METHODS AND ANALYSIS

Study design

This prospective, multicenter cohort study, which started in June 2016, will enroll a total of 680 PWID by October 2017 in 4 different French cities with different geographical and health characteristics (Bordeaux, Marseilles, Paris and Strasbourg). The study design and data collection tools were partly inspired by an evaluation of the Vancouver Downtown Eastside DCR (Insite)[26] and the Vancouver Injection Drug User Study.[27] Individual follow-up will last 12 months. PWID in the DCR in Paris and Strasbourg constitute the "treatment" group (hereafter "DCR-exposed"), while PWID already enrolled in harm reduction programs constitute the "control" group (hereafter "DCR-unexposed"). These four cities were chosen because they were all candidates for the opening of DCR when the law permitting experimentation with DCR passed (Public Health Law from January 2016). Data collection consists in face-to-face interviews (each lasting approximately 20 to 35 minutes) administered by a trained interviewer at baseline, 3 months, 6 months and 12 months. Data collection is coordinated by the logistics department of methodology and management (CMG) of ORS PACA – INSERM-IRD UMR1252 (SESSTIM) in Marseilles, under the supervision of the cohort's four PIs (Marc Auriacombe for Bordeaux, Perrine Roux for Marseilles, Marie Jauffret-Roustide for Paris and Laurence Lalanne-Tongio for Strasbourg), and is managed by each site-investigator. Participants are compensated for their time with 10 euros worth of service vouchers after each of the 4 interviews. The study protocol was approved by the

Institutional Review Board (IRB00003888) of the French institute of medical research and health (opinion number: 14-166).

Participants

Subjects were eligible if they reported injecting illicit drugs except cannabis (heroin, cocaine / crack, amphetamines, ecstasy), and/or prescription drugs (methylphenidate, buprenorphine, benzodiazepines, morphine sulphate, oxycodone, methadone) at least once during the previous month. Participants must be over 18 years old and French-speaking. They must also provide informed consent to participate in the study. They were recruited mainly in the DCR (in the cities where there is one) and in other harm reduction facilities that currently outreach to PWID likely to attend a DCR if available in each city. This mix of recruitment sites was chosen in order to be able to compare PWID between cities. To avoid duplicate enrollment, the month, year and place of birth are recorded for each participant.

Measures

The evaluation of DCR is based on the following main outcome: the proportion of participants reporting at least one injection-related HIV-HCV risk practice (sharing of syringes/needles, sharing of other injecting paraphernalia (filter, swab, water, cup, etc.)) in the previous month.

The other variables that will be collected are: sociodemographic characteristics (gender, age, housing, employment, living in a couple, ethnicity, parenthood, social allowances, country of birth); history of drug use (age at first drug use, first injection and related context); current drug and alcohol use (type, frequency, quantity of drugs used, context of drug use, use disorder diagnostic criteria, craving); overdoses and suicide risk; drug use-related HIV-HCV risk practices (injecting, snorting, smoking, sharing and reusing injecting equipment); addiction treatments; DCR attendance; health conditions and access to care and prevention

(type and frequency of care, satisfaction with care, HIV, HCV and HBV screening and self-reported HIV and HCV status, education in injection, other HR services); criminality (illegal activities and experience of prison); negative life events (violence, sexual assault, loss of a relative, etc.); psychosocial assessment (anxiety, ADHD, PTSD, etc.); injection initiation (experience and context); cognitive assessments (GONOGO, mnesic test); sexual health (sexual risk practices, contraception); discrimination and life course (parents, childhood).

This interview questionnaire includes the full version or some items from several already validated questionnaires as follows: i) the Blood-Borne Virus Transmission Risk Assessment (BBV-TRAQ)[28] to evaluate the risk practice; ii) a section of the Addiction Severity Index, which is a multi-dimensional questionnaire which measures drug use based on participants' self-report;[29 30] iii) the Alcohol Use Disorders Identification Test (AUDIT-C) questionnaire to measure alcohol consumption;[31] iv) a set of questions from the PRIMER study to examine injection initiation;[32] v) three validated questionnaires to measure psychiatric outcomes: the 25-item Wender Utah Rating Scale (WURS) for attention-deficit/hyperactivity disorder screening,[33] the Beck Anxiety Inventory to measure anxiety[34] and the Post-traumatic stress event questionnaire;[35 36] vi) finally, two questionnaires measure participants' cognitive ability: the go-no go task[37] and the mnesic test.[38]

Table 1 displays the schedule for each assessment.

Table 1. Summary of data collection at each follow-up visit

	M0	M3	M6	M12

Socio-demographic characteristics	x	x	x	x
Socio-economic characteristics	x	x	x	x
History of substance use	x			
Current drug use	x	x	x	x
Alcohol and tobacco use	x	x	x	x
Overdoses and suicidal risk	x		x	x
Drug use-related HIV-HCV risk practices	x	x	x	x
Addiction treatment	x	x	x	x
Health conditions and access to care	x		x	x
Screening for HIV and HCV	x		x	x
Criminality	x	x	x	x
Prison experience	x		x	x
Negative life events	x			x
Initiation injection	x		x	x
HR services user satisfaction	x		x	x
Sexual health		x		
Other practices at risk of dermal contamination		x		
DCR attendance and other services	x	x	x	x
Life course		x		
Attention Deficit Hyperactivity Disorder – ADHD		x		

Anxiety: Beck anxiety inventory			x	
Post-traumatic stress disorder			x	
Discrimination		x		
GONOGO Task		x		x
Mnemonic Test		x		x

Sample size

The main outcome is the comparison of the percentage of PWID reporting at least one injection-related HIV-HCV risk practice during the previous month between the DCR-exposed and DCR-unexposed groups. The sample size needed was calculated according to this main outcome. Many studies from different countries with DCR have shown that between 30%[39 40] and 60%[41] of users regularly attend them (at least once a week). In the French context, the proportion of PWID reporting at least one injection-related HIV-HCV risk practice varies according to the context and the characteristics of PWID recruited in different studies, from 25%[25] to 50%[42]. We hypothesize 33% of regular (i.e., at least once a week) DCR attending participants will report at least one of these events. Supposing that one third of participants will regularly attend DCR, with an alpha=5 % and a power of 80 %, we need a total of 131 participants in each group. Given an expected attrition rate of 40% after 12 months of follow-up,[43] the sample size is therefore 680 (Paris=250, Marseilles=200, Bordeaux=150, Strasbourg=80).

Statistical methods

COSINUS was developed to show the impact of DCR on HIV-HCV risk practices. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual

factors (sociodemographic, behavioral and cognitive data) and structural factors, including DCR attendance and exposure to other HR services (access to OMT, social services, education to safer injection, etc.), on the main outcome (reporting at least one injection-related HIV-HCV risk practice during the previous month). Data analysis will be carried out with logistic regression models for qualitative data in two ways, multinomial regression for qualitative data of more than two terms, or linear regression for continuous data. In addition, to study the impact of the combined effect of different services (DCR, education about safe injection, other HR services) on the main outcome, we will use mixed-model regression analysis by adjusting for these different structural factors and other covariates. A Cox model-based approach (or duration models) will be used to study the impact of DCR attendance (or other HR services) for a certain event at a certain time (transition from injection to another mode of use, access to care). To take into account bias due to missing data and loss to follow-up, we will perform sensitivity analyses using the Heckman model, which adjusts for this potential source of statistical bias .[44] Analyses will be performed using several statistical software packages (SPSS v. 12.0, Intercooled Stata® v. 10.0 and SAS; statistical v 10.0).

Patient and Public Involvement

Although participants did not directly contribute to the design of the study or to the development of the research questions, their needs and preferences were considered throughout the process. Feedback to the participants regarding scientific results, will be organized on each study site.

DISCUSSION

The COSINUS cohort study is the first in France designed to assess the impact of DCR on HIV-HCV risk practices. It is important to note that DCR in France are seen as an additional

tool to existing NEP and OMT programs, as well as the recently education program for safer injecting practices.[25]

To date, most of the data published on the effects of DCR are from the Vancouver INSITE research team,[45] whose work greatly contributed to the preliminary design of our cohort study. However, the French and Vancouver contexts are very different in terms of substances available on the black market, access to OMT, sharing practices, sero-prevalence of HIV and HCV, and harm reduction policy. In France, an estimated 180 000 drug users are currently on OMT,[46] corresponding to an estimated coverage of 80% in urban areas.[7 25] Two thirds of individuals receiving OMT are treated with buprenorphine. This figure contrasts with other high-level income countries, where methadone is more accessible.[47] This high coverage of OMT may have played a role in decreasing long-term HCV prevalence over recent years.[2 9-11] The decrease in prevalence of HCV has been slower than that seen for HIV. This reflects the situation in other European countries such as the Netherlands and Switzerland.[48] Overall, despite high coverage of prevention and treatment services, HCV prevalence data suggest that PWID – including those receiving OMT[49] - still have a high risk of transmitting HCV.[15 50] DCR can therefore be an addition to existing HCV prevention tools by engaging difficult-to-rich PWID in OMT and safer injection practices.

Although there are differences between the French and Vancouver contexts in terms of black market substance abuse (see above), and despite some heterogeneity across and within the four different metropolitan areas where our study is being conducted,[7] similarities between the two contexts exist, specifically regarding reduced access to sterile syringes, low socioeconomic levels, and a high proportion of PWID injecting in public spaces.[7 42] COSINUS will help us understand the dynamic of HIV-HCV risk practices at a national level, both in already existing DCR and in sites providing other HR services. In France, incidence of fatal overdoses among PWID is low, making it difficult to reduce it significantly over a 12-

month period. This could be related to the national harm reduction policy implemented in the 1990s including access to OST[6] and a high level of OST coverage.[7 46]

Many prospective studies have tested, evaluated and validated DCR worldwide and have shown several benefits for public health.[20] Although public opinion on DCR is mixed and has seen shifting attitudes over time,[24 51] DCR acceptance by drug users and the drug-using community has been positive to date.[52-55] Any evaluation of DCR needs to take into account the social environment where DCR are implemented, especially social acceptability by the neighborhood.[56] DCR facilitate access to needles and provide safer places for users at high risk both to themselves and to their environment.[41 57 58] They provide hygienic and safe conditions for intravenous users and staff. They reduce morbidity and mortality associated with overdoses and with HIV and HCV infections, which is not only beneficial to PWID but increases healthcare cost-effectiveness.[59] They promote access to opioid dependence treatment[60] and to prevention interventions related to drug injecting practices.[61 62] However, few existing DCR provide education programs for safer injection[63] or have a space to inhale drugs. Moreover, data about the combined effect of DCR with other HR services are sparse. The Canadian experience has shown the importance of the evaluation process of such a controversial HR tool.[64 65] More specifically, evidence-based findings from an evaluation process of the DCR "Insite" helped to advocate against its closure, which was threatened by the Federal Government.[66] The COSINUS cohort study will not only study the impact of regularly attendance in DCR on HIV-HCV risk practices in PWID in France, but will also assess the combined effect of DCR together with other HR services (e.g., education about safer injection, access to OMT, social activities) on these practices.

Some limitations have to be acknowledged. First, all the data collected were self-reported. Although the use of self-reports may be subject to social desirability bias, studies have shown their reliability in drug-using populations.[67 68] To control any such bias, we used trained

interviewers independent of the participating harm reduction facilities. In terms of the diversity of our sample, all the PWID were recruited through easily accessible harm reduction facilities which conduct outreach actions, and which constitute the main contact that the PWID population has with the health care system. Another limitation is that, due to cost limitations of our study, we enrolled only French-speaking participants. Further studies are planned to better investigate the impact of DCRs in all the population of PWID including non French-speaking PWID that represent around 20% of people who attend DCRs.[69]

In addition to evaluating DCR and other HR services, this cohort will be used for a more global assessment of the needs of the PWID population in terms of access to treatment for addictive disorders. It will also examine the reasons for not seeking treatment, while identifying users who may benefit from it. It will help to provide a greater understanding of users' social conditions, practices, their access to prevention and treatment services, and of the role of incarceration and violence in this population often excluded from the health care system.

ETHICS AND DISSEMINATION

This study was approved by the Institutional Review Board (IRB00003888) of the French institute of medical research and health (opinion number: 14-166). All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. All participants in the survey gave their informed consent.

The results from this cohort will enable health authorities shape health and harm reduction policies according to PWID needs, as well as improve and create novel harm reduction and therapeutic interventions. All relevant results will be published in peer-reviewed international scientific journals and presented at conferences, nationally and internationally.

LIST OF ABBREVIATIONS

ADHD: Attention Deficit Hyperactivity Disorder

CEEI/IRB: Institutional Review Board

CMG: the logistics department of methodology and management

COSINUS: COhort to identify Structural and INdividual factors associated with drug Use

DCR: Drug Consumption Rooms

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

HR: Harm Reduction

INSERM: National Institute of Health and Medical Research

NEP: Needle Exchange Programs

OMT: Opiate Maintenance Treatment

PWID: People Who Inject Drugs

DECLARATIONS

Authors' contributions

Study conception and design: PC, CD, LL, MA, MJR, PR. Drafting of Manuscript: MA, MJR, LL, PR, CK, CD drafted the first version of the manuscript. MA, LL, MJR, and PR are the COSINUS cohort study PIs. SK, LBM, MG, CK, CC are the study-site interviewers and

contributed to improving the design of the study. All authors significantly contributed to the manuscript and approved the final version.

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Competing interests

The authors declare that they have nothing to disclose regarding funding or conflict of interest with respect to this manuscript.

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The impact of drug consumption rooms on risk practices and access to care in people who inject drugs in France: the COSINUS prospective cohort study protocol.

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ABSTRACT

Introduction: The high prevalence of hepatitis C and the persistence of HIV and HCV risk practices in people who inject drugs (PWID) in France underlines the need for innovative prevention interventions. The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of drug consumption rooms (DCR) on PWID outcomes. Secondary objectives are to assess how DCR a) influence other drug-related practices, such as the transition from intravenous to less risky modes of use, b) reduce drug use frequency/quantity, c) increase access to treatment for addiction and comorbidities (infectious, psychiatric and other), d) improve social conditions, and e) reduce levels of violence experienced and drug-related offenses. COSINUS will also give us the opportunity to investigate the impact of other harm reduction tools in France and their combined effect with DCR on reducing HIV-HCV risk practices. Furthermore, we will be better able to identify PWID needs.

Methods and analysis: Enrolment in this prospective multisite cohort study started in June 2016. Overall, 680 PWID in 4 different cities (Bordeaux, Marseilles, Paris and Strasbourg) will be enrolled and followed up for 12 months through face-to-face structured interviews administered by trained staff to all eligible participants at baseline (M0), 3-month (M3), 6-month (M6) and 12-month (M12) follow-up visits. These interviews gather data on socio-demographic characteristics, past and current drug and alcohol consumption, drug-use related practices, access to care and social services, experience of violence (as victims), offenses, other psychosocial issues, and perception and needs about harm reduction interventions and services. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual and structural factors, including DCR attendance and exposure to other harm reduction services, on the main outcome (HIV-HCV risk practices).

Ethics and dissemination: This study was reviewed and approved by the institutional review

board of the French institute of medical research and health (opinion number: 14-166). The findings of this cohort study will help to assess the impact of DCR on HIV-HCV risk practices and other psychosocial outcomes and trajectories. Moreover, they will enable health authorities to shape health and harm reduction policies according to PWID needs. Finally, they will also help to improve current harm reduction and therapeutic interventions and to create novel ones.

Strengths and limitations of this study

- This is the first multisite harm reduction focused cohort of PWID conducted in France.
- The study's findings will help to assess the impact of DCR and other harm reduction services on HIV-HCV risk practices in PWID.
- The findings will also assess the needs of PWID in France by providing a greater understanding of their social conditions, access to prevention and treatment services.
- Non French-speaking PWID are excluded from the cohort so their specific needs are not assessed, they may represent up to 20% of people who attend harm reduction facilities in some sites.

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INTRODUCTION

Rationale

In France, as elsewhere, people who inject drugs (PWID) faced a dramatic HIV epidemic in the 1990s. In response, the French government's harm reduction policy - which first developed programs for access to sterile injection material in 1987 - extended access in 1994 to include syringe vending machines and the sale of ready-to-use injection kits (Steribox®) in community pharmacies[1], as well as new state-funded needle exchange programs (NEP)[2]. These public health initiatives were concomitant with opiate maintenance treatment (OMT) programs with methadone (available since 1994) and buprenorphine (available since 1995)[3 4] and highly active antiretroviral therapy (HAART) for HIV-infected individuals.[5] HIV prevalence in PWID dramatically decreased from 40% to 20% in 14 years from 1988 to 2002,[2 6] with a prevalence in 2011 of 10%.[7] An estimated 77% to 85% of opioid-dependent individuals in France are currently treated with OMT.[7]

Despite this progress, and just as in many countries where OMT and NEP are available,[8] the impact of this harm reduction policy on the hepatitis C virus (HCV) epidemic in France has not been as great as that for HIV.[2 9-12] This is because this policy was adopted when HCV prevalence was already too high to be rapidly controlled. In 2011, HCV infection prevalence in the country was 64% among many PWID.[7] HCV incidence was also very high, between 11% and 22%,[13] compared with neighboring countries such as the Netherlands.[14] The delay in implementing an efficient harm reduction policy may explain the persistent high national prevalence of HCV in PWID today.[15] Besides HCV and HIV infections, numerous other physical problems can result from injecting drug use, including soft tissue infections,[16 17] cardiovascular and pulmonary complications,[18] and bacterial and fungal infections.[19] In addition, research on existing drug consumption rooms (DCR) showed that they improve access to primary health care and improve safer injection conditions.[20] By attracting the most

marginalized PWID,[21] they also reduce the level of public injection and so the number of used syringes has dropped in public spaces.[22] Finally, it has also been shown that DCR are effective in reducing fatal overdoses.[23]

Despite the French health authorities' reluctance to open DCR for many years, mostly because of the country's persistent repressive policy toward drug use and general negative public opinion,[24] their success in other countries encouraged the French government to reconsider DCR as a possible additional harm reduction (HR) tool. Two DCR, in Paris and Strasbourg, were opened in 2016 as part of a 6-year experiment granted on the condition that the health and social impact of the facilities would be rigorously evaluated. These two DCR accept all PWID 18 years or older and provide the following services: the possibility to administer drugs by injection (or inhalation in some cases, only for PWID), access to social, medical and psychiatric consultations, the provision of sterile equipment, the collection and disposal of used injection equipment, primary care, harm reduction counselling and HCV, HBV and HIV testing. In this perspective, the COSINUS cohort (COhort to identify Structural and INdividual factors associated with drug Use) was set up in 2016 to prospectively evaluate the impact of DCR on the reduction of risk-taking behaviors in PWID.

The main objective of this article is to describe the design of the COSINUS cohort study and outline which issues it will explore to evaluate the impact of the DCR on PWID outcomes.

Research objectives and hypothesis

The main objective of COSINUS is to evaluate the impact of regular DCR use on HIV and HCV risk practices. The hypothesis is that PWID with regular access to DCR have fewer practices at risk of HCV and HIV transmission than PWID with no access. It will also investigate the impact of regular DCR use on access to care. Furthermore, data from COSINUS will be used to study the impact of other individual (e.g., age, gender, ethnicity, housing) and structural (e.g., exposure to social services, harm reduction services including education about

safer injection)[25] factors on several outcomes (other risk practices, criminality, current drug use, negative life events, etc.). More specifically, it will help provide a greater understanding of the combined effect of different harm reduction services on PWID health and risk practices.

METHODS AND ANALYSIS

Study design

This prospective, multicenter cohort study, which started in June 2016, will enroll a total of 680 PWID by October 2017 in 4 different French cities with different geographical and health characteristics (Bordeaux, Marseilles, Paris and Strasbourg). The study design and data collection tools were partly inspired by an evaluation of the Vancouver Downtown Eastside DCR (Insite)[26] and the Vancouver Injection Drug User Study.[27] Individual follow-up will last 12 months. PWID in the DCR in Paris and Strasbourg constitute the "treatment" group (hereafter "DCR-exposed"), while PWID already enrolled in harm reduction programs constitute the "control" group (hereafter "DCR-unexposed"). These four cities were chosen because they were all candidates for the opening of DCR when the law permitting experimentation with DCR passed (Public Health Law from January 2016). Data collection consists in face-to-face interviews (each lasting approximately 20 to 35 minutes) administered by a trained interviewer at baseline, 3 months, 6 months and 12 months. Data collection is coordinated by the logistics department of methodology and management (CMG) of ORS PACA – INSERM-IRD UMR1252 (SESSTIM) in Marseilles, under the supervision of the cohort's four PIs (Marc Auriacombe for Bordeaux, Perrine Roux for Marseilles, Marie Jauffret-Roustide for Paris and Laurence Lalanne-Tongio for Strasbourg), and is managed by each site-investigator. Participants are compensated for their time with 10 euros worth of service vouchers after each of the 4 interviews. The study protocol was approved by the Institutional Review Board (IRB00003888) of the French institute of medical research and health (opinion

number: 14-166).

Participants

Subjects were eligible if they self-reported injecting illicit drugs except cannabis (heroin, cocaine / crack, amphetamines, ecstasy), and/or prescription drugs (methylphenidate, buprenorphine, benzodiazepines, morphine sulphate, oxycodone, methadone) at least once during the previous month. Participants must be over 18 years old and French-speaking. There are no specific exclusion criteria, except if the PWID does not fulfil the inclusion criteria, for example non French-speaking PWID are excluded. Participants must also provide informed consent to participate in the study. They were recruited mainly in the DCR (in the cities where there is one) and in other harm reduction facilities that currently outreach to PWID likely to attend a DCR if available in each city. This mix of recruitment sites was chosen in order to be able to compare PWID between cities. To avoid duplicate enrollment, the month, year and place of birth are recorded for each participant.

Measures

The evaluation of DCR is based on the following main outcome: the proportion of participants reporting at least one injection-related HIV-HCV risk practice (sharing of syringes/needles, sharing of other injecting paraphernalia (filter, swab, water, cup, etc.)) in the previous month.

The other variables that will be collected are: sociodemographic characteristics (gender, age, housing, employment, living in a couple, ethnicity, parenthood, social allowances, country of birth); history of drug use (age at first drug use, first injection and related context); current drug and alcohol use (type, frequency, quantity of drugs used, context of drug use, use disorder diagnostic criteria, craving); overdoses and suicide risk; drug use-related HIV-HCV risk practices (injecting, snorting, smoking, sharing and reusing injecting equipment); addiction treatments; DCR attendance; health conditions and access to care and prevention (type and

frequency of care, satisfaction with care, HIV, HCV and HBV screening and self-reported HIV and HCV status, education in injection, other HR services); criminality (illegal activities and experience of prison); negative life events (violence, sexual assault, loss of a relative, etc.); psychosocial assessment (anxiety, ADHD, PTSD, etc.); injection initiation (experience and context); cognitive assessments (GONOGO, mnesic test); sexual health (sexual risk practices, contraception); discrimination and life course (parents, childhood).

This interview questionnaire includes the full version or some items from several already validated questionnaires as follows: i) the Blood-Borne Virus Transmission Risk Assessment (BBV-TRAQ)[28] to evaluate the risk practice; ii) a section of the Addiction Severity Index, which is a multi-dimensional questionnaire which measures drug use based on participants' self-report;[29 30] iii) the Alcohol Use Disorders Identification Test (AUDIT-C) questionnaire to measure alcohol consumption;[31] iv) a set of questions from the PRIMER study to examine injection initiation;[32] v) three validated questionnaires to measure psychiatric outcomes: the 25-item Wender Utah Rating Scale (WURS) for attention-deficit/hyperactivity disorder screening,[33] the Beck Anxiety Inventory to measure anxiety[34] and the Post-traumatic stress event questionnaire;[35 36] vi) finally, two questionnaires measure participants' cognitive ability: the go-no go task[37] and the mnesic test.[38]

Table 1 displays the schedule for each assessment.

Table 1. Summary of data collection at each follow-up visit

	M0	M3	M6	M12

Socio-demographic characteristics	x	x	x	x
Socio-economic characteristics	x	x	x	x
History of substance use	x			
Current drug use	x	x	x	x
Alcohol and tobacco use	x	x	x	x
Overdoses and suicidal risk	x		x	x
Drug use-related HIV-HCV risk practices	x	x	x	x
Addiction treatment	x	x	x	x
Health conditions and access to care	x		x	x
Screening for HIV and HCV	x		x	x
Criminality	x	x	x	x
Prison experience	x		x	x
Negative life events	x			x
Initiation injection	x		x	x
HR services user satisfaction	x		x	x
Sexual health		x		
Other practices at risk of dermal contamination		x		
DCR attendance and other services	x	x	x	x
Life course		x		
Attention Deficit Hyperactivity Disorder – ADHD		x		

Anxiety: Beck anxiety inventory			x	
Post-traumatic stress disorder			x	
Discrimination		x		
GONOGO Task		x		x
Mnemonic Test		x		x

Sample size

The main outcome is the comparison of the percentage of PWID reporting at least one injection-related HIV-HCV risk practice during the previous month between the DCR-exposed and DCR-unexposed groups. The sample size needed was calculated according to this main outcome. Many studies from different countries with DCR have shown that between 30%[39 40] and 60%[41] of users regularly attend them (at least once a week). In the French context, the proportion of PWID reporting at least one injection-related HIV-HCV risk practice varies according to the context and the characteristics of PWID recruited in different studies, from 25%[25] to 50%[42]. We hypothesize 33% of regular (i.e., at least once a week) DCR attending participants will report at least one of these events. Supposing that one third of participants will regularly attend DCR, with an alpha=5 % and a power of 80 %, we need a total of 131 participants in each group. Given an expected attrition rate of 40% after 12 months of follow-up,[43] the sample size is therefore 680 (Paris=250, Marseilles=200, Bordeaux=150, Strasbourg=80).

Statistical methods

COSINUS was developed to show the impact of DCR on HIV-HCV risk practices. Longitudinal data analysis will use a mixed logistic model to assess the impact of individual factors (sociodemographic, behavioral and cognitive data) and structural factors, including

DCR attendance and exposure to other HR services (access to OMT, social services, education to safer injection, etc.), on the main outcome (reporting at least one injection-related HIV-HCV risk practice during the previous month). Data analysis will be carried out with logistic regression models for qualitative data in two ways, multinomial regression for qualitative data of more than two terms, or linear regression for continuous data. In addition, to study the impact of the combined effect of different services (DCR, education about safe injection, other HR services) on the main outcome, we will use mixed-model regression analysis by adjusting for these different structural factors and other covariates. A Cox model-based approach (or duration models) will be used to study the impact of DCR attendance (or other HR services) for a certain event at a certain time (transition from injection to another mode of use, access to care). To take into account bias due to missing data and loss to follow-up, we will perform sensitivity analyses using the Heckman model, which adjusts for this potential source of statistical bias .[44] Analyses will be performed using several statistical software packages (SPSS v. 12.0, Intercooled Stata® v. 10.0 and SAS; statistical v 10.0).

Patient and Public Involvement

Although participants did not directly contribute to the design of the study or to the development of the research questions, their needs and preferences were considered throughout the process. Feedback to the participants regarding scientific results, will be organized on each study site.

DISCUSSION

The COSINUS cohort study is the first in France designed to assess the impact of DCR on HIV-HCV risk practices. It is important to note that DCR in France are seen as an additional tool to existing NEP and OMT programs, as well as the recently education program for safer injecting practices.[25]

To date, most of the data published on the effects of DCR are from the Vancouver INSITE research team,[45] whose work greatly contributed to the preliminary design of our cohort study. However, the French and Vancouver contexts are very different in terms of substances available on the black market, access to OMT, sharing practices, sero-prevalence of HIV and HCV, and harm reduction policy. In France, an estimated 180 000 drug users are currently on OMT,[46] corresponding to an estimated coverage of 80% in urban areas.[7 25] Two thirds of individuals receiving OMT are treated with buprenorphine. This figure contrasts with other high-level income countries, where methadone is more accessible.[47] This high coverage of OMT may have played a role in decreasing long-term HCV prevalence over recent years.[2 9-11] The decrease in prevalence of HCV has been slower than that seen for HIV. This reflects the situation in other European countries such as the Netherlands and Switzerland.[48] Overall, despite high coverage of prevention and treatment services, HCV prevalence data suggest that PWID – including those receiving OMT[49] - still have a high risk of transmitting HCV.[15 50] DCR can therefore be an addition to existing HCV prevention tools by engaging difficult-to-rich PWID in OMT and safer injection practices.

Although there are differences between the French and Vancouver contexts in terms of black market substance abuse (see above), and despite some heterogeneity across and within the four different metropolitan areas where our study is being conducted,[7] similarities between the two contexts exist, specifically regarding reduced access to sterile syringes, low socioeconomic levels, and a high proportion of PWID injecting in public spaces.[7 42] COSINUS will help us understand the dynamic of HIV-HCV risk practices at a national level, both in already existing DCR and in sites providing other HR services. In France, incidence of fatal overdoses among PWID is low, making it difficult to reduce it significantly over a 12-month period. This could be related to the national harm reduction policy implemented in the 1990s including access to OMT[6] and a high level of OMT coverage.[7 46]

Many prospective studies have tested, evaluated and validated DCR worldwide and have shown several benefits for public health.[20] Although public opinion on DCR is mixed and has seen shifting attitudes over time,[24 51] DCR acceptance by drug users and the drug-using community has been positive to date.[52-55] Any evaluation of DCR needs to take into account the social environment where DCR are implemented, especially social acceptability by the neighborhood.[56] DCR facilitate access to needles and provide safer places for users at high risk both to themselves and to their environment.[41 57 58] They provide hygienic and safe conditions for intravenous users and staff. They reduce morbidity and mortality associated with overdoses and with HIV and HCV infections, which is not only beneficial to PWID but increases healthcare cost-effectiveness.[59] They promote access to opioid dependence treatment[60] and to prevention interventions related to drug injecting practices.[61 62] However, few existing DCR provide education programs for safer injection[63] or have a space to inhale drugs. Moreover, data about the combined effect of DCR with other HR services are sparse. The Canadian experience has shown the importance of the evaluation process of such a controversial HR tool.[64 65] More specifically, evidence-based findings from an evaluation process of the DCR "Insite" helped to advocate against its closure, which was threatened by the Federal Government.[66] The COSINUS cohort study will not only study the impact of regularly attendance in DCR on HIV-HCV risk practices in PWID in France, but will also assess the combined effect of DCR together with other HR services (e.g., education about safer injection, access to OMT, social activities) on these practices.

Some limitations have to be acknowledged. First, all the data collected were self-reported. Although the use of self-reports may be subject to social desirability bias, studies have shown their reliability in drug-using populations.[67 68] To control any such bias, we used trained interviewers independent of the participating harm reduction facilities. In terms of the diversity of our sample, all the PWID were recruited through easily accessible harm reduction facilities

which conduct outreach actions, and which constitute the main contact that the PWID population has with the health care system. Another limitation is that, due to cost limitations of our study, we enrolled only French-speaking participants. Further studies are planned to better investigate the impact of DCRs in all the population of PWID including non French-speaking PWID that represent around 20% of people who attend DCRs.[69]

In addition to evaluating DCR and other HR services, this cohort will be used for a more global assessment of the needs of the PWID population in terms of access to treatment for addictive disorders. It will also examine the reasons for not seeking treatment, while identifying users who may benefit from it. It will help to provide a greater understanding of users' social conditions, practices, their access to prevention and treatment services, and of the role of incarceration and violence in this population often excluded from the health care system.

ETHICS AND DISSEMINATION

This study was approved by the Institutional Review Board (IRB00003888) of the French institute of medical research and health (opinion number: 14-166). All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. All participants in the survey gave their informed consent.

The results from this cohort will enable health authorities shape health and harm reduction policies according to PWID needs, as well as improve and create novel harm reduction and therapeutic interventions. All relevant results will be published in peer-reviewed international scientific journals and presented at conferences, nationally and internationally.

LIST OF ABBREVIATIONS

ADHD: Attention Deficit Hyperactivity Disorder

CEEI/IRB: Institutional Review Board

CMG: the logistics department of methodology and management

COSINUS: COhort to identify Structural and INdividual factors associated with drug Use

DCR: Drug Consumption Rooms

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

HR: Harm Reduction

INSERM: National Institute of Health and Medical Research

NEP: Needle Exchange Programs

OMT: Opiate Maintenance Treatment

PWID: People Who Inject Drugs

DECLARATIONS

Authors' contributions

Study conception and design: PC, CD, LL, MA, MJR, PR. Drafting of Manuscript: MA, MJR, LL, PR, CK, CD drafted the first version of the manuscript. MA, LL, MJR, and PR are the COSINUS cohort study PIs. SK, LBM, MG, CK, CC are the study-site interviewers and contributed to improving the design of the study. All authors significantly contributed to the manuscript and approved the final version.

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Competing interests

The authors declare that they have nothing to disclose regarding funding or conflict of interest with respect to this manuscript.

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Members of the Cosinus study group has contributed to the design and/or the monitoring of the cohort: Auriacombe M, Bertoia G, Briand Madrid L, Carrieri MP, Célérier I, Chauvin C, Danion JM, Denis C, Grelli N, Gutowski M, Hamelin N, Jauffret-Roustide M, Kervran C, Kirchherr S, Lalanne L, Le Breton M, Roux P, Vilotitch A.

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