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Individual-level needle and syringe coverage amongst people who inject drugs

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Table of contents

Table of figures

Abbreviations and acronyms

Aboriginal and Torres Strait Islander: ATSI

Antiretroviral Therapy: ART

Blood-Borne Virus: BBV/s

Fixed-site Needle and Syringe Program: Fixed-site NSP/s

Hepatitis B Virus: HBV

Hepatitis C Virus: HCV

Human Immunodeficiency Virus: HIV

Injecting Drug Use: IDU

Joint United Nations Programme on HIV/AIDS: UNAIDS

Low and Middle Income Countries: LMIC/s

Melbourne Injecting Drug User Cohort Study: MIX Study

Opioid Substitution Therapy: OST

People Who Inject Drugs: PWID/s

Safe Injecting Facility: SIF/s

Syringe Vending Machine: SVM/s

United Nations Office on Drugs and Crime: UNODC

World Health Organisation: WHO

Abstract

People who inject drugs (PWID) experience many deleterious health outcomes, such as blood-borne virus (BBV) infection via the sharing of unsterile needles and syringes (hereafter "syringe/s"). Needle and syringe programs distribute sterile injecting equipment to PWID to reduce BBV transmission. The evidence base for needle and syringe programs is strong, but there remain barriers to access.

"Coverage" is a term used in program evaluation, referring to the extent to which a service reaches its target population. Traditionally, syringe distribution coverage is measured at the population-level. However, population-level measurements have limitations: they use uncertain population estimates, they mask the most at-risk individuals, and they homogenise the levels of need and risk amongst PWID. In response to these limitations, syringe coverage measurements at the individual-level have been proposed, most prominently by Bluthenthal et al. (2007). Individual-level syringe coverage measurement calculates the percentage of a person's injecting episodes that are "covered" by a sterile syringe. It aims to account for the variability between people, assisting in targeting interventions. However, there remain knowledge gaps with the individual-level syringe coverage measurement. The longitudinal patterns of individual-level syringe coverage haven't been explored, additional refinement of the measure is needed, and, the measures use has largely been restricted to high-income settings, limiting generalisability of findings.

The aims of this thesis were to: 1) explore individual-level syringe coverage longitudinally, 2) identify associations with insufficient individual-level syringe coverage as targets for intervention, 3) develop recommendations for increasing individual-level syringe coverage, 4) improve the methodology for measuring individual-level syringe coverage, and 5) measure individual-level syringe coverage in a low and middle income (LMIC) setting.

In Papers One to Three, I explored individual-level syringe coverage longitudinally using data from a prospective cohort of regular PWID in Melbourne, Australia. In Paper One, I categorised participants according to their temporal patterns of individual-level

syringe coverage, showing that 45% of the sample fluctuated between states of sufficient and insufficient individual-level syringe coverage, potentially as the result of time-varying factors. Paper Two explored these factors, finding that changes in methamphetamine injection, hepatitis C virus-positivity, initiating opioid substitution therapy, and the common use of fixed-site needle and syringe programs either positively or negatively predicted changes in individual-level syringe coverage levels. Paper Three showed that changes to injecting frequency had twice the effect upon individual-level syringe coverage compared to other behaviours mediating this coverage (such as syringe acquisition), thereby prioritising harm reduction efforts. Papers Three and Four sought to improve the individual-level syringe coverage measure, assisting in the eventual creation of a standardised tool for international harm reduction monitoring. Finally, Papers Five and Six examined harm reduction in LMICs. Paper Five explored the implementation of harm reduction in LMICs and made recommendations moving forward. Paper Six measured individual-level syringe coverage in Myanmar. The study showed substantial differences in individual-level syringe coverage between recruitment sites, providing information for harm reduction services for future planning and monitoring.

This thesis highlights the important role individual-level syringe coverage measurement can have in international harm reduction efforts. Using the measure, harm reduction services can identify those PWID most in need of intervention and target interventions accordingly.

Publications during enrolment

Thesis including published works declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes five original papers published in peer reviewed journals and one submitted publication. The core theme of the thesis is individual-level needle and syringe coverage amongst people who inject drugs. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the School of Public Health and Preventive Medicine under the supervision of Prof. Paul Dietze and Dr. Campbell Aitken.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of *Chapters two to five,* my contribution to the work involved the following:

Thesis Chapter	**Publication Title**	**Status** *(published, in press, accepted or returned for revision, submitted)*	**Nature and % of student contribution**	**Co-author name(s) Nature and % of Co-author's contribution***	**Co-author(s), Monash student Y/N***
Chapter Two	Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis	Published	70%, Study design, data collection, data analysis and interpretation, manuscript preparation and revision	1) Nick Scott, data analysis, manuscript revision, 10% 2) Campbell Aitken, study design, manuscript revision, 10% 3) Paul Dietze, study design, manuscript revision, 10%	No No No
Chapter Three	Longitudinal analysis of change in individual-level needle and syringe coverage amongst people who	Published	70%, Study design, data collection, data analysis and interpretation, manuscript	1) Nick Scott, data analysis, manuscript revision, 10% 2) Campbell Aitken, study design, manuscript revision, 10%	No No

	inject drugs in Melbourne, Australia		preparation and revision	3) Paul Dietze, study design, manuscript revision, 10%	No
Chapter Three	Assessing individual-level needle and syringe coverage parameters and the measurement of coverage in Melbourne, Australia: methods and impacts	Published	70%, Study design, data collection, data analysis and interpretation, manuscript preparation and revision	1) Nick Scott, data analysis, manuscript revision, 10% 2) Campbell Aitken, study design, manuscript revision, 10% 3) Paul Dietze, study design, manuscript revision, 10%	No No No
Chapter Four	How does the use of multiple needles/syringes per injecting episode impact on the measurement of individual-level needle and syringe program coverage?	Published	60%, Study design, data collection, data analysis and interpretation, manuscript preparation and revision	1) Angus McCormack, data collection, manuscript revision, 5% 2) Shelley Cogger, data collection, study design manuscript revision, 10% 3) Campbell Aitken, manuscript revision, 5% 4) Lucinda Burns, manuscript revision, 2.5% 5) Raimondo Bruno, manuscript revision, 5% 6) Jenny Stafford, manuscript revision, 2.5% 7) Kerryn Butler, manuscript revision, 2.5% 8) Courtney Breen, manuscript revision, 2.5% 9) Paul Dietze, manuscript revision, 5%	No No No No No No No No No
Chapter Five	Injecting drug use in low and middle-income countries: Opportunities to improve care and prevent harm	Published	60%, review planning and design, manuscript preparation and revision	1) Mark Stoove, concept, manuscript revision, 10% 2) Joseph Doyle, concept, manuscript revision, 10% 3) Paul Dietze, concept, manuscript revision, 10% 4) Margaret Hellard concept, manuscript revision, 10%	No No No No
Chapter Five	Measuring individual-level needle and syringe coverage among people who inject drugs in	Returned for revision	60%, Study design, data analysis and interpretation, manuscript preparation and	1) Soe Moe Aung, study design, data collection, manuscript revision, 5% 2) Naanki Pasricha, study design, manuscript revision, 5% 3) Thu Wun, data	No No

	Myanmar		revision	collection, manuscript revision, 5% 4) Soe Khaing Linn, data collection, manuscript revision, 5% 5) Nay Lin, data collection, manuscript revision, 5% 6) Campbell Aitken, study design, manuscript revision, 5% 7) Chad Hughes, study design, manuscript revision, 5% 8) Paul Dietze, study design, manuscript revision, 5%	No No No No No No

I have not renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student signature: [redacted] **Date:** 28/12/2017

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor signature: [redacted] **Date:** 28/12/2017

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Outcomes during candidature

A list of publications and oral presentations during the PhD candidature is presented below. Asterisks identify publications included as thesis chapters; hashes identify publications included as appendices.

Peer-reviewed publications

1. * **O'Keefe D.,** Scott N., Aitken N., Dietze P. (2016) Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis. *BMC Health Services Research* 16:411 (epub)
2. # **O'Keefe D.,** Horyniak D., Dietze P. (2016) From initiating injecting drug use to regular injecting: Retrospective survival analysis of injecting progression within a sample of people who inject drugs regularly. *Drug and Alcohol Dependence* 158: 177-180
3. *** O'Keefe D.,** Scott N., Aitken C., Dietze P. (2017) Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia. *Drug and Alcohol Dependence* 176: 7-13
4. * **O'Keefe D.,** McCormack A., Cogger S., Aitken C., Burns L., Bruno R., Stafford J., Butler K., Breen C., Dietze P. (2017) How does the use of multiple needles/syringes per injecting episode impact on the measurement of individual level needle and syringe program coverage? *International Journal of Drug Policy* 46: 99-106
5. # **O'Keefe D.,** Bowring A., Aitken C., Dietze P. (2017) The association between intentional overdose and same-sex sexual intercourse in a cohort of people who inject drugs in Melbourne, Australia. *Substance Use and Misuse,* epub 29 Sept 2017
6. *** O'Keefe, D.,** Stoove, M., Doyle, J., Dietze, P., Hellard, M. (2017) Injecting drug use in low and middle income countries: opportunities to improve care and prevent harm. *Journal of Viral Hepatitis* 24(9): 714-724
7. *** O'Keefe D.,** Scott N., Aitken C., Dietze P. (2017) Assessing individual-level

needle and syringe coverage parameters and the measurement of coverage in Melbourne, Australia: methods and impacts. *Journal of Public Health*, epub 22 Dec 2017

8. # Peach E., Cogger S., Byron K., Francis P., **O'Keefe D.,** Higgs P., Stoove M., Elmore K., Dietze P., Hellard M. (2017) Blood-borne virus transmission in an urban, culturally diverse neighbourhood: results from a cross-sectional bio-behavioural survey using innovative outreach methods in a hard-to-reach population. *Sexual Health,* epub 12 Oct 2017

Submitted manuscripts

1. * **O'Keefe D.,** Soe Moe Aung, Pasricha N., Thu Wun, Soe Khaing Linn, Nay Lin, Aitken C., Hughes C., Dietze P. Measuring individual-level needle and syringe coverage among people who inject drugs in Myanmar. *International Journal of Drug Policy* (under review)

Conference presentations – oral

1. **O'Keefe D.,** Dietze P. The progression from initiating injecting drug use to regular injecting: comparisons of time difference. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference,* November 2014, Adelaide, Australia
2. **O'Keefe D.,** Aitken C., Dietze P. Longitudinal analysis of individual harm reduction coverage in an Australian cohort of people who inject drugs. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference,* November 2015, Perth, Australia
3. **O'Keefe D.,** Aitken C., Dietze P. Longitudinal analysis of individual harm reduction coverage in an Australian cohort of people who inject drugs. *International Harm Reduction Conference (IHRC),* October 2015, Kuala Lumpur, Malaysia
4. **O'Keefe D.,** McCormack A., Cogger S., Aitken C., Burns L., Bruno R., Stafford J., Butler K., Breen C., Dietze P. Use of multiple needles/syringes per injecting episode: potential parameter inclusion within measures of coverage.

Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference, November 2016, Sydney, Australia

5. **O'Keefe D.,** Scott N., Aitken C., Dietze P. Longitudinal analysis of change in individual-levels of needle and syringe coverage in a cohort of people who inject drugs. *World Congress of Public Health*, April 2017, Melbourne, Australia.
6. **O'Keefe D.,** Aitken C., Dietze P. The relationship between needle and syringe program operating hours and time of drug use: effects on individual-level needle and syringe coverage. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference,* November 2017, Melbourne, Australia

Conference presentations – posters

1. **O'Keefe D.,** Bowring A., Aitken C., Dietze P. The association between intentional overdose and same-sex sexual intercourse amongst a cohort of PWID in Melbourne, Australia. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference*, November 2016, Sydney, Australia.
2. Peach E., Francis P., Cogger S., Morris M., Stoove M., Hellard M., Elmore K., **O'Keefe D.,** Higgs P., Dietze P. Relational and contingent risk and harm reduction: blood-borne virus prevention and care in an urban, culturally diverse neighbourhood. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference,* November 2015, Perth, Australia.
3. Peach E., Francis P., Cogger S., Morris M., Stoove M., Hellard M., Elmore K., **O'Keefe D.,** Higgs P., Dietze P. Hazardous alcohol use and concomitant blood-borne virus infection in a local urban population of people who inject drugs: Implications for approaches to harm reduction. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference*, November 2015, Perth, Australia.
4. **O'Keefe D.,** Nay Lin, Myo Thant, Zaw Min Oo, Hla Htay, Than Win, Hughes C., Pasricha N., Soe Moe Aung, Dietze P. Measuring individual-level needle and syringe coverage among people who inject drugs (PWID) in Myanmar: risk predictors and outcomes. *Australasian Professional Society on Alcohol and other Drugs (APSAD) Conference*, November 2017, Melbourne, Australia.

Invited presentations

1. **O'Keefe, D.,** Aitken, C., Dietze, P. Syringe coverage: definitions and outcomes. *Centre for Research Excellence into Injecting Drug Use (CREIDU) research update*, August 2015, Melbourne, Australia.
2. **O'Keefe, D.** Needle and syringe coverage amongst people who inject drugs: national and international experiences. *Monash University, Masters of Public Health (Drugs in Society course)*, April 2017, Melbourne Australia
3. **O'Keefe, D.** Harm reduction in Australia: policies and programs. *Australian Awards Fellowship*, November 2017, Melbourne Australia

Awards

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Chapter One: Introduction

The concept of "coverage", as a means of evaluating program effectiveness, can be applied to any public health intervention. Coverage has been defined as "the proportion of the population at risk reached by an intervention, ideally with sufficient intensity to have probable impact" (1). However, the conceptualisation and measurement of coverage is not uniform. The methodology required to generate coverage estimates is specific to the intervention being measured and the public health domain in question.

The coverage of needle and syringe programs, which provide sterile injecting equipment to people who inject drugs (PWID) (2), can be measured at both the population level and the individual level (3). Needle and syringe programs service a heterogeneous population (4), with differing risk profiles and barriers to serve access. Population-level measures are not sensitive to this heterogeneity in people, behaviours (such as injecting frequencies) or the contexts in which drug use occurs; hence the need for measures that account for individual-level differences (3). Importantly, needle and syringe (hereafter "syringe/s") coverage measurement at the individual level allows for exploring the associations (e.g. demographics, drug use characteristics) of insufficient individual-level syringe coverage to identify individuals susceptible to low syringe coverage and assist in the creation of targeted interventions.

Despite the value of individual-level measures for evaluating the effectiveness of needle and syringe programs, their construction and utilisation is a relatively recent advance. The most prominent method of measuring individual-level syringe coverage was first proposed by Bluthenthal et al. in 2007 (5). Since then, the method has been used in multiple studies, though conducted in only a few countries (nearly all high-income), until now all using a cross-sectional design. Furthermore, other individual-level syringe coverage measurements have varied in terms of their method of calculation, hampering comparability of findings across studies. If individual-level syringe coverage measures are to be used as an evaluative tool (as population-level measures currently are (6, 7)), a specific, consistent methodology needs to be developed and agreed upon. The absence of longitudinal individual-level syringe coverage findings, research in diverse international contexts and an established calculation methodology are key gaps in the

literature. In response to these gaps in methodology and knowledge, I studied how individual-level syringe coverage changes over time and the drivers of this change. I also explored ways of refining individual-level syringe coverage measurement, and broadened the understanding of syringe coverage by measuring it in a setting without previous individual-level syringe coverage estimates; Myanmar.

The first chapter of this thesis provides an introduction to the relevant literature. First, I present the epidemiology of, and public health response to, injecting drug use (IDU), both globally and in Australia. This is followed by a summary of syringe coverage – its conceptualisation, measurement and the strengths and deficiencies of this measurement. I compare syringe coverage measurement at the population level and individual level. I discuss the development and benefits of individual-level syringe coverage measurement, including findings from past research using the measure. Finally, I provide an overview of the thesis and present the rationale and aims of my research.

1.1 Background and rationale

1.1.1 Epidemiology of injecting drug use

There are an estimated 15.6 million PWID globally, with 179 of the world's 206 countries and territories reporting evidence of IDU (8, 9). IDU carries the risk of attendant harms, such as transmission of blood-borne viruses (BBVs) (10-13) injection-related morbidity (such as bacterial infections due to non-sterile injecting practices) (14, 15), and mortality due to both drug overdose (16, 17) and other causes exacerbated by IDU (such as BBV-related mortality) (18, 19). PWID are highly stigmatised and marginalised and experience greater levels of unemployment (20), homelessness (21), mental illness (22), and involvement with criminal justice systems (23), compared to non-IDU populations.

Public health interventions that target the deleterious effects of IDU are available, but coverage is inadequate, contributing to these effects (8, 24). In many countries, IDU is the dominant means of transmission of human immunodeficiency virus (HIV) and viral

hepatitis (25, 26) with the sharing of unsterile syringes, needles and other injecting equipment the key vector in transmission (27-30). Globally, it is estimated that 2.8 million (17.8%) PWID are HIV-positive, 8.2 million (52.3%) are hepatitis C virus (HCV) antibody positive (a measure of exposure, rather than current infection) and 1.4 million (9%) are hepatitis B virus (HBV) positive (9).

1.1.2 The risk environment of injecting drug use

The receptive use of another person's unsterile and potentially BBV-contaminated syringe ("receptive syringe sharing") remains common amongst PWID, despite the establishment of effective interventions to reduce the practice (29, 31, 32). The persistence of syringe sharing, though often a result of the simple absence or inaccessibility of sterile injecting equipment, is motivated by more than just access to equipment (29). Instead, the sharing of syringes may be the result of various individual choices, interpersonal social functions, or environmental factors that promote this risk behaviour (29, 33, 34).

Though without the same level of risk as receptive syringe sharing, syringe re-use (re-using one's own unsterile syringes) carries its own risks, such as bacterial infection (14, 35) and vein damage due to needle blunting (36). Like receptive syringe sharing, syringe re-use can be a marker of inadequate syringe coverage (37).

The context and conditions in which IDU occurs influences levels of associated risk (38, 39). Conceptualisations of health and health interventions have emphasised the importance of the environment in the production and reproduction of harm (38). Broadly speaking, the risk environment can be defined as "the space – whether social or physical – in which a variety of factors interact to increase the chances of drug-related harm" (38) (p.88). Both micro- and macro-environmental factors influence the production of risks associated with IDU (39). These factors can extend as far as national conflict and war, or narrow down to the interpersonal dynamics within PWID peer-groups (39). For example, different drug types increase the risk of specific harms (e.g. heroin and overdose; cocaine and high-frequency injecting) and the dominance of certain drug types in particular geographic areas – potentially as a result of globalised drug distribution routes (39) – confer localised risks for harm (40). PWID recently

released from prison are at substantially increased risk of fatal drug overdose (41, 42), whilst PWID experiencing homelessness – potentially as a result of macro-environmental factors – often inject in unsterile, public locations, performing rushed injections (43), placing them at increased risk of vein damage and infection (44). Additionally, the perception of risk is determined in-part by social norms, rules and values (38), meaning that PWID may have subjective perceptions of risk that are reinforced by their peer groups. The intersection of these mediating factors within the environment in which IDU occurs means that the safest methods of IDU, with the lowest risk for BBV transmission, overdose, and other related hazards, may be unachievable sometimes, or all of the time, for many PWID.

The focus of intervention around IDU should include all elements of the risk environment. Risk environments need to be understood to determine the best way to create "enabling environments" for the reduction of drug-related harm (38). Access to sterile syringes and other injecting equipment is of critical importance within the IDU risk environment but many barriers limit and even prevent access, such as service-level policy decisions, service opening hours or geographical service access. Many of these are beyond the control of individual PWID, and they can consequently serve to lower syringe coverage at both the population and individual level.

1.1.3 Harm reduction

Many of the public health interventions that service PWID and non-injecting drug users are categorised under the umbrella term "harm reduction". Harm reduction contends that drug use is an ineradicable health and social behaviour, the harms of which should be minimised as much as possible (45). Prominent harm reduction interventions for PWID are needle and syringe programs and opioid substitution therapy (OST: the receipt of opioid agonist medication, such as methadone or buprenorphine, as a replacement for illicitly procured opioids). Both have been shown to be efficacious and cost-effective means of reducing the harms associated with IDU (46-51), with no evidence of increasing IDU levels amongst the general population (52). The World Health Organization (WHO), Joint United Nations Programme on HIV/AIDS (UNAIDS) and the United Nations Office on Drugs and Crime (UNODC) all support comprehensive

packages of harm reduction interventions including needle and syringe programs and OST, with benchmarks for effective implementation specified (8), as discussed in section 1.1.8.

Decreases in BBV transmission and injecting risk, following the introduction of harm reduction have been reported (53, 54), and the prompt and comprehensive implementation of harm reduction programs has stalled or even prevented BBV epidemics (48, 55, 56). However, harm reduction requires sustained and reliable implementation for maximum effectiveness (50). Sudden reductions in service delivery (e.g. via service closure) have resulted in increased injecting risk behaviour (57).

1.1.4 Needle and syringe programs

Needle and syringe programs are designed to reduce BBV transmission by minimising the potential for the sharing of injecting equipment. They involve provision of sterile injecting equipment to PWID clients irrespective of the drug of injection and are typically implemented as a low-threshold intervention, meaning there are minimal requirements for clients to access the service. In this frame, needle and syringe programs are easily implemented and operated by staff with minimal training. Many allow clients anonymous access, though in some countries, PWID are required to register with the services in order to acquire syringes (58). Needle and syringe programs may provide unlimited syringes, or place limits on distribution numbers, or alternatively, they may operate as "exchanges", whereby used syringes are returned and exchanged for sterile syringes (59). In addition to providing sterile syringes, needle and syringe programs may also provide other sterile drug injecting equipment, such as alcohol swabs, drug filters and tourniquets. Syringe dispensation need not occur from fixed-sites, with fixed-site needle and syringe programs (hereafter "fixed-site NSPs") often complemented by other models of syringe dispensation, such as mobile-outreach syringe delivery (48) and syringe vending machines (SVMs) for 24-hour access (60, 61). There is evidence that these adjunct modalities may service different segments of PWID populations compared to programs operating from fixed-sites (62, 63).

In the needle and syringe program literature the term “needle and syringe program” often refers to different services and programs. It can be used to describe the overall program operating in different countries and contexts in which the range of syringe distribution modalities are described as one. In other circumstances the term is used to refer specifically to fixed-site NSPs that are distinguished from other dispensation points, such as SVMs or pharmacies. However, these fixed-site NSPs can serve as a hub from which other models of service delivery (e.g. outreach) may operate. Throughout this thesis I will make explicit reference to “fixed-site NSPs” to distinguish free, fixed-site operations from other forms of syringe distribution such as SVMs, outreach and pharmacies which will also be specified as such. Otherwise, the term “needle and syringe program” will be used to refer to either services or the overall program of syringe distribution (e.g. at the country level). The research papers in this thesis revert to describing needle and syringe programs or “NSP” as assessed through participants’ questionnaires, and so, as is used in wider literature the term is generally equivalent to fixed-site services.

Pharmacies are a private enterprise and may provide sterile syringes at a cost. Pharmacies are considered separate from publically funded and operated needle and syringe programs. Nevertheless, pharmacies provide an important adjunct to needle and syringe programs (64), particularly where needle and syringe program access may be low (65).

Evidence shows that needle and syringe programs reduce harms associated with IDU, particularly the transmission of HIV (12, 56, 66). MacDonald et al. (2003), in an analysis of harm reduction performance in 99 cities worldwide, showed that HIV prevalence decreased over time in cities with needle and syringe programs compared to cities without (67, 68). However, even in locations with low PWID-specific HIV prevalence, high HCV incidence has often persisted (69), due in part to the higher transmissibility of HCV compared to HIV (70). Current levels and methods of needle and syringe program implementation may be ineffective at averting HCV transmission. Whilst there is some empirical evidence showing reductions in HCV transmission as a result of needle and syringe programs (71, 72), in general, this evidence is considered less robust than the evidence of effectiveness on HIV (2, 73). The actual impact of needle and syringe programs on HCV transmission remains unclear (2).

Many needle and syringe programs services operate as part of "enhanced" services, offering supplementary interventions such as condom distribution, OST provision, BBV testing and counselling, HIV anti-retroviral therapy (ART) provision, drug counselling, social and welfare assistance, drug consumption rooms, overdose prevention education, on-site medical staff and facilitation of drug treatment access (68, 74, 75). Indeed, evidence suggests that needle and syringe programs are most effective when implemented in conjunction with other harm reduction interventions (8, 56, 76). Needle and syringe programs, coupled with OST provision, has previously been termed "full harm reduction" (37, 72, 77), and has been associated with reductions in HCV incidence and needle sharing (72) and higher individual-level syringe coverage (37) for those PWID simultaneously accessing both needle and syringe programs and OST.

Needle and syringe programs have been described as fundamentally altering the risk environment for PWID (78). Heimer (2008) compares the epidemiological impact of needle and syringe programs to vector-control programs that seek to eliminate the vector of disease, being the contaminated syringe in the case of IDU (79). Kaplan and Heimer (1994) previously developed what they termed the "circulation theory of needle exchange", showing that needle and syringe programs reduce the amount of time unsterile syringes circulate in the PWID population, and therefore reduce the potential for these vectors of disease to infect disease-free individuals (80). These effects are typically thought of in relation to direct service access. However, they may be amplified as needle and syringe programs can also provide reach to PWID not directly accessing services, via informal peer-to-peer syringe distribution. In this way, needle and syringe programs can help increase the volume of sterile syringes amongst PWID networks (78).

1.1.5 Needle and syringe coverage

Despite the evidence of public health benefit, global syringe provision is inadequate. Some type of needle and syringe program is reported to operate in 93 countries worldwide, equating to only 52% of countries with reported IDU (8). Further, these needle and syringe programs are estimated to distribute only 33 sterile syringes per PWID per year (8). However, PWID injection frequencies can be far in excess of this (e.g.

47% of Australian PWID reported injecting ≥30 times a month (32)), and disparity exists in syringe coverage, both between and within countries (8, 47, 72, 81). Russia, for example, with one of the world's largest populations of PWID (estimated at 1.9 million) has severely limited needle and syringe program access (8, 82, 83). Of the 75 countries with available data for population-level syringe coverage estimate, only nine reach levels of syringe distribution considered "high coverage" according to the WHO (8).

1.1.6 Consequences of inadequate needle and syringe coverage

Without sufficient syringe coverage, BBVs can spread rapidly via IDU (84, 85). After HIV is introduced into PWID populations, prevalence can reach 40% within one to two years without appropriate intervention (84). Such dramatic BBV prevalence increases have been observed in India, where in Manipur, PWID-population prevalence of HIV increased from 0% to 50% within six months, and in southern China, where one of the highest recorded incidence rates of HCV (at the time of publication) was reported at 37.6 per 100 person-years (86, 87). Inadequate harm reduction was cited as a contributing factor in both cases (86, 87). The reduction in injecting risk behaviour as a result of harm reduction implementation has been shown in multiple locations. Between cities, Neaigus et al. (2008) reported greater injecting risk behaviour in a US city without formal syringe distribution than in a city which had legalised needle and syringe programs (88). Even within cities, disparities can occur. Zamani et al. (2010) compared neighbourhoods in Tehran with and without active needle and syringe programs; PWID from the neighbourhood with a needle and syringe program had 76% lower odds of receptive syringe sharing (81).

1.1.7 Barriers to sufficient needle and syringe coverage

Numerous factors impact the ability of both needle and syringe programs and clients to maximise syringe coverage, and can be broadly classified as *structural, individual* and *environmental* barriers. These barriers cannot always be eliminated entirely, but the

more they can be anticipated, planned for and mitigated, the greater the potential of maximising syringe coverage.

Structural barriers

Structural barriers refer to the institutional, policy and organisational elements that affect needle and syringe program delivery and access (89). Structural barriers may stem from service-level policy and practices (such as syringe dispensation policies) (59), or from top-down governmental decisions (such as funding levels) (55). Importantly, they are barriers over which consumers typically have little control.

Restrictive syringe dispensation policies, which limit the number of syringes PWID can acquire at any one visit, or which require the exchange of used syringes for new sterile syringes, are implemented in many countries (28, 59). Though these policies seek to increase client contact and reduce the circulation of unsterile syringes (90), needle and syringe programs with restrictive syringe dispensation distribute fewer syringes (91) and clients of restrictive services have lower syringe coverage (59) and higher levels of syringe sharing (28). The UNODC, UNAIDS and WHO recommend syringe dispensation without restrictions or conditions (92).

Fixed-site NSP operating hours often do not correspond with times of drug purchasing and use, which may occur at any time of the day or on weekends (93), when fixed-site NSPs may be closed (65, 94). Limited opening hours hinders PWIDs in covering spontaneous, unplanned-for injecting episodes, and has been repeatedly cited as a barrier to syringe acquisition (60, 94-96).

Not all interventions complementary to needle and syringe programs, some of which have mutual benefits on coverage, are available to all PWID. Despite the benefits of "full harm reduction" described above, and its demonstrated effectiveness in reducing injecting risk and increasing individual-level syringe coverage (13, 72), OST is offered in only 86 countries worldwide (8). Also, prison-based needle and syringe programs operate in only eight countries (82), even though large proportions of prison populations are PWID (97, 98), often imprisoned for drug-related crimes (98). IDU continues to occur in prisons, despite the inherent difficulty of attaining both drugs and syringes (98). The absence of prison-based needle and syringe programs represents a

distinct structural barrier to the reduction of injecting risk to imprisoned PWID. Moreover, many international harm reduction programs, particularly in low and middle-income countries (LMICs), operate on donor funding, often as temporary pilot projects (99).

Harm reduction interventions are often politically and socially unpalatable and commonly underfunded (56, 82), directly impacting the reach of services including syringe coverage (55). This social and political disapproval can result in local opposition to establishing harm reduction interventions, thereby imposing a significant barrier to their implementation and effective functioning. Wilton (1998) posited that this kind of opposition emerges as a protection of individual and collective identity in response to perceived threat by "outsiders" (100). This can occur despite the community's tacit acceptance of the target population in general (100). Such opposition to the proximal siting of controversial interventions is an example of "NIMBYism" (Not In My Backyard). Examples specific to NSPs have been documented. Shaw et al. (2003) detailed intense community opposition to a proposed NSP in Massachusetts, USA, with opposition arguments based around the potential for "bad elements" being attracted to the NSP and the suggested need for an abstinence-based response to drug use (101). This expression of NIMBYism, even in communities hardest hit by IDU-related consequences, is often supported by political and institutional figures (102) who may be unrelated to the community in question. The blocking of NSP implementation is an obvious barrier to access and syringe coverage amongst PWID and community opposition has previously led to the closure of existing NSPs, with attendant increases in injecting risk (57). This barrier is one largely overcome within the Australian context, where over 3000 points of syringe distribution exist (103) in both affluent and poorer suburbs. Even so, community opposition to NSPs is a significant issue in many countries and can have detrimental effects on syringe coverage.

Environmental barriers

The environment in which IDU occurs can refer to both the social as well as the physical, and there are negative influences or barriers to syringe coverage evident within both the physical and social environments.

Fixed-site NSPs are often located close to street-based drug markets (104). Police activity in these areas, and therefore police interaction with PWID, is commonly a part of the social environment for PWID (105). Many needle and syringe programs foster collaborative relationships with police as a means of protecting their clients, but police harassment of PWID in drug-using and service provision environments remains a problem, and along with saturation police operations, can pose a significant deterrent to service access (106-108).

Spatial access influences the use of health services (109-111). Inconvenient distances between client and service (what is inconvenient may differ depending on the client) may result in an inability to reach services, or make a service unattractive (112). Poor geographical access to needle and syringe programs increases levels of injecting risk, and therefore, potential for BBV transmission (109). Even within urban centres, large distances to needle and syringe programs have been associated with increased injecting risk (109). This barrier is particularly relevant in rural locations, where dispersed populations may have reduced or no access to needle and syringe programs (62, 112, 113). Also, in rural locations, where fixed-site NSPs may be limited to a single service, client anonymity may be a particular concern (104), making individuals reluctant to enter services that identify them as PWID.

The health risks of different drugs types are not uniform (40, 114, 115), and certain drug types are more prevalent in specific geographic areas (116-118). Localised dynamics of drug availability and preference can create uniquely risky contexts. For example, the influx of high-purity heroin in Australia in the 1990s led to dramatic increases in overdose deaths (119), whilst the recent (and rapid) change from powdered methamphetamine ("speed") to the higher purity crystalline form ("ice") has produced increases in indicators of harm, such as increased methamphetamine-related ambulance attendances and treatment presentations (120). Differences in drug-type risk profiles affect syringe coverage, such as the relatively higher injecting frequencies associated with cocaine injection (121, 122). Frequent injecting has previously been associated with inadequate individual-level syringe coverage (123).

Despite difficulties of trafficking drugs into prisons, injectable drugs are accessible, as are syringes (98). Used, unsterile syringes become commodified and circulate amongst prisoners (98), meaning imprisoned PWID are at an elevated risk of BBV infection

compared to PWID in non-prison settings (124). In such environments, the absence of prison-based needle and syringe programs makes the acquisition of adequate sterile syringes is impossible.

The peer networks of PWID shape and reproduce perceptions of injecting risk (125). Positive or negative attitudes towards risk are normalised and perpetuated amongst networks (125), meaning that inconsistent syringe acquisition, or syringe sharing practices, may be reinforced by PWID peers. Hence, injecting networks play an important role in the transmission dynamics of BBVs (27).

Individual barriers

PWID populations are highly variable in demographics (126-128), drug use (32, 128) and risk behaviours (4, 108, 127-129). These characteristics may drive barriers to service access. Within Australia, for example, fixed-site NSP attendees are characterised as predominantly white, male, heroin injectors with longer injecting careers (94, 130). Research exploring SVM use has shown how the characteristics of clients who use SVMs can differ to typical fixed-site NSP clientele, with a higher proportion of women (61) and younger PWID (60) accessing SVMs. This finding suggests barriers for these particular sub-groups in accessing fixed-site NSPs. Female PWID may be uncomfortable accessing male-dominated services (62) and experience greater stigma as PWID than men (131), meaning they may be additionally reluctant to enter services known to be frequented by PWID. Young PWID may not use services populated by mainly older clients (132), and age restrictions exist at some needle and syringe programs and have been reported as barriers to service use (104, 132). Fixed-site NSPs and syringe dispensing pharmacies may be culturally inappropriate for, and underutilised by, ethnic minorities (133-135), and some groups report experiencing stigma in fixed-site NSPs as a result of their ethnicity (104). Whilst this highlights service-level program deficiencies, the barriers are a result of individual characteristics. Importantly, PWID who do not use fixed-site NSPs, or use them inconsistently, have been found to have insufficient individual-level syringe coverage levels (123).

1.1.8 Measurement of needle and syringe coverage

The meaning, significance and indicators of syringe coverage are related to the intervention under consideration, the population involved and the intervention's intended outcome. For example, the assessment of coverage of a vaccination program may be derived by combining census data for all children of a certain age with the number who were given a vaccine. ART coverage for HIV-positive individuals defines its population according to the number who receive a specified diagnosis, which is then combined with the number who receive treatment as an ongoing intervention. Measuring syringe distribution presents its own challenges. IDU is an ongoing behaviour, characterised by periods of abstinence, relapse (136) and varying injecting frequencies (4). Moreover, so long as they are injecting, PWID will require ongoing intervention. Sharma et al. (2007) asked:

> *So what is meant by the term (coverage)? And what are the conceptual elements of coverage in the context of interventions for the prevention of HIV among IDUs? At the most simple level, it is important to ask who is being covered and what is being covered? Is coverage a proxy for effectiveness, accessibility and utilization of interventions—and do they all matter equally? Does coverage refer to any contact, prolonged contact or "effective contact" with a target population? Or does it refer to the coverage of certain behaviours or events—for instance, the percentage of injections with a clean syringe? Is the key issue perhaps to consider who and what is being or not being served?* (3) (p.93)

Because of the ambiguities and inconsistencies these questions reveal, syringe coverage has proved confusing in regards to its application, specifications and meaning (3). As a result, syringe coverage has often been seen purely as a way of evaluating the extent of service delivery, rather than as a way to better understand how PWID interact with needle and syringe programs (3). The tools used to calculate syringe coverage can be used to both evaluate effectiveness and explore person-level variations in engagement and need, but the focus has been on the former.

Syringe coverage has traditionally been measured at the population level. However, population-level syringe coverage cannot account for individual variations in risk, need

and service engagement. As a result, recent research has proposed new methods for measuring syringe coverage at the individual level (5) to better reflect the heterogeneity of PWID.

1.1.9 Population-level needle and syringe coverage

Syringe coverage measurement at the population level is crucial for program evaluation, with two measures of population-level syringe coverage in common usage: 1) the proportion of an estimated PWID population accessing a service, and 2) the averaged distribution of sterile syringes per estimated PWID per annum (3). International public health organisations, such as the WHO and UNAIDS, regard these measurements as indicators of needle and syringe program effectiveness and subsequently recommend targets (137) for program performance, assessed against international benchmarks, using routine service data. The development of international targets for syringe coverage is an attempt to define the critical level at which to achieve public health impact (56). It is not necessary to eliminate all IDU-related risk behaviours to impact upon BBV transmission, but syringe coverage should be sufficient to reduce harms significantly, even though risk behaviours may continue (138).

The first measure of population-level syringe coverage specifies the "reach" of a program. In practice, reach is categorised to mean those PWID "ever" reached and those "regularly" reached (139). "Regular reach" is defined as monthly service access within a 12-month period (3, 6). Whilst a "high coverage" target of ≥60% of the estimated PWID population having regular reach has been recommended in WHO guidelines (6), and is utilised consistently in international harm reduction efforts (3), there is little evidence that this target is meaningful in controlling HIV transmission (58).

The second measure is defined by the WHO as "the number of syringes distributed per PWID per year" (6, 74). Using syringe distribution data, the measure is calculated by dividing the total number of syringes distributed by a PWID population estimate. Targets have been recommended based on previous research findings and statistical modelling (6, 140). According to the WHO, 200 sterile syringes distributed per PWID per annum constitutes the "high" syringe coverage needed to have impact on HIV

incidence (6). An HCV-specific recommendation of 300 sterile syringes per PWID per annum has recently been established to reduce HCV transmission (141).

Additional population-level measures have been proposed that try to account for injecting frequencies amongst PWID populations, thereby assessing levels of overall need in the population. Both Tempalski et al. (142) and Arnaud et al. (74) used a variation on the WHO measure, that included an estimate of injecting frequencies within the denominator: the number of syringes distributed, divided by the PWID-population estimate, multiplied by an estimate of injecting frequency per PWID. The measures rely not only on an estimate of the PWID population size but also an estimate of the injecting frequency per PWID. The issue of estimate uncertainty is doubled with these measures, with the estimate of injecting frequency across the PWID population particularly prone to a wide margin of uncertainty. Despite the attempt to assess how population-level syringe distribution meets the actual injecting needs of the PWID population, the measures have a high potential for error (139), and are therefore not in widespread use amongst international harm reduction programs (139).

Internationally consistent methods for evaluating and comparing harm reduction services are vital. The population-level measurements described above enable the setting of aspirational targets and the comparison of program performance against recommended benchmarks. However, their limitations are clear. First, both population-level methods rely upon PWID population estimates. Such estimates are difficult to produce, have a wide margin of error (143), and have problems with definitions (e.g. how to define “regular” and “occasional” injectors) (56). Second, the “regular reach” indicator requires registration systems in order to capture and record the use of services by unique PWID and the frequency with which they present. This practice is common in some countries (Asian countries in particular (3)), but certainly not all (Australia specifies needle and syringe programs as “anonymous” services (144), meaning Australia doesn’t calculate “reach”) making between-country comparison difficult (3). Third, recording those “ever” reached means clients are continually added as long as the service is in operation (139), regardless of death, relocation or drug use cessation, thereby inadequately representing the current situation. Fourth, the assumption of homogeneity in PWID’s need and risk is inherent to both methods. The WHO’s 200–300 per annum syringe distribution recommendation only has meaning for

PWID injecting at per annum frequencies within this range, if the standard of a new, sterile syringe for every injection is applied (142). Importantly, these single specified targets fail to account for individual and population variability amongst PWID, which can be pronounced. Some PWID will require many more syringes than the WHO recommends; some will require far fewer. Finally, to conceptualise syringe coverage only as the number of syringes distributed, or the proportion of PWID reached, does not consider the quality of the service being provided (3). This limitation gives little sense of how needle and syringe programs reach clients of differing risk or need, or how syringe distribution may interact across the suite of harm reduction services, such as OST or ART, and the mutual benefits in risk/BBV reductions they may provide when implemented in conjunction with needle and syringe programs (56).

1.1.10 Individual-level needle and syringe coverage

In response to the limitations of population-level syringe coverage measurement, syringe coverage measures at the individual level have been proposed. These measures account for variability between individuals, capture key behaviours influencing individual-level syringe coverage and provide a more nuanced assessment of syringe coverage overall. The most prominent method of individual-level syringe coverage assessment is that devised by Bluthenthal et al. in 2007, which assessed the level of syringe access required to reduce injecting risk behaviours. Bluthenthal et al. directly related injecting frequency to syringe acquisition amongst individual PWID using primary data collection (5). Their method records the syringes *retained* (syringes acquired minus those intended to be distributed, or already given away) at the last fixed-site NSP visit. The syringes retained are multiplied by the number of fixed-site NSP visits in the past 30 days (assuming the number of retained syringes is stable), in order to extrapolate a total estimate of past month syringe retention. The retention estimate is then divided by the person's injecting frequency. The resultant figure is multiplied by 100 to create an estimated percentage of past-30-day injecting episodes that are "covered" by a sterile syringe (5). Accordingly, ≥100% individual-level syringe coverage is considered sufficient, as this means all injecting episodes were covered by at least one sterile syringe (76). The percentage of PWID experiencing either sufficient or

insufficient individual-level syringe coverage, after accounting for variations in syringe acquisition and injecting behaviours, can then be estimated, using the equation below.

Bluthenthal et al. equation to measure individual-level syringe coverage (5)

$$\frac{(new\ syringes\ retained\ from\ last\ NSP\ visit\ x\ monthly\ NSP\ visits)}{past\ month\ injecting\ episodes}\ x\ 100$$
$$= \%\ of\ monthly\ injecting\ episodes\ covered\ by\ a\ sterile\ syringe$$

Individual-level syringe coverage measures have multiple benefits as policy and program relevant indicators. First, they can account for the cluster of behaviours associated with syringe acquisition and utilisation. PWID often acquire syringes not only for themselves, but also for their peers, which will then be distributed on (130, 145). PWID may also acquire syringes from a variety of sources, rather than just fixed-site NSPs, and stockpile sterile syringes for later use (5, 146). These mediating factors can be included within the individual-level syringe coverage measurement, providing a more accurate representation of actual syringe coverage-related behaviours. Second, whilst population-level syringe coverage measurement does not account for variations in PWID behaviour, individual-level syringe coverage measurement calculates syringe coverage according to the circumstances of each unique PWID. Third, because individual-level syringe coverage measurements require primary data collection, they enable simultaneous collection of demographic, behavioural and other exposure variables that may be tested for association with individual-level syringe coverage outcomes. As already noted, the barriers PWID face to achieving sufficient individual-level syringe coverage are particular to their social and environmental context, and knowing the factors that positively and negatively affect syringe coverage facilitates better service targeting.

However, a standardised individual-level syringe coverage measurement methodology is yet to be decided upon. Formulas other than that proposed by Bluthenthal et al. have been devised and implemented in attempts to improve accuracy. McCormack et al. developed an adapted version of the Bluthenthal et al. method. Forgoing Bluthenthal et

al.'s extrapolation method, McCormack et al. favoured directly enumerating individual-level syringe coverage behaviours (146). Here they recorded numerical data on syringe acquisition, peer-to-peer syringe distribution and injecting frequency for the past month. Importantly, data on syringe acquisition in the McCormack et al. measure can include acquisition from any source (needle and syringe programs, pharmacies, peers), as opposed to the Bluthenthal et al. measure which was limited to fixed-site NSP acquisition. The outcome (percentage of injecting episodes covered by a sterile syringe) remains the same. Crucially, McCormack et al.'s work also demonstrated that the omission of certain behaviours may introduce bias into the measure. McCormack et al. showed that a new measure, inclusive of "syringe stockpiling" as a formula parameter, reduced estimates of insufficient individual-level syringe coverage by eight percentage points. Furthermore, 75% of the sample reported syringe stockpiling (146), suggesting a highly common practice with importance in relation to syringe coverage. Additional, currently unidentified behaviours may similarly, and inadvertently, bias the individual-level syringe coverage estimate through unmeasured confounding or similar processes. The differences between Bluthenthal et al.'s extrapolation method and McCormack et al.'s enumeration method (including syringe stockpiling) is presented in Figure 1.

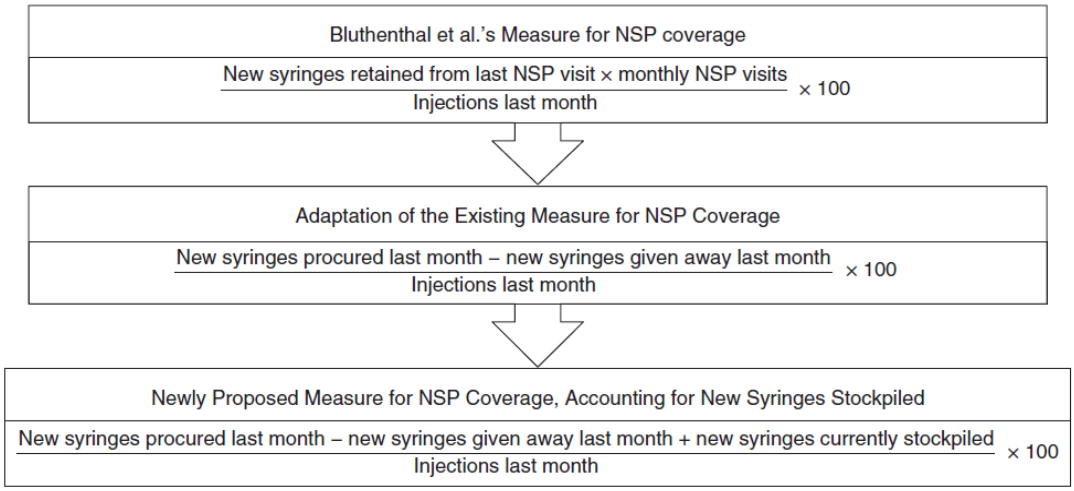

Figure 1: Different methods of measuring individual-level syringe coverage

Adapted from: (146), Figure 1

The inconsistency of measurement methodology is a limitation of individual-level syringe coverage measurement research. Another limitation is the requirement of primary data collection, which may be unfeasible for services with minimal resources or capacity to perform such collection. Despite these limitations, individual-level measurement captures vital public health information that population-level measurements cannot. Individual-level measurement accounts for differences between people. By considering highly variable factors, like injecting frequency, individual-level syringe coverage measurement directly captures service need and service engagement for each person measured. Though difficult to collect, these measures account for the heterogeneity between PWID, and can be employed to identify unique barriers to sufficient individual-level syringe coverage.

1.1.11 Findings from individual-level needle and syringe coverage research

In their original publication, Bluthenthal et al. categorised individual-level syringe coverage, stratifying participants who had ≤49%, 50-99%, 100-149% and ≥150% individual-level syringe coverage (5). This categorisation assessed the relationship between injecting risk and different degrees of individual-level syringe coverage. Importantly, it also specified those participants who had sufficient individual-level syringe coverage (≥100% individual-level syringe coverage) and insufficient individual-level syringe coverage (<100%), addressing the "one shot for one syringe" recommendation proposed by the American Centre for Disease Control and Prevention (5). The demarcation of individual-level syringe coverage as either sufficient or insufficient has subsequently been utilised across multiple studies. Bluthenthal et al. reported that 53% of their sample was insufficiently covered. They found an inverse relationship between individual-level syringe coverage and injecting risk: the lower the individual-level syringe coverage, the higher the proportions of PWID reporting syringe sharing and syringe re-use (5). Significantly, participants who reported higher than sufficient individual-level syringe coverage (≥150%) had the lowest rates of reported injecting risk behaviours (5), suggesting that excessive syringe acquisition for unplanned injecting episodes is most protective. Work by the same research group

compared individual-level syringe coverage across 24 Californian needle and syringe programs with syringe dispensation policies that varied in restrictiveness. Insufficient individual-level syringe coverage prevalence ranged from 39% at those needle and syringe programs with the least restrictive policy to 74% at those with the most restrictive policies (59). In a further study, the group compared individual-level syringe coverage amongst Californian PWID of different ethnicities, with Mexican American PWID reporting the highest level of insufficient individual-level syringe coverage (60%), then white PWID (53%), then African American PWID (48%) (128).

Multiple international studies have reported similarly high prevalence of insufficient individual-level syringe coverage. Heller et al. (2009) recruited 478 PWID in New York City, USA, where 54% were insufficiently covered (147), largely matching the prevalence amongst the Bluthenthal et al.'s Californian samples. Australian researchers estimated that 16-37% of three separate samples were insufficiently covered (37, 123, 146). In Kermanshah province, Iran, a prevalence of 56% was reported (148). Finally, in a pooling of six UK samples, Turner et al. (2011) reported insufficient individual-level syringe coverage between 18% in Glasgow to 46% in Bristol (72).

In the Heller et al. study, younger (19–25 years) PWID and those reporting current homelessness had higher levels of insufficient individual-level syringe coverage, as did those reporting past-month public injecting (147) (quite possibly as a result of their homelessness). Noroozi et al. estimated significantly higher odds of receptive syringe sharing and syringe re-use in those with insufficient individual-level syringe coverage (148), with the syringe re-use association replicated in Australian work by Bryant et al. (2012). Additional findings in Australian samples showed those injecting drugs at either daily or greater frequency had increased odds of insufficient individual-level syringe coverage (123) (matching the finding of decreasing coverage with increasing injecting in Bluthenthal et al. (5)), as did the non-use or inconsistent use of fixed-site NSPs as the main source of syringe acquisition (123). Iversen et al. (2012) showed an association between self-reported HCV antibody positivity and sufficient individual-level syringe coverage (an association with serological evidence of HCV exposure was not significantly associated (37)). Iversen et al. also showed that currently receiving OST, coupled with needle and syringe program use ("full harm reduction") increased the odds of sufficient individual-level syringe coverage (37). The benefits of "full harm

reduction" were supported by Turner et al. (2011), showing that those PWID in receipt of OST and with at least 100% individual-level syringe coverage, reported reductions in syringe sharing by 48% and injecting frequency by 20.8 injections per month (72).

Finally, recent modelling work was used to predict HIV incidence amongst Iranian PWID after classifying those with sufficient or insufficient individual-level syringe coverage. Those with insufficient individual-level syringe coverage reported more injections, more incidents of syringe sharing, and a greater number of people that syringes were shared amongst (149). The annual rate of new HIV infection due to the sharing of syringes was estimated in the author's modelling as 40.4 per 1000 PWID in those with insufficient individual-level syringe coverage, compared to 10.2 per 1000 in those with sufficient individual-level syringe coverage (149).

This brief review demonstrates the replication of particular findings across international settings. The syringe coverage benefit of combining OST with needle and syringe programs; the associations between insufficient individual-level syringe coverage, receptive syringe sharing and syringe-reuse; and the lower individual-level syringe coverage experienced by those injecting at higher frequencies were all independently reported in multiple studies. Receipt of OST reduces injecting frequency for opioid injectors (13, 150), and therefore, receipt of OST enhances a person's ability to cover their injecting episodes (37), an interpretation supported by the association between high-frequency injecting and insufficient individual-level syringe coverage (5, 123). When PWID experience insufficient individual-level syringe coverage, they are more likely to re-use unsterile syringes, increasing the risk of bacterial infections (5, 14, 148, 151). PWID who utilised fixed-site NSPs inconsistently, or not at all, had higher odds of insufficient individual-level syringe coverage (123). This finding supports the value of needle and syringe programs providing free and consistent syringe distribution, as is the case with Australian fixed-site NSPs. Furthermore, it positions freely accessible needle and syringe programs as superior to either commercial syringe sources (e.g. pharmacies) or potentially unreliable sources (e.g. injecting peers). Important to note, however, is that all the studies described were based on cross-sectional data. With only one time point of observation, it is not possible to determine how these figures may change over time for individual PWID. Intra-individual variability may mean that a much larger percentage of PWID may experience

insufficient coverage over an extended period than ascertained through cross-sectional studies that typically only assess past-month behaviours.

1.1.12 Needle and syringe coverage in Australia

Australia's early and comprehensive adoption of needle and syringe programs – and harm reduction more broadly – is credited with averting a similar HIV epidemic in the PWID population as experienced in other countries (152). Harm reduction was effectively incorporated as one component of Australia's National Drug Strategy since 1985 (153), with the first fixed-site NSP opening the following year on a pilot basis (152, 154). Whilst harm reduction was initially established as a response to HIV spread amongst PWID, HCV transmission prevention quickly became a key objective (152). By 1991, needle and syringe programs, mostly as fixed-site NSPs, were well established across all Australian states, except Tasmania (155). Australia now delivers sterile injecting equipment to an estimated PWID population (as of 2017) of 93,000 (156), via a combination of syringe distribution service-types: primary fixed-site NSPs, secondary fixed-site NSPs and pharmacies (103). Primary fixed-site NSPs are specialised services for PWID, operated by specially trained staff. Often providing a full complement of fixed-site dispensation, outreach and SVM, primary fixed-site NSPs use syringe dispensation to facilitate access to enhanced services, such as OST and BBV testing, commonly provided within the same fixed-site building (75, 103). Secondary fixed-site NSPs are attached to other health services, such as hospitals and community health centres, with variable training of staff in drug issues and with variability ability to facilitate access to drug treatment (103). Pharmacies sell sterile injecting equipment. Across Australia, up to 2016, there were 3,209 fixed-site syringe distribution services, operating under this service mixture (102 primary fixed-site NSPs, 786 secondary fixed-site NSPs and 2,321 pharmacies) (103). These outlets are supplemented by 300 SVMs, generally managed by primary fixed-site NSPs (103). Needle and syringe program access is often poorer in rural locations than urban locations (112), but even so, the number of services and population-level syringe distribution in Australia is amongst the highest in the world (and is complemented by high levels of OST access) (8, 82). It has been estimated that Australian needle and syringe programs prevented 25,000 cases of

HIV and 21,000 cases of HCV (152) by the year 2000, and saved $70-220 million in healthcare costs between 2000 and 2010 (157).

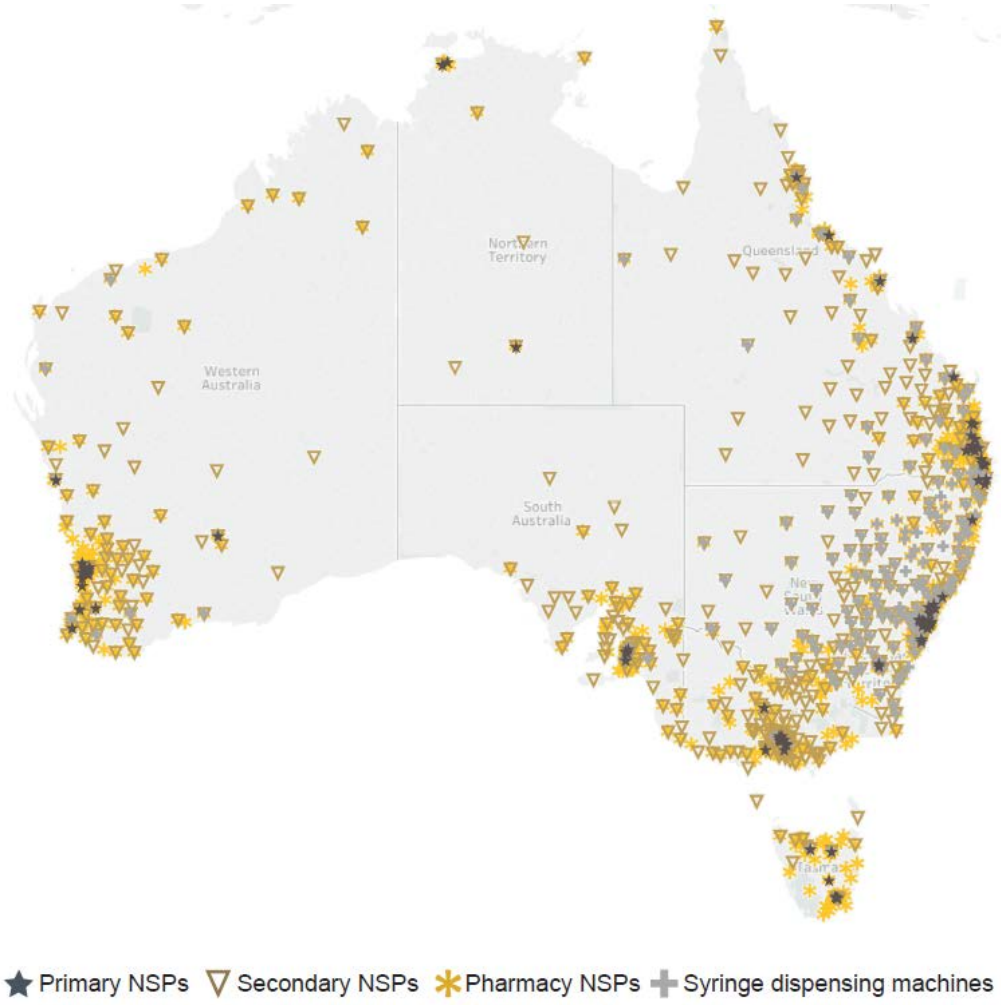

Figure 2. Australian map of needle and syringe program services, 2015/16
Adapted from: (103), Figure 2.5

Since program introduction, the number of sterile syringes distributed annually has increased year-on-year. In the 2015/16 financial year, 49.4 million syringes were distributed nationally, approximately 90% via public needle and syringe programs (as opposed to private pharmacies) (103); whilst the most recent PWID population estimate (amongst people aged 15-64 years) was 93,000 individuals (156). In 2017, an

estimated 461 sterile syringes were distributed per PWID (8). Consequently, Australia's syringe distribution exceeds WHO population-level syringe coverage recommendations.

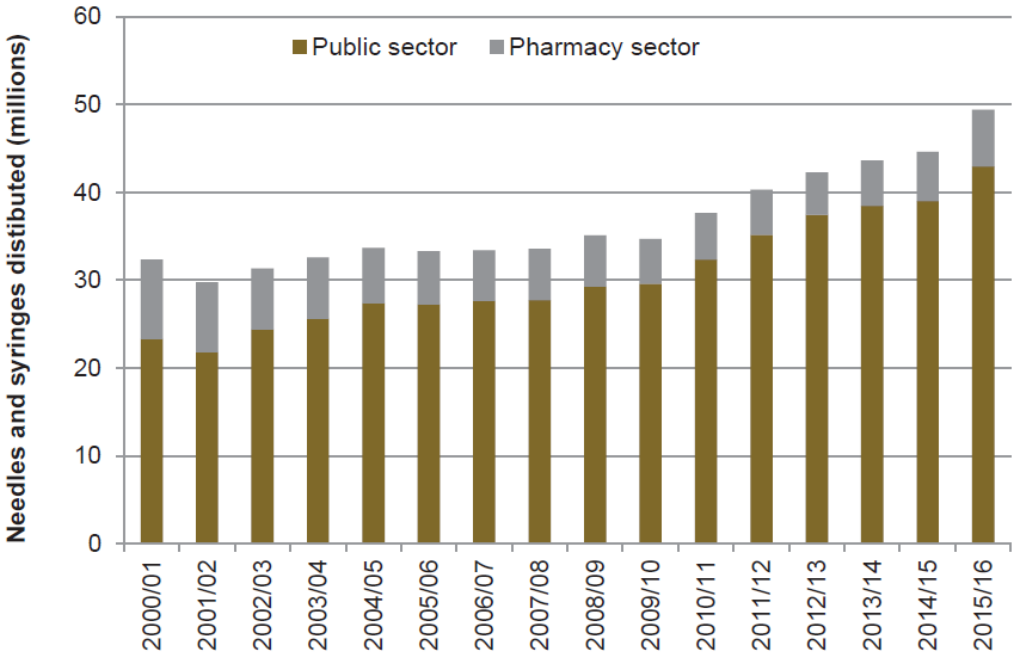

Figure 3. Australian needle and syringe distribution by service-type, 2000/01-2015/16

Adapted from: (103), Figure 4.1

Despite high population-level syringe coverage, many Australian PWID do not acquire sufficient sterile syringes to cover their injecting episodes (37, 123), reflecting the complex interplay between service delivery, client need and engagement. The implication is that even large-scale and liberal syringe distribution is not enough to meet the unique needs of all PWID. Maximising syringe coverage may not be achieved through generalised increases in syringe provision, but instead as a consequence of varied and co-ordinated modalities of syringe distribution, tailored to meet the idiosyncratic needs of individual PWID.

1.1.13 Gaps in the research

There remain significant gaps in the research literature, limiting a more complete understanding of the barriers to syringe coverage, those who experience deficiencies in individual-level syringe coverage and how to improve syringe coverage overall. All studies reviewed above were cross-sectional, precluding examination of intra-individual syringe coverage variability, and effective causal inference between exposure variables and individual-level syringe coverage as an outcome. Accordingly, a key gap is the absence of longitudinal individual-level syringe coverage research; Bluthenthal et al.'s first individual-level syringe coverage paper specified this need (5).

In addition, the individual-level syringe coverage formula has been implemented inconsistently across studies, limiting comparability of findings. Whilst Bluthenthal et al. used a method of extrapolating the individual-level syringe coverage estimate (5), McCormack et al. explicitly enumerated each individual-level syringe coverage parameter, whilst also recommending an additional parameter for inclusion in the individual-level syringe coverage formula (syringe stockpiling (146)). Further testing and refinement is required to establish an optimal methodology for measuring individual-level syringe coverage, improving the accuracy of individual-level syringe coverage estimates and the development of an accepted and consistent individual-level syringe coverage structure.

Finally, all but one of the reviewed studies was conducted in high-income settings, limiting the generalisability of findings to LMICs, in which the ability to respond to high PWID-specific BBV prevalence is often poor. Iranian research demonstrated that individual-level syringe coverage measurement can be implemented in such settings (148). Further research should be conducted in a more diverse range of countries and locations to gain greater insights into syringe acquisition behaviours amongst PWID in a variety of contexts, for example, in LMICs where stigma against PWID or police interference is higher (99). These heightened barriers may inspire novel methods of syringe acquisition and service delivery, improving syringe coverage for services and individuals. These methods may go unreported without appropriate research.

1.1.14 Conclusions

Even in countries with high population-level syringe coverage, substantial deficiencies at the individual-level may persist, and have been associated with injecting risk behaviours, which in turn, are associated with increased risk of BBV transmission and infection (5). The barriers to sufficient syringe coverage exist at the structural, environmental and individual level, and these barriers may affect different PWID to different degrees. Furthermore, different PWID have different levels of need and risk. Syringe coverage measurement at the population-level is not sensitive to these differences. Individual-level syringe coverage accounts for this lack of sensitivity, by explicitly relating injecting frequency to syringe acquisition for individual PWID, providing a much more nuanced and detailed assessment of syringe coverage. PWID interact with harm reduction services to varying degrees. To think of PWID as active in their own syringe coverage provision (provided the opportunity is there) (3) recognises the unique and varied obstacles they may experience, and the need for tailored services. Individual-level syringe coverage measurement can identify PWID sub-groups and contexts in need of targeting. However, significant gaps in the research literature exist, such as the absence of longitudinal research and research in LMICs. These gaps limit the understanding of syringe coverage and its effects, and the generalisability of current research findings.

1.2 Thesis Overview

1.2.1 Rationale and aims

Syringe coverage is a vital measure of intervention effectiveness. Throughout section 1.1, I explained why it is important to measure syringe coverage at the individual level.

This thesis addresses gaps in the current literature on longitudinal individual-level syringe coverage measurement, measurement refinement and research in LMICs. My research had the following aims:

1) examine the interrelationships between the temporal patterns of individual-level syringe coverage, risk behaviours and health outcomes;
2) identify associations with insufficient individual-level syringe coverage as potential targets for intervention;
3) develop recommendations for increasing individual-level syringe coverage amongst PWID;
4) improve the methodology for measuring individual-level syringe coverage;
5) measure individual-level syringe coverage and describe service provision modalities in a low/middle income setting.

An example of the research documents needed for the studies contained within this thesis are provided in Appendix A: Myanmar study ethics documents and questionnaire

1.3 Thesis Outline

This thesis contains six chapters, including this introductory chapter. Chapters Two to Five present original research in six papers (five published in peer-reviewed journals and one currently under review). Chapter Six provides an integrated discussion of the combined research.

Chapter Two

Chapter Two presents research in which individual-level syringe coverage is analysed longitudinally. Using data from a cohort of regular PWID in Melbourne, Australia, I explore the patterns of individual-level syringe coverage over time and the demographic, drug-use characteristics and service access associations with these patterns. This research provides a foundation that Chapter Three expands upon by exploring longitudinal individual-level syringe coverage more fully. The manuscript was published in *BMC Health Services Research.*

Chapter Three

Chapter Three expands upon the findings from Chapter Two, presenting two complementary papers. The first builds on the findings in Chapter Two, exploring the relationships between time-varying covariates and changes in individual-level syringe coverage, directly testing the assertion that individual-level syringe coverage is influenced, both positively and negatively, by changes in these covariates. The second paper explores how changes in the behaviours included in the individual-level syringe coverage formula affect assessment of individual-level syringe coverage, with the aim of identifying areas of prioritisation for harm reduction services. The second paper also suggests improvements to the individual-level syringe coverage measure. The first manuscript in this chapter was published in *Drug and Alcohol Review.* The second was published in the *Journal of Public Health*.

Chapter Four

Behaviours that mediate syringe acquisition and injecting frequency may bias individual-level syringe coverage calculation if not included as parameters in the individual-level syringe coverage formula. In Chapter Four, I replicate McCormack et

al.'s methodology to examine whether including a parameter measuring the use of multiple sterile syringes per injecting episode improves the measurement of individual-level syringe coverage. This manuscript was published in the *International Journal of Drug Policy*.

Chapter Five

The bulk of individual-level syringe coverage research (and indeed, most PWID research) has been conducted in high-income settings, despite ongoing BBV epidemics amongst PWID populations, and the acknowledged paucity of PWID research in LMICs (99, 143). The first paper within Chapter Five presents a review of harm reduction in LMICs; the difficulties and successes, the consequences of poor implementation, and recommendations for the future. The second paper describes research on individual-level syringe coverage in Myanmar, calculating estimates of, and exploring associations with, insufficient individual-level syringe coverage across three characteristically different urban locations. The first manuscript in this chapter was published in the *Journal of Viral Hepatitis;* the second has been submitted to the *International Journal of Drug Policy*.

Chapter Six

Chapter Six presents an integrated discussion of the research in this thesis. I consider the key findings of each paper, their interconnection and relationship with past research, the implications of these findings and recommendations for future work. Finally, I discuss the strengths and limitations of my research.

Chapter Two: A longitudinal, descriptive analysis of individual-level needle and syringe coverage

2.1 Overview of Chapter Two

In previous work, injecting risk behaviours were associated with insufficient individual-level syringe coverage at the cross-sectional level (5, 148). However, directions of causation in these associations, and the variability of what may be temporary and infrequent events, cannot be discerned with only a single time-point of observation. Bluthenthal et al. suggested examining the longitudinal relationship between needle and syringe program dispensation policies, service utilisation patterns and individual-level syringe coverage (5). Though they referred to the specific need to explore the effect of needle and syringe program dispensation policy, the authors acknowledged the importance of analysing individual-level syringe coverage over time.

Whilst cross-sectional research has the advantage of typically being less resource intensive than longitudinal research, it is incapable of establishing the temporal relationship between exposures and outcomes, or capturing intra-individual change over time. For example, the association between HCV-positivity and receptive syringe sharing has been reported in numerous cross-sectional studies (158-160). This association has a logical causal relationship, in that the sharing of unsterile, potentially infected syringes leads to BBV transmission (31, 33), and repeated instances of sharing represents cumulative risk. However, with only one time-point of observation, the interpretation may be either; that the reuse of unsterile syringes leads to HCV infection, or alternatively, that individuals currently HCV-positive are more likely to share syringes due to an existing infection and subsequent negligence. The latter is an example of reverse causation, which at the cross-sectional level, cannot be ruled out. To identify the temporal sequence of cause and effect, longitudinal research is required.

Existing individual-level syringe coverage research has been cross-sectional (5, 123, 146, 148). It is important to understand the changes in individual-level syringe

coverage, and the patterns to these changes, over time. Such an examination will provide a deeper and more nuanced appreciation of the experience of syringe coverage and the characteristics of individuals experiencing changes to their syringe coverage, allowing for more innovative methods of intervention.

The paper presented in this Chapter is the first of three studies exploring individual-level syringe coverage longitudinally in this thesis. All use data from the Melbourne Injecting Drug User Cohort (MIX) Study (126). MIX is a prospective cohort of 757 PWID, recruited primarily in 2009. As of February 2015, 2862 observations were available for analysis, to a maximum of seven interview waves per participant and high study retention. Consequently, the cohort provided an excellent opportunity to explore individual-level syringe coverage longitudinally. Paper One uses an adapted version of the Bluthenthal et al. methodology that follows McCormack et al.'s enumeration method (though without the syringe stockpiling parameter). Participants are categorised according to their longitudinal experience of individual-level syringe coverage. Associations with insufficient individual-level syringe coverage are tested via regression analysis. In this way, I intend to identify PWID sub-groups at risk of insufficient individual-level syringe coverage, and the potential time-varying influences on insufficient individual-level syringe coverage. Not only does Paper One meet the stated research need for longitudinal examination of individual-level syringe coverage (5), and hence aim number one, but also provides the foundation for further, more complex, longitudinal examination.

The manuscript presented in this chapter was published as:

O'Keefe D., Scott N., Aitken C., Dietze P. (2016) Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis, *BMC Health Services Research* 16:411 (epub)

2.2 Publication: Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis

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RESEARCH ARTICLE Open Access

Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis

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Abstract

Background: Coverage is used as one indicator of needle and syringe program (NSP) effectiveness. At the individual level, coverage is typically defined as an estimate of the proportion of a person who injects drugs' (PWID) injecting episodes that utilise a sterile syringe. In this paper, we explore levels of individual syringe coverage and its changes over time.

Methods: Data were extracted from 1889 interviews involving 502 participants drawn from the Melbourne drug user cohort study (MIX).
We asked questions relating to participants syringe acquisition, distribution and injecting frequency within the two weeks before interview. We created a dichotomous coverage variable that classified participants as sufficiently (≥100 %) covered if all their injecting episodes utilised at least one sterile syringe, and insufficiently (<100 %) covered if not. We categorised participants as "consistently covered" if they were sufficiently covered across interviews; as "consistently uncovered" if they were insufficiently covered across interviews; and "inconsistently covered" if they oscillated between coverage states.
Chi-square statistics tested proportions of insufficient coverage across sub-groups using broad demographic, drug use and service utilisation domains. Logistic regression tested predictors of insufficient coverage and inconsistently covered categorisation.

Results: Across the sample, levels of insufficient coverage were substantial (between 22–36 % at each interview wave). The majority (50 %) were consistently covered across interviews, though many (45 %) were inconsistently covered.
We found strong statistical associations between insufficient coverage and current hepatitis C virus (HCV) infection (RNA +). Current prescription of opioid substitution therapy (OST) and using NSPs as the main source of syringe acquisition were protective against insufficient coverage.

Conclusion: Insufficient coverage across the sample was substantial and mainly driven by those who oscillated between states of coverage, suggesting the presence of temporal factors. We recommend a general expansion of NSP services and OST prescription to encourage increases in syringe coverage.

Keywords: Injecting drug use, Syringe coverage, Harm reduction, Longitudinal analysis

Abbreviations: AOR, Adjusted odds ratio; BBV, Blood-borne virus; 95 % CIs, 95 % Confidence intervals; HCV, Hepatitis C virus; IQR, Interquartile range; MIX, Melbourne injecting drug user cohort study; NSP, Needle and syringe program; OST, Opioid substitution therapy; PWID, People/person who injects drugs; WHO, World Health Organisation

Background

The coverage of a public health program can be defined as the extent to which it reaches its intended population [1]. It is an indicator of the effectiveness of public health interventions in reducing public health risks.

Needle and syringe programs (NSPs) seek to avert blood-borne virus (BBV) spread amongst people who inject drugs (PWID) via the distribution of sterile needles and syringes (hereafter referred to as syringe/s). The coverage achieved by NSPs at the population level refers to the proportion of PWID reached by services. At the individual level, coverage is typically defined as the proportion of a PWID's injecting episodes that utilise a sterile syringe [2].

The sharing of used syringes is a significant contributor to the transmission of BBVs amongst PWID [3, 4]. It is es-timated that globally, only 1–4 syringes are distributed per PWID per month [5], well below the World Health Organization (WHO) recommended rate of 200 syringes per PWID per year [6].

Syringe coverage is mediated by context. Service management and funding [7], dispensation policy [8], intensive policing practices [1, 9], cohesiveness of PWID networks [2], spatial service access [10], and individual demographics [11, 12] influence the ability of individuals to attain sufficient syringes and service systems to provide sufficient coverage.

Previous research has shown that insufficient coverage at the individual level is significantly associated with high-frequency injecting and not using NSPs as a primary source of syringe acquisition [2]. Insufficient individual-level coverage has also been associated with syringe re-use and receptive/distributive syringe sharing [11–13]. Despite these findings, current understanding of the causes of in-sufficient coverage is poor. Most research on individual coverage has been cross-sectional and consequently un-able to capture variation over time – hence Bluthenthal et al.'s call for longitudinal investigation [11]. A greater un-derstanding of coverage over time will also provide better knowledge of the predictors of insufficient coverage and enable better interventions.

The Australian context provides the ideal setting for research on patterns of syringe coverage over time. Australia's early and comprehensive adoption of NSPs prevented an HIV epidemic in PWID, in contrast to many other countries [14, 15]. An estimated 3000+ syringe outlets service an estimated population of 90,000 PWID [16], distributing approximately 213 syringes per PWID per year [12], in excess of WHO population-level recommendations [6]. Despite greater opportunity to acquire syringes than many of their international counterparts, an estimated 16–37 % of Australian PWID experience insufficient coverage [2, 12, 17]. Consequently, research exploring the individual and structural determinants of insufficient coverage in Australia provides important information for other settings.

In this paper we analyse six years of data from an ongoing cohort of PWID in Melbourne, Australia. We aim to:

- describe the characteristics of individuals with recent insufficient coverage (insufficient syringe acquisition to cover injecting episodes within the past two weeks) across broad demographic, drug use and service utilisation domains;
- explore how the proportion of individuals with recent insufficient coverage changes over time;
- categorise participants according to their longitudinal patterns of coverage; and
- identify exposure sub-groups independently associated with individual coverage and longitudinal coverage pattern trajectories.

Methods

Melbourne injecting drug user cohort study

Data are drawn from the Melbourne injecting drug user cohort study (MIX), which has been described in detail elsewhere [18]. The cohort includes PWID recruited through the original MIX recruitment phase in 2008–2010 ($n = 688$), and those rolled into the study in 2011 via past involvement in the Networks II cohort ($n = 69$) [19], resulting in 757 participants. Both MIX and Networks II sought to recruit regular injectors, and despite some demographic differences between the MIX and Networks II cohorts at the 2011 roll-in (mean age in 2011 was 29 in MIX, 35 in Networks II; 16 % in MIX were born overseas, 31 % in Networks II; 54 % were currently on OST in MIX, 62 % in Networks II), the characteristics of the cohorts at baseline (2005 for Networks II) were comparable [19–21].

Eligibility criteria for the original MIX cohort were being aged 18–30 years and reporting injecting of heroin and/or methamphetamine regularly (at least once a month in the six months prior to recruitment).

Participant sample

As of February 2015 (dataset end), 2862 separate interviews had been collected over a maximum of seven annual interview waves per participant. As the necessary coverage questions were not introduced into the questionnaire until June 2010, all interviews prior to this date (902 interviews, 184 participants) were excluded from analysis. Furthermore, as we intended to analyse changes to coverage longitudinally, only participants with two or more interviews after June 2010 were retained, excluding a further 71 participants. This process resulted in an amended dataset of 502 participants and 1889 interviews across a maximum of six separate interview waves. Study retention was high, with 85 % of these participants having at least three interviews.

The demographic and drug use patterns of the total cohort and the amended sample used in analysis were similar, though current employment was 7 percentage points higher, and current OST prescription 21 percentage points higher, among the amended sample. Comparisons between the two sets of data at first interview are presented in Additional file 1.

Measures

To measure syringe retention, we asked the following questions:

"In the last two weeks, how many new syringes in total did you get?"
"In the last two weeks, how many syringes did you give away or sell to others?"

The MIX questionnaire records past week use and injecting frequency for 18 drug types. Past week injecting frequencies for each drug type were summed to create a total injecting frequency variable.

Using a method of calculating individual syringe coverage adapted from Bluthenthal et al. [11], we subtracted the number of syringes sold or given away from the number of syringes acquired. We then multiplied past week injecting frequency by two to create a consistent time frame for the measure (rather than syringe collection being halved, as initial inspection showed less variance for injection frequency, suggesting it is the more consistent practice). We then divided the number of syringes retained by past two-week injecting frequency and then multiplied by 100, resulting in a percentage of injecting episodes that utilised a sterile syringe. The formula for individual coverage measurement was therefore:

$$\frac{(syringes\ acquired - syringes\ distributed)}{(past\ week\ injecting\ frequency\ x\ 2)} \times 100$$

Recent individual coverage was considered to be sufficient if every reported episode of injecting was covered by at least one reported sterile syringe, or ≥100 % individual coverage. A dichotomous variable, "recent coverage" (≥100 % coverage / <100 % coverage), was applied to each interview with valid data, classifying participants as either sufficiently or insufficiently covered for the two weeks before interview.

Coverage was only calculated for participants who reported both syringe acquisition and injecting within the two-week period (as the absence of either parameter precludes calculation). Missing data accounted for 44 % (832 observations) of all coverage responses. Of these missing data, most (602 observations, 72 % of all missing responses) resulted from injecting abstinence.

Sub-group selection

We chose exposure variables a priori, including predictors in Bluthenthal et al.'s [11] original coverage paper and recent work by McCormack et al. [17]. Broadly, these subgroups fall within demographic, drug use characteristics and service utilisation domains. **Demographic:** "sex" (male/female), "Indigenous status" (yes/no), "WHO definition of youth" (≤24 years/>24 years); "highest level of education" (<year 10/year 10–11/year 12, higher education, trade), "weekly income" (around median: <$400/≥$400), "employment status" (employed/unemployed), "stable accommodation" (yes/no), "country of birth" (Australia/other), "arrest (past twelve months)" (yes/no). **Drug use characteristics**: "injecting career" (around median: <13 years/≥13 years), "heroin injection (past month)" (yes/no), "methamphetamine injection (past month)" (yes/no), "Hazardous drinking scale score – *derived from Audit-C scale*" (abstinent/<8 points/≥8 points) [22], "receptive syringe sharing (past month) - *derived from BBV-TRAQ-SV*" (yes/no), "injection of another person (past month) - *derived from BBV-TRAQ-SV*" (yes/no), "been injected by another person (past month) – *derived from BBV-TRAQ-SV*" (yes/no), "BBV-TRAQ-SV injecting risk scale score" (continuous measure) [23], "hepatitis C virus serology (HCV) status" (three categories: positive (RNA+)/exposed (Antibody+, RNA-)/negative (Antibody-, RNA-), "injecting more than usual in the past six months" (yes/no), "solitary injecting >80 % of the time" (yes/no). **Service utilisation:** "current opioid substitution therapy prescription (OST)" (yes/no), "NSP as usual source of syringe acquisition (past month)" (yes/no). An amended version of the MIX questionnaire, relevant to this analysis, is presented in Additional file 2: Appendix 1.

Analysis strategy

We categorised participants with at least two instances of valid coverage data into three distinct subgroups according to longitudinal experience of the dichotomised recent coverage variable: "consistently covered" if all valid coverage data was recorded as sufficient, "consistently uncovered" if all valid coverage data was recorded as insufficient, and "inconsistently covered" if participants had at least one change between the two states of coverage across interviews.

The three coverage pattern groups were comparable in terms of missing data and attrition patterns. In the consistently covered group, 91 % of participants had three or more interviews and 27 % missing coverage data. In the consistently uncovered group, 82 % had three or more interviews and 26 % missing data. The inconsistently covered group had 92 % with three or more interviews and 22 % missing data.

Statistical analysis

Proportional differences between participants experiencing sufficient or insufficient coverage at their first interview and

their most recent interview were tested using chi-square statistics for categorical variables and Wilcoxon rank-sum testing for non-parametric continuous variables. Proportional differences between the three coverage pattern groups at first interview were tested using chi-square statistics for categorical variables and Kruskal-Wallis testing for non-parametric continuous variables.

Logistic regression was used to determine cross-sectional predictors of insufficient coverage from the dichotomous recent coverage variable. Initial inspection suggested that a binary coverage pattern variable of consistently covered/inconsistently covered be examined (placement in the inconsistently covered group as the outcome of interest), with too few cases of those consistently uncovered to allow analysis. The chosen time point of analysis was the first interview for each participant so as to minimise any bias across time due to differences in number of interviews.

Statistical significance was set at $p < 0.05$. All analyses were carried out using Stata 13.1 for Windows (StataCorp LP, TX, USA).

Results

Participant demographics

At first interview, the amended sample of 502 participants was predominately male (64 %), Australian-born (82 %), largely non-indigenous (95 %), unemployed (78 %) and living in stable accommodation (85 %). Mean age at first interview was 30. For those reporting injecting within the month prior to interview ($n = 416$), heroin was the most commonly injected drug (73 %), followed by methamphetamine (11 %). The remaining 16 % of participants most commonly injected either some form of OST or other pharmaceutical opioid.

Coverage characteristics across the cohort

Participants who reported syringe acquisition in the two weeks before interview collected syringes from any source a median of two times (interquartile range (IQR): 1–3) at both first and most recent interview. Participants collected a median of 20 syringes at first and most recent interview (IQRs of 10–70 and 10-100 respectively), and gave away/sold a median of one syringe (IQR: 0–8) at first interview and zero syringes (IQR: 0–10) at most recent interview. After subtraction of distributed syringes, participants retained a median of 16 syringes at both their first and most recent interview (IQRs of 6–48 and 5–65 respectively).

For those not reporting injecting abstinence in the week before interview, median self-reported injecting frequency was five times (IQR: 2–11) at both first and most recent interview (IQR: 2–14).

Median coverage percentages at first and most recent interview were 165 % (IQR: 92–353 %) and 175 % (IQR: 100–357 %) respectively. Despite the median percentage coverage being greater than 100 %, recent insufficient coverage was substantial; 26 % and 25 % of the sample were insufficiently covered at their first and most recent interview respectively.

The percentages of participants with recent sufficient coverage across all interviews are presented in Fig. 1.

Cross-sectional sufficient/insufficient coverage across exposure sub-groups

Proportions of sufficient and insufficient coverage were stable over time across many sub-groups. Those with insufficient coverage were more likely to report episodes of increased injecting frequency lasting ≥1 month in the past six months ($X^2 = 4.28$, $p = 0.039$) and recent injection of methamphetamine ($X^2 = 15.18$, $p = <0.001$). Those with sufficient coverage were more likely to report injecting careers equal to or longer than 13 years ($X^2 = 15.63$, $p = <0.001$) and current OST prescription ($X^2 = 12.11$, $p = 0.001$). These findings were significant at most recent interview, but not at first interview.

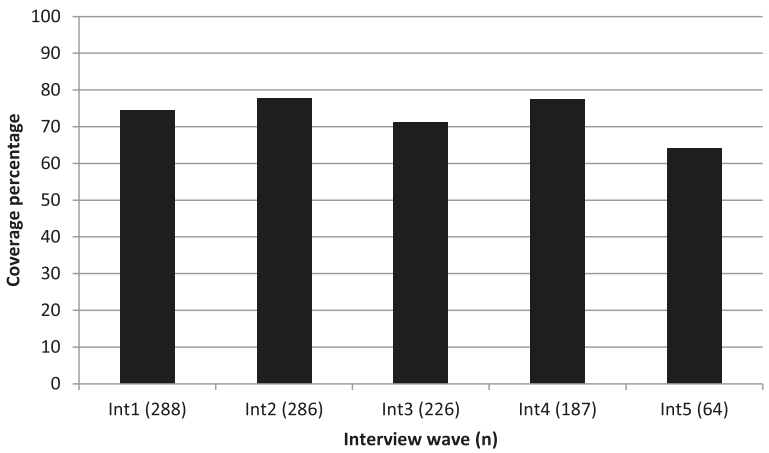

Fig. 1 Percentages of sufficient coverage across interview waves

Participants arrested within the past twelve months were more likely to report insufficient coverage at first interview ($X^2 = 3.91$, $p = 0.048$), but not at most recent.

Insufficient coverage was also associated with risk practices. Those with insufficient coverage were more likely to report receptive syringe sharing within the past month at first interview ($X^2 = 7.49$, $p = 0.006$). Furthermore, those with insufficient coverage recorded higher injecting risk scores on the BBV-TRAQ-SV scale at both interviews, a difference that was significant at most recent interview ($p = 0.022$), but not first.

At first interview, participants with current HCV infection were more likely to report insufficient coverage ($X^2 = 8.78$, $p = 0.012$). This finding was confirmed in regression analysis, which identified greater odds of insufficient coverage for those with a current HCV infection (adjusted odds ratio (AOR)) = 4.44 (95 % confidence intervals (CIs): 1.43, 13.73)). There was little difference in coverage between HCV status subgroups at most recent interview. Regression analysis also showed reduced odds of insufficient coverage for participants who reported most commonly acquiring syringes from NSPs (as opposed to pharmacies or informal sources) (AOR = 0.27 (95 % CIs: 0.09, 0.77)).

Full descriptive and regression results are presented in Table 1.

Coverage pattern group categorisation

Of participants with valid data for coverage pattern categorisation ($n = 322$), 162 (50 %) were consistently covered, 17 (5 %) were consistently uncovered and 143 (45 %) were inconsistently covered.

Median coverage across interviews for the total cohort was 150–167 %. The consistently covered group had greater median levels at every interview wave (214–250 %); the reverse was true for the consistently uncovered group, who experienced at least a 50 % shortfall in median coverage (45–50 %). Inconsistently covered participants recorded over 100 % median coverage (102–117 %).

Longitudinal median coverage data are presented in Fig. 2.

Correlates of coverage pattern groups at first interview

Most exposure sub-groups were proportionally similar between coverage pattern groups. However, some significant differences were found.

Those consistently covered were significantly less likely to have receptively shared syringes within the past month ($X^2 = 9.58$, $p = 0.008$) than the other coverage pattern groups. They were also significantly more likely to have injecting careers equal to or longer than 13 years ($X^2 = 6.58$, $p = 0.037$) and current OST prescription ($X^2 = 12.60$, $p = 0.002$).

In regression analysis, two significant results were found. Those with a current prescription of OST had decreased odds of being classified as inconsistently covered (AOR = 0.41 (95 % CIs: 0.22, 0.76)), whilst those with a current HCV infection had increased odds of being classified as inconsistently covered (AOR = 2.73 (95 % CIs: 1.12, 6.64)).

Full descriptive and regression results are presented in Table 2.

Discussion

We conducted longitudinal analysis of individual syringe coverage to address the gap noted in previous research [11] and to better understand the characteristics and predictors of coverage.

We found substantial levels of insufficient coverage. Across interview waves, the percentage of participants experiencing insufficient coverage was between 22–36 %, a finding that accords with previous Australian research [2, 12]. The fact that, at any time point, between a fifth to a third of the sample have "uncovered" injecting episodes is of serious concern, particularly considering that insufficiently covered participants in this study had a greater tendency to report receptive sharing of syringes, another finding that confirms past research [2, 11].

Analysis of longitudinal coverage patterns showed that most participants were consistently able to achieve sufficient coverage across interviews. The levels of insufficient coverage seen at each interview wave were driven then, not by those consistently uncovered but by those who fluctuated between states of coverage over time. This oscillating group should be the focus of interventions designed to reduce insufficient coverage. That so many participants were able to cover themselves at some time points but not at others, suggests a relationship between individual coverage and temporal context, rather than a consistent pattern of deficient coverage.

Cross-sectional analysis revealed that NSP access was associated with higher levels of coverage. This finding is plausible and highlights the advantages of harm reduction services from which PWID can reliably acquire syringes for free. These services overcome the inherent barriers of commercial sources (such as pharmacies) and potentially inconsistent or unreliable sources (such as friends and partners).

The association between insufficient coverage and current HCV infection (RNA positive) was strong. Previous research has shown that knowledge of HCV negativity can moderate injecting risk behaviours, such as receptively sharing syringes or injecting equipment [24]. A similar association between HCV status and coverage may be hypothesised, whereby a current HCV infection confers a consequent negligence with regards to sufficient syringe acquisition. Conversely, the shortfall in coverage might be a driver of HCV transmission.

Table 1 Analysis of recent sufficient and insufficient coverage at first and most recent interview

	First interview <100 %, *n* (%)	First interview ≥100 %, *n* (%)	Chi-squared *p*-value	Most recent interview <100 %, *n* (%)	Most recent interview ≥100 %	Chi-squared *p*-value	AOR[a] at first interview, AOR (95 % CI)	AOR *p*-value
Sex								
Female	27 (36 %)	84 (39 %)	0.673	23 (32 %)	81 (38 %)	0.393	1	
Male	47 (64 %)	130 (61 %)		47 (68 %)	132 (62 %)		1.37 (0.61, 3.09)	0.442
Indigenous status								
No	66 (92 %)	200 (93 %)	0.606	62 (91 %)	202 (95 %)	0.270	1	
Yes	6 (8 %)	14 (7 %)		6 (9 %)	11 (5 %)		1.04 (0.26, 4.20)	0.956
WHO definition of youth								
≤24 years	11 (15 %)	41 (19 %)	0.408	3 (4 %)	9 (4 %)	0.983	1	
>24 years	63 (85 %)	173 (81 %)		67 (96 %)	204 (96 %)		0.77 (0.23, 2.51)	0.661
Highest level of education								
<yr10	23 (31 %)	63 (29 %)	0.515	15 (22 %)	59 (28 %)	0.620	1	
Year 10–11	26 (36 %)	92 (43 %)		26 (38 %)	74 (35 %)		0.56 (0.23, 1.39)	0.210
Year 12/higher educ/trade	24 (33 %)	59 (28 %)		28 (40 %)	80 (37 %)		1.61 (0.63, 4.13)	0.324
Employment status								
No	63 (85 %)	175 (82 %)	0.511	56 (80 %)	168 (79 %)	0.840	1	
Yes	11 (15 %)	39 (18 %)		14 (20 %)	45 (21 %)		0.94 (0.29, 3.01)	0.919
Weekly income								
<$400	52 (70 %)	144 (67 %)	0.635	35 (50 %)	113 (53 %)	0.657	1	
≥$400	22 (30 %)	70 (33 %)		35 (50 %)	100 (47 %)		0.97 (0.40, 2.35)	0.943
Stable accommodation								
No	16 (22 %)	31 (14 %)	0.152	17 (25 %)	34 (16 %)	0.104	1	
Yes	58 (78 %)	183 (86 %)		52 (75 %)	179 (84 %)		1.03 (0.39, 2.71)	0.956
Country of birth								
Other	17 (24 %)	40 (19 %)	0.366	18 (26 %)	36 (17 %)	0.081	1	
Australia	55 (76 %)	174 (81 %)		50 (74 %)	177 (83 %)		0.96 (0.37, 2.46)	0.934
Injecting career								
<13 years	32 (45 %)	96 (45 %)	0.951	31 (46 %)	45 (21 %)	**<0.001***	1	
≥13 years	40 (55 %)	118 (55 %)		37 (54 %)	168 (79 %)		0.65 (0.28, 1.53)	0.325
Heroin injection (past month)								
No	9 (12 %)	38 (18 %)	0.262	10 (14 %)	39 (18 %)	0.440	1	
Yes	65 (88 %)	176 (82 %)		60 (86 %)	174 (82 %)		2.30 (0.70, 7.56)	0.171
Methamphetamine injection (past month)								
No	40 (54 %)	141 (66 %)	0.069	20 (29 %)	118 (55 %)	**<0.001***	1	
Yes	34 (46 %)	73 (34 %)		50 (71 %)	95 (45 %)		1.94 (0.86, 4.39)	0.112
Hazardous drinking scale score (8 point cut-off)								
abstinent	24 (33 %)	71 (33 %)	0.588	28 (40 %)	85 (40 %)	0.675	1	
<8 points	27 (37 %)	90 (42 %)		23 (31 %)	77 (36 %)		0.82 (0.34, 1.98)	0.656
≥8 points	22 (30 %)	52 (25 %)		20 (29 %)	51 (24 %)		1.66 (0.63, 4.36)	0.304
Current OST prescription								
No	35 (47 %)	86 (40 %)	0.199	45 (64 %)	86 (40 %)	**0.001***	1	
Yes	29 (53 %)	127 (60 %)		25 (36 %)	127 (60 %)		1.02 (0.49, 2.11)	0.952

Table 1 Analysis of recent sufficient and insufficient coverage at first and most recent interview *(Continued)*

BBV-TRAQ-SV injecting risk scale score (continuous measure)								
Mean	8.91	6.04	0.083	9.64	5.58	**0.022***	1.01 (0.98, 1.03)	0.652
Receptive sharing (past month)								
No	58 (78 %)	193 (91 %)	**0.006***	57 (81 %)	191 (90 %)	0.054	1	
Yes	16 (22 %)	20 (9 %)		13 (19 %)	21 (10 %)		1.01 (0.31, 3.36)	0.982
Injecting others (past month)								
No	56 (76 %)	173 (81 %)	0.343	60 (86 %)	184 (86 %)	0.888	1	
Yes	18 (24 %)	41 (19 %)		10 (14 %)	29 (14 %)		1.20 (0.47, 3.05)	0.699
Injected by others (past month)								
No	66 (89 %)	186 (87 %)	0.610	68 (97 %)	192 (90 %)	0.063	1	
Yes	8 (11 %)	28 (13 %)		2 (3 %)	21 (10 %)		0.32 (0.69, 1.50)	0.148
Injecting more than usual (past six months)								
No	45 (61 %)	133 (62 %)	0.838	38 (54 %)	144 (68 %)	**0.039***	1	
Yes	29 (39 %)	81 (38 %)		32 (46 %)	68 (32 %)		1.27 (0.59, 2.76)	0.541
Solitary injecting >80 % of the time								
No	48 (65 %)	152 (71 %)	0.321	52 (74 %)	154 (73 %)	0.788	1	
Yes	26 (35 %)	62 (29 %)		18 (26 %)	58 (27 %)		1.43 (0.64, 3.18)	0.384
Arrest (since last interview)								
No	28 (38 %)	109 (51 %)	**0.048***	31 (45 %)	114 (54 %)	0.202	1	
Yes	46 (62 %)	104 (49 %)		38 (55 %)	98 (46 %)		1.53 (0.70, 3.34)	0.281
HCV serology status								
Negative	6 (10 %)	43 (24 %)	**0.012***	6 (10 %)	19 (11 %)	0.607	1	
Positive	42 (70 %)	87 (49 %)		42 (68 %)	105 (61 %)		**4.44 (1.43, 13.73)**	**0.010***
Exposed	12 (20 %)	47 (27 %)		14 (22 %)	59 (28 %)		1.66 (0.46, 6.01)	0.436
NSP as usual source of syringe acquisition (past month)								
No	12 (16 %)	20 (9 %)	0.105	20 (29 %)	31 (15 %)	**0.008***	1	
Yes	62 (84 %)	194 (91 %)		50 (71 %)	182 (85 %)		**0.27 (0.09, 0.77)**	**0.015***

Regression number of observations: 215; Prob(chi^2): 0.12; R^2: 0.14
*Indicates statistically significant result at the <0.05 alpha level (bold data)
[a]Adjusted Odds Ratio, adjusted for all variables in the table

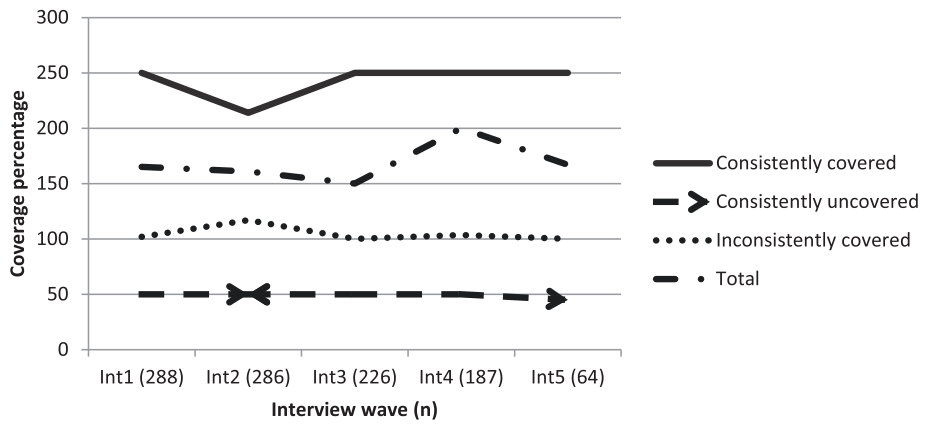

Fig. 2 Median coverage percentage across interview waves by coverage pattern groups

Table 2 Descriptive and logistic regression analysis of coverage pattern groups at first interview

	Consistently covered, *n* (%)	Consistently uncovered, *n* (%)	Inconsistently covered, *n* (%)	Chi squared *p*-value	AOR[a] at first interview, AOR (95 % CI)	AOR *p*-value
Sex						
Female	67 (41 %)	6 (35 %)	49 (34 %)	0.433	1	
Male	95 (59 %)	11 (65 %)	94 (66 %)		1.43 (0.72, 2.83)	0.311
Indigenous status						
No	152 (94 %)	14 (88 %)	136 (96 %)	0.361	1	
Yes	10 (6 %)	2 (12 %)	6 (4 %)		0.33 (0.07, 1.62)	0.172
WHO definition of youth						
≤24	22 (14 %)	2 (12 %)	28 (19 %)	0.321	1	
>24	140 (86 %)	15 (88 %)	115 (81 %)		1.50 (0.18, 1.37)	0.177
Highest level of education						
<yr10	53 (33 %)	6 (35 %)	36 (25 %)	0.613	1	
yr 10–11	64 (39 %)	6 (35 %)	66 (47 %)		1.73 (0.82, 3.62)	0.148
yr 12/higher educ/trade	45 (28 %)	5 (30 %)	40 (28 %)		2.14 (0.92, 5.01)	0.078
Employment status						
No	125 (77 %)	15 (88 %)	118 (83 %)	0.348	1	
Yes	37 (23 %)	2 (12 %)	25 (17 %)		0.91 (0.37, 2.23)	0.838
Weekly income						
<$400	109 (68 %)	10 (59 %)	101 (71 %)	0.581	1	
≥$400	52 (32 %)	7 (41 %)	42 (29 %)		1.01 (0.48, 2.13)	0.976
Stable accommodation						
No	21 (13 %)	2 (12 %)	22 (15 %)	0.801	1	
Yes	141 (87 %)	15 (88 %)	121 (85 %)		1.03 (0.44, 2.41)	0.946
Country of birth						
Other	24 (15 %)	5 (31 %)	29 (20 %)	0.169	1	
Australia	138 (85 %)	11 (69 %)	113 (80 %)		0.93 (0.38, 2.25)	0.873
Injecting career						
<13 years	58 (36 %)	8 (50 %)	71 (50 %)	**0.037***	1	
≥13 years	104 (64 %)	8 (50 %)	71 (50 %)		0.62 (0.30, 1.25)	0.181
Heroin injection (past month)						
No	41 (25 %)	2 (12 %)	24 (17 %)	0.120	1	
Yes	121 (75 %)	15 (88 %)	119 (83 %)		1.26 (0.47, 3.34)	0.645
Methamphetamine injection (past month)						
No	108 (67 %)	11 (65 %)	92 (64 %)	0.910	1	
Yes	54 (33 %)	6 (35 %)	51 (36 %)		0.93 (0.46, 1.87)	0.842
Hazardous drinking scale score (8 point cut-off)						
abstinent	53 (33 %)	5 (29 %)	41 (29 %)	0.827	1	
<8 points	69 (43 %)	9 (53 %)	62 (44 %)		1.17 (0.57, 2.40)	0.673
≥8 points	39 (24 %)	3 (18 %)	39 (27 %)		1.42 (0.59, 3.42)	0.437
Current OST prescription						
No	54 (33 %)	11 (65 %)	72 (50 %)	**0.002***	1	
Yes	108 (67 %)	6 (35 %)	71 (50 %)		**0.41 (0.22, 0.76)**	**0.005***
BBV-TRAQ-SV injecting risk scale score (continuous measure)						
Mean	6.03	9.88	5.96	0.293	0.97 (0.97, 1.02)	0.776

Table 2 Descriptive and logistic regression analysis of coverage pattern groups at first interview *(Continued)*

Receptive sharing (past month)						
No	150 (93 %)	12 (71 %)	124 (87 %)	**0.008***	1	
Yes	11 (7 %)	5 (29 %)	19 (13 %)		1.10 (0.36, 3.35)	0.865
Injecting others (past month)						
No	137 (85 %)	13 (76 %)	119 (83 %)	0.686	1	
Yes	25 (15 %)	4 (24 %)	24 (17 %)		0.97 (0.40, 2.32)	0.945
Injected by others (past month)						
No	145 (90 %)	16 (94 %)	128 (90 %)	0.830	1	
Yes	17 (10 %)	1 (6 %)	15 (10 %)		1.66 (0.44, 6.23)	0.452
Injecting more than usual (past six months)						
No	107 (66 %)	12 (71 %)	88 (62 %)	0.625	1	
Yes	54 (34 %)	5 (29 %)	54 (38 %)		1.55 (0.80, 3.00)	0.191
Solitary injecting >80 % of the time						
No	101 (67 %)	8 (50 %)	96 (71 %)	0.240	1	
Yes	50 (33 %)	8 (50 %)	40 (29 %)		0.99 (0.50, 1.96)	0.985
Arrest (since last interview)						
No	89 (55 %)	6 (35 %)	64 (45 %)	0.090	1	
Yes	45 (45 %)	11 (65 %)	79 (55 %)		1.28 (0.68, 2.40)	0.439
HCV serology status						
Negative	27 (21 %)	2 (17 %)	16 (14 %)	0.451	1	
Positive	65 (50 %)	8 (66 %)	68 (61 %)		**2.73 (1.12, 6.64)**	**0.027***
Exposed	37 (29 %)	2 (17 %)	28 (25 %)		2.31 (0.87, 6.13)	0.093
NSP as usual source of syringe acquisition (past month)						
No	14 (9 %)	4 (25 %)	18 (13 %)	0.149	1	
Yes	137 (91 %)	12 (75 %)	120 (87 %)		0.96 (0.36, 2.54)	0.933

Regression number of observations: 212; Prob(chi2): 0.25; R^2: 0.10
*Indicates statistically significant result at the <0.05 alpha level (bold data)
[a]Adjusted Odds Ratio, adjusted for all variables in the table

We identified a persistent association between coverage and OST prescription. Cross-sectionally, those with a current OST prescription had significantly higher proportions of sufficient coverage (an outcome Bluthenthal et al. [11] also identified), and longitudinally, current OST prescription was significantly associated with being in the "consistently covered" group. We suspect that the key driver here is the efficacy of OST in reducing opiate use [20, 25]. Receipt of OST has been shown to reduce the risk of HCV incidence amongst Australian heroin injecting PWID almost five-fold [26], whilst internationally, combined OST prescription with sufficient individual-level coverage (termed "full harm reduction") has been associated with an almost 80 % decrease in the risk of HCV acquisition [27]. The role of OST prescription in reducing HCV transmission is reflective of a reduction in injecting risk. Subsequently, the expansion of OST provision may play an important role in increasing coverage levels. Victorian OST services, however, are currently hampered by insufficient prescribers and inefficiencies in service co-ordination [28]. Increasing the numbers of PWID in receipt of OST would require strategies to overcome these barriers.

Though Australia's harm reduction provision is comprehensive, with at least one source of syringe distribution per 30 PWID [16], the proportions of insufficient coverage in this and similar Australian research [2, 12, 17] indicate ongoing shortfalls. One explanation is that the PWID population is dynamic and diverse. The variance in individual coverage is undoubtedly due to more factors than we've captured here (as evidenced by the regression model's low R^2 value). To appropriately account for this diversity, harm reduction services must be adaptive and flexible. Consequently, the acquisition of sterile syringes should be facilitated as much as possible by expanding hours of NSP operation and implementing novel methods of syringe distribution (such as syringe vending machines, which are not widely available in

Melbourne) [29–31]. NSPs are an efficacious, cost-effective means of limiting disease spread [14, 32, 33], and recent modelling suggests increases in service coverage would decrease BBV prevalence [34, 35].

Finally, research on individual coverage levels highlight the inadequacy of population-level measurements (such as the WHO measure). Though logistically difficult to determine, individual-level measurements capture the micro-details of coverage that are often diluted in population-wide averages. For example, at first interview in our cohort, 14,525 syringes were reportedly acquired by 338 currently injecting participants within the two weeks before interview, or an average of 43 syringes per person. If this average was multiplied by 26 to extrapolate to the total weeks in the year, this equals 1118 syringes per PWID, nearly six times the WHO recommendation for syringe distribution to curtail HIV spread [6]. However, it is clear that in aggregate, the PWID who cover their injecting episodes mask those who do not, and those who do not cover themselves are at most risk.

Limitations

To measure individual levels of coverage, separate parameters are required, all prone to reporting bias. Such a limitation is an unavoidable element of this field of study [11, 12]. However, PWID recall reliability has been demonstrated [36], and we chose the past two weeks as the recall period for the questions to minimise recall bias.

Recent research has shown that many PWID exploit Australia's unlimited dispensation policy and stockpile syringes for future use [17], meaning that participants who reported no past two-week syringe acquisition may still have been sufficiently covered. These findings came after MIX survey development and we were unable to account for stockpiling in our dataset. However, McCormack et al. found that the inclusion of a stockpiling question decreased levels of insufficient coverage (also using Bluthenthal et al.'s measure) by only eight percentage points (24 to 16 %) across their sample [17], so we are confident in the patterns we observed.

A substantial amount of coverage data was missing from our dataset. Approximately 45 % of our observations lacked coverage data, mostly (72 %) due to past week injection abstinence. However, the remaining 28 % of missing data was due to no reported syringe acquisition within the past two weeks and, with many of these participants also reporting injecting (sometimes in significant frequencies), syringe stockpiling was probably occurring. Therefore, we restricted analysis to those participants reporting both injecting and concurrent syringe acquisition.

Finally, our participants were recruited from a population with unknown parameters, limiting the generalisability of our findings [37].

Conclusion

We explored individual needle and syringe coverage longitudinally. We replicated previous Australian research and found substantial insufficient coverage amongst our group. This coverage shortfall is driven mainly by participants who cover themselves intermittently, suggesting the influence of temporal factors. Statistical analysis showed the protective effects of current OST prescription and NSPs as the main source of syringe acquisition, and an increased risk for those currently infected with HCV. An increase in OST coverage would potentially see a concurrent increase in syringe coverage, whilst more generally, to ensure PWID have every opportunity to avoid BBV infections and other injecting-related problems, the best response is the general expansion of NSP services.

Additional files

Additional file 1: Appendix 1. Demographic comparison between total and amended MIX samples at first interview. Comparative statistics between the full MIX cohort and the amended cohort used in this analysis. (DOCX 14 kb)

Additional file 2: Amended MIX questionnaire for longitudinal coverage analysis. Selected questions from the MIX questionnaire, relevant to the analysis within this article. Variables are presented in their original state, prior to data cleaning. (DOCX 22 kb)

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Availability of data and materials

Data cannot be shared for this study due to the highly confidential nature of the data, obtained from a vulnerable, marginalised population.

Authors' contributions

DO'K led the analysis and writing of the article. NS, CA & PD assisted with conceptualisation and provided essential input and support during analysis and writing. All authors have read the article and approve of its submission to BMC Health Services Research.

Competing interests

PD has received funding from Gilead Sciences Inc and Reckitt Benckiser for work unrelated to this study. Other authors have nothing to declare.

Consent for publication

Not applicable.

Ethics approval and consent to participate
The Victorian Department of Health Human Research Ethics Committee and the Monash University Human Research Ethics Committee approved the study. All participants provided informed consent to be involved in the study. Reference number 28/13.

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References

1. Jolley E, Rhodes T, Platt L, Hope V, Latypov A, Donoghoe M, et al. HIV among people who inject drugs in Central and Eastern Europe and Central Asia: a systematic review with implications for policy. BMJ Open. 2012;2(5).
2. Bryant J, Paquette D, Wilson H. Syringe coverage in an Australian setting: does a high level of syringe coverage moderate syringe sharing behaviour? AIDS Behav. 2012;16(5):1156–63.
3. Marshall BD, Shoveller JA, Wood E, Patterson TL, Kerr T. Difficulty accessing syringes mediates the relationship between methamphetamine use and syringe sharing among young injection drug users. AIDS Behav. 2011;15(7): 1546–53.
4. Pouget ER, Deren S, Fuller C, Blaney S, McMahon JM, Kang S, et al. Receptive syringe sharing among injection drug suers in Harlem and the Bronx during New York state expanded syringe access demonstration program. J Acquir Immune Defic Syndr Hum Retrovirol. 2005;39(4):471–7.
5. MacArthur GJ, van Velzen E, Palmateer N, Kimber J, Pharris A, Hope V, et al. Interventions to prevent HIV and Hepatitis C in people who inject drugs: a review of reviews to assess evidence of effectiveness. Int J Drug Policy. 2014;25(1):34–52.
6. WHO. Technical guide for countries to set targets for universal HIV services for injecting drug users. Geneva: World Health Organisation; 2012.
7. Burrows D. Advocacy and coverage of needle exchange programs: results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. Cad Saude Publica. 2006; 22(4):871–9.
8. Bluthenthal RN, Ridgeway G, Schell T, Anderson R, Flynn NM, Kral AH. Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. Addiction. 2007;102(4):638–46.
9. Walensky RP, Losina E, Malatesta L, Barton GE, O'Connor CA, Skolnik PR, et al. Effective HIV case identification through routine HIV screening at urgent care centers in Massachusetts. Am J Public Health. 2005;95(1):71–3.
10. Cooper HLF, Des Jarlais DC, Ross Z, Tempalski B, Bossak B, Friedman SR. Spatial access to syringe exchange programs and pharmacies selling over-the-counter syringes as predictors of drug injectors' use of sterile syringes. Res Pract. 2011;101(6):1118–25.
11. Bluthenthal RN, Anderson R, Flynn NM, Kral AH. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. Drug Alcohol Depend. 2007;89(2-3):214–22.
12. Iversen J, Topp L, Wand H, Maher L. Individual-level syringe coverage among Needle and Syringe Program attendees in Australia. Drug Alcohol Depend. 2012;122(3):195–200.
13. Shaw SY, Shah L, Jolly AM, Wylie JL. Determinants of injection drug user (IDU) syringe sharing: the relationship between availability of syringes and risk network member characteristics in Winnipeg, Canada. Addiction. 2007; 102(10):1626–35.
14. Wodak A, Cooney A. Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence. Subst Use Misuse. 2006;41(6-7):777–813.
15. Kwon JA, Anderson J, Kerr CC, Thein HH, Zhang L, Iversen J, et al. Estimating the cost-effectiveness of needle-syringe programs in Australia. AIDS. 2012; 26(17):2201–10.
16. IHRA. Global state of harm reduction. London, United Kingdon: International Harm Reduction Association, 2014.
17. McCormack A, Aitken C, Burns LA, Cogger S, Dietze P. Syringe stockpiling by people who inject drugs: an evaluation of current measures for needle and syringe program coverage. Am J Epidemiol. 2015;183(9):852-60.
18. Horyniak D, Higgs P, Jenkinson R, Degenhardt L, Stoove M, Kerr T, et al. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. Harm Reduction J. 2013;10(11).
19. Sacks-Davis R, Daraganova G, Aitken C, Higgs P, Tracy L, Bowden S, et al. Hepatitis C virus phylogenetic clustering is associated with the social-injecting network in a cohort of people who inject drugs. PLoS One. 2012;7(10):e47335.
20. Scott N, Caulkins JP, Ritter A, Dietze P. How patterns of injecting drug use evolve in a cohort of people who inject drugs. Trends & issues in crime and criminal justice. 2015;502:1-7.
21. O'Keefe D, Horyniak D, Dietze P. From initiating injecting drug use to regular injecting: Retrospective survival analysis of injecting progression within a sample of people who inject drugs regularly. Drug Alcohol Depend. 2015;158:177–80.
22. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. The alcohol use disorders identification test: guidelines for use in primary care. 2nd ed. Geneva: World Health Organisation; 2001.
23. Stoove M, Fry CL. The Blood Borne Virus Transmission Risk Assessment Questionnaire - Short Version (BBV-TRAQ-SV): Administration and Procedures Manual. Victoria: Turning Point Alcohol and Drug Centre Inc; 2006.
24. Palmateer N, Anderson N, Wadd S, Hutchinson S, Taylor A, Goldberg D. Exploring associations between perceived HCV status and injecting risk behaviors among recent initiates to injecting drug use in Glasgow. Subst Use Misuse. 2008;43(3-4):375–88.
25. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. J Subst Abuse Treat. 2005;28:321–9.
26. White B, Dore GJ, Lloyd AR, Rawlinson WD, Maher L. Opioid substitution therapy protects against hepatitis C virus acquisition in people who inject drugs: the HITS-c study. Med J Aust. 2014;201(6):326–9.
27. Turner KM, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011;106(11):1978–88.
28. King T, Ritter A, Berends L. Victorian Pharmacotherapy Review. Sydney: National Drug and Alcohol Research Centre; 2011.
29. Islam MM, Conigrave KM. Syringe vending machines as a form of needle syringe programme: advantages and disadvantages. J Substance Use. 2007; 12(3):203–12.
30. Wood E, Kerr T, Small W, Jones J, Schechter MT, Tyndall MW. The impact of police presence on access to needle exchange programs. J Acquir Immune Defic Syndr. 2003;34(1):116–7.
31. Islam MM, Conigrave KM. Assessing the role of syringe dispensing machines and mobile van outlets in reaching hard-to-reach and high-risk groups of injecting drug users (IDUs): a review. Harm Reduct J. 2007;4:14.
32. Strathdee SA, Vlahov D. The effectiveness of needle exchange programs: a review of the science and policy. AIDScience. 2001;1(16).
33. Laufer FN. Cost-effectiveness of syringe exchange as an HIV prevention strategy. J Acquir Immune Defic Syndr. 2001;28:272–8.
34. Vickerman P, Martin N, Turner K, Hickman M. Can needle and syringe programmes and opiate substitution therapy achieve substantial reductions in hepatitis C virus prevalence? Model projections for different epidemic settings. Addiction. 2012;107(11):1984–95.
35. Vickerman P, Hickman M, Rhodes T, Watts C. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. Epidemiol Soc Sci. 2006;42(3):355–61.
36. Darke S. Self-report among injecting drug users: a review. Drug Alcohol Depend. 1998;51:252–63.
37. Horyniak D, Stoove M, Degenhardt L, Aitken C, Kerr T, Dietze P. How do drug market changes affect characteristics of injecting initiation and subsequent patterns of drug use? Findings from a cohort of regular heroin and methamphetamine injectors in Melbourne, Australia. Int J Drug Policy. 2015;26(1):43–50.

2.3 Summary of Chapter Two

Paper One presents the first longitudinal examination of individual-level syringe coverage. Across interviews, I showed consistently high levels of insufficient individual-level syringe coverage (between 22%-36%), levels comparable with previous Australian cross-sectional samples (37, 123, 146). At initial interview, insufficient individual-level syringe coverage was significantly associated with HCV-positivity (RNA+) and the non- or inconsistent use of fixed-site NSPs as the usual source of syringe acquisition. Again, the latter result according with previous Australian research (123). Importantly, I categorised participants according to their longitudinal experience of individual-level syringe coverage, as either: "consistently covered" (50% of the sample), "consistently uncovered" (5%) and "inconsistently covered" (45%), meaning only 50% of the sample had consistently adequate individual-level syringe coverage. Those currently on OST had reduced odds of being categorised as "inconsistently covered", whilst those HCV-positive had increased odds of being categorised as such. Importantly, the large percentage of participants fluctuating between states of sufficient and insufficient individual-level syringe coverage suggests the influence of time-varying factors on the ability to cover one's injecting episodes. Alternatively, weaknesses in the measure may produce these variations, suggesting the need to strengthen the measure's accuracy.

There are numerous, varied barriers to syringe acquisition and many of these barriers may not be permanent. For example, PWID on OST may experience decreases in injecting frequency (13), thereby improving their individual-level syringe coverage. However, retention in OST may be temporary (161), meaning that if PWID are still injecting, once OST is stopped, injecting frequency may increase, and individual-level syringe coverage consequently decrease. Other impermanent barriers such as these may influence syringe coverage at certain points for certain individuals, resulting in temporary states of sufficient and insufficient individual-level syringe coverage.

The findings in this chapter suggest the need for further longitudinal analysis, whereby I specifically analyse the 45% of the sample experiencing individual-level syringe coverage fluctuations. In this manner, I seek to identify the time-varying covariates of

changes in individual-level syringe coverage, exploring the interpretation of temporal influences on individual-level syringe coverage more fully in Chapter Three.

Chapter Three: Exploring changes to individual-level needle and syringe coverage over time

3.1 Overview of Chapter Three

Approximately half the sample in Paper One fluctuated between states of sufficient and insufficient individual-level syringe coverage over time, suggesting time-varying factors, such as initiating injection of methamphetamine, or a new OST prescription may impact syringe coverage over time. However, Chapter Two explored longitudinal individual-level syringe coverage in only a descriptive manner. Chapter Three builds on this foundation to more fully explore transient changes in individual-level syringe coverage and how these may relate to transient changes in exposure.

Again using the MIX dataset, Paper Two directly expands the methodology of Paper One, by analysing data from the 152 participants classified as "inconsistently covered" (the sample slightly increased from Paper One due to the more recent dataset). Using time-varying covariates (e.g. housing status) Paper Two aimed to identify the temporal changes in the lives of PWID that may influence related changes to individual-level syringe coverage.

Paper Three explores how changes to the parameters included in the individual-level syringe coverage formula (*instances of syringe acquisition, total syringes acquired, peer-to-peer syringe distribution, injecting frequency)* (5, 123, 146) influences change in overall individual-level syringe coverage. These behaviours can vary between and within individuals over time, and these changes may exert different levels of influence on individual-level syringe coverage. Paper Three specifically tests and compares the effect size each individual-level syringe coverage parameter has upon individual-level syringe coverage overall, aiming to identify the parameter of greatest influence to help prioritise areas for intervention. For example, the key effect of OST is on injecting frequency (13). If individual-level syringe coverage is most influenced by injecting

frequency, then emphasising interventions that affect this variable should have the biggest impact on individual-level syringe coverage.

Finally, the individual-level syringe coverage formula has been implemented inconsistently across studies, with different parameters included in individual-level syringe coverage calculation. Establishing a consistent method of measuring individual-level syringe coverage, with an optimal collection of parameters, will facilitate the production of comparable individual-level syringe coverage estimates across settings and over time. In Paper Three, I explore the potential inclusion/exclusion of the variously utilised individual-level syringe coverage parameters, with the aim of improving and refining the individual-level syringe coverage measure.

The first manuscript presented in this chapter was published as:

O'Keefe D., Scott N., Aitken C., Dietze P. (2017) Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia, *Drug and Alcohol Dependence* 176: 7-13

The second manuscript presented in this chapter was published as:

O'Keefe D., Scott N., Aitken C., Dietze P. (2017) Assessing individual-level needle and syringe coverage parameters and the measurement of coverage in Melbourne, Australia: methods and impacts, *Journal of Public Health,* (epub ahead of print)

3.2 Publication: Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia

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Full length article

Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia

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ABSTRACT

Background: Needle and syringe program (NSP) coverage is often calculated at the individual level. This method relates sterile needle and syringe acquisition to injecting frequency, resulting in a percentage of injecting episodes that utilise a sterile syringe. Most previous research using this method was restricted by their cross-sectional design, calling for longitudinal exploration of coverage.

Methods: We used the data of 518 participants from an ongoing cohort of people who inject drugs in Melbourne, Australia. We calculated individual-level syringe coverage for the two weeks prior to each interview, then dichotomised the outcome as either "sufficient" (≥100% of injecting episodes covered by at least one reported sterile syringe) or "insufficient" (< 100%). Time-variant predictors of change in recent coverage (from sufficient to insufficient coverage) were estimated longitudinally using logistic regression with fixed effects for each participant.

Results: Transitioning to methamphetamine injection (AOR:2.16, p = 0.004) and a newly positive HCV RNA test result (AOR:4.93, p = 0.001) were both associated with increased odds of change to insufficient coverage, whilst change to utilising NSPs as the primary source of syringe acquisition (AOR: 0.41, p = 0.003) and opioid substitution therapy (OST) enrolment (AOR:0.51, p = 0.013) were protective against a change to insufficient coverage.

Conclusions: We statistically tested the transitions between time-variant exposure sub-groups and transitions in individual-level syringe coverage. Our results give important insights into means of improving coverage at the individual level, suggesting that methamphetamine injectors should be targeted, whilst both OST prescription and NSP should be expanded.

1. Introduction

Needle and syringe program (NSP) coverage is often calculated at the individual level, according to the method devised by Bluthenthal et al. (2007a). This method relates sterile needle and syringe (hereafter "syringe/s") acquisition to injecting frequency, resulting in a percentage of injecting episodes that utilise a sterile syringe. Compared to population-level measurements, such as those proposed by UNAIDS (Burrows, 2006a) and the WHO (WHO, 2011), which often distort coverage estimates via aggregation, individual-level measures of syringe coverage capture the individual risk elements of people who inject drugs (PWID) and rightly consider PWID as a heterogeneous population.

Previous research on individual-level coverage amongst PWID using Bluthenthal et al.'s measure (Bluthenthal et al., 2007a; Bryant et al., 2012; Iversen et al., 2012; McCormack et al., 2016; Noroozi et al., 2015; O'Keefe et al., 2016) shows consistent findings that opioid substitution therapy (OST) prescription and the utilisation of NSPs as a source of syringe acquisition (as opposed to acquiring syringes from pharmacies or informal sources such as friends/partners/dealers) are associated with sufficient coverage (defined as ≥100% of injecting episodes that utilise a sterile syringe) (Bryant et al., 2012; Iversen et al., 2012; O'Keefe et al., 2016). Insufficient coverage (< 100%) has been associated with receptive syringe sharing, syringe reuse, increased injecting frequency and hepatitis C virus (HCV) infection (Bluthenthal et al., 2007a; Bryant et al., 2012; Iversen et al., 2012; Noroozi et al., 2015; O'Keefe et al., 2016). However, most of these studies were restricted by their cross-sectional designs, and their inferences subsequently limited by only a single point of observation.

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The need to analyse individual-level coverage longitudinally was identified by Bluthenthal et al. in their original 2007 paper (Bluthenthal et al., 2007a). Whilst they made specific reference to the causal association between syringe dispensation policy and coverage, the cross-sectional associations found in other research show that there are many causative paths to low coverage. For example, levels of service funding (Burrows, 2006b), syringe dispensation policy (Bluthenthal et al., 2007b), aggressive police operations (Cooper et al., 2005; Wood et al., 2003), geographic proximity to services (Cooper et al., 2012), hours of operation (Wood et al., 2002) and injecting network characteristics (Bryant et al., 2012) have been shown to impact upon service access and therefore, coverage. Longitudinal analysis is required to identify temporal factors that influence an individual's ability to achieve sufficient coverage. The results of such analysis would enable the design of policies that minimise exposure to any detrimental factors.

We previously described the longitudinal characteristics of individual-level syringe coverage amongst a cohort of PWID in Melbourne, Australia. We showed that many participants in the Melbourne Injecting Drug User Cohort (MIX) study (Horyniak et al., 2013) fluctuated between states of sufficient and insufficient coverage over time (O'Keefe et al., 2016) and that at each interview wave between 22% and 36% of the cohort reported insufficient coverage, percentages similar to those found in other cross-sectional Australian research (Bryant et al., 2012; Iversen et al., 2012; McCormack et al., 2016). However, we did not examine factors associated with these fluctuations. Such an examination is needed, as 45% of the sample oscillated between states of sufficient and insufficient coverage over time, suggesting the presence of temporal mediators of the ability to adequately cover injecting episodes (O'Keefe et al., 2016). These can be identified using a fixed effects regression analysis, which controls for individual characteristics and measures only associations between changes in temporal variables and changes in coverage (Scott et al., 2016).

In this study, we expand upon our previous analysis and explore the temporal factors of change in syringe coverage (from sufficient to insufficient coverage). We analysed seven years of data from an ongoing cohort of PWID in Melbourne, Australia, aiming to:

- describe and analyse the longitudinal successions between states of sufficient and insufficient coverage; and
- identify time-varying predictors of change between states of sufficient and insufficient coverage via logistic regression using fixed effects to control for individual characteristics.

2. Methods

Our data come from the MIX study, which has been described in detail elsewhere (Horyniak et al., 2013). Briefly, participants are administered an annual, structured questionnaire with blood sample testing for HIV, HCV and hepatitis B virus. Recruitment of the original 688 MIX participants occurred between 2008 and 2010, though an additional 69 participants were included in the cohort in 2011 via past involvement in the Networks II cohort (Sacks-Davis et al., 2012), resulting in 757 participants. Both MIX and Networks II sought to recruit PWID who injected regularly. The characteristics of the cohorts at baseline (2005 for Networks II) were comparable (Scott et al., 2016).

Eligibility criteria for the original MIX cohort were being aged 18–30 years and reporting injecting of heroin and/or methamphetamine regularly (at least once a month in the six months prior to recruitment).

2.1. Participant sample

The most recently available MIX dataset (May 2016) includes 3312 interviews over nine interview waves. Coverage questions were not introduced into the MIX questionnaire until June 2010. Consequently, all interviews prior to this date (902 interviews, including 176 participants who were not interviewed after June 2010) were excluded from analysis. Due to the longitudinal nature of this study, we further excluded those participants with only one interview after June 2010 (63 interviews, 63 participants). The final, amended dataset consisted of 518 participants and 2347 interviews across a maximum of seven separate interview waves, occurring between June 2010 and May 2016. Attrition was low, with 88% of remaining participants completing at least three interviews within the amended dataset, and a mean 1851 (range: 308, 2889) days of study time within our sample, equivalent to a mean 5.1 years.

The exclusion process is described in Fig. 1.

2.2. Coverage parameters

The MIX questionnaire includes the following questions to record the three primary coverage parameters (syringe acquisition, peer-to-peer syringe distribution and injecting frequency):

*"In the last **two weeks** how many new (needles and) syringes in total did you get?"*

*"In the last **two weeks** how many new (needles and) syringes did you give away or sell to others?"*

Past week injecting frequencies for 18 different drug types were

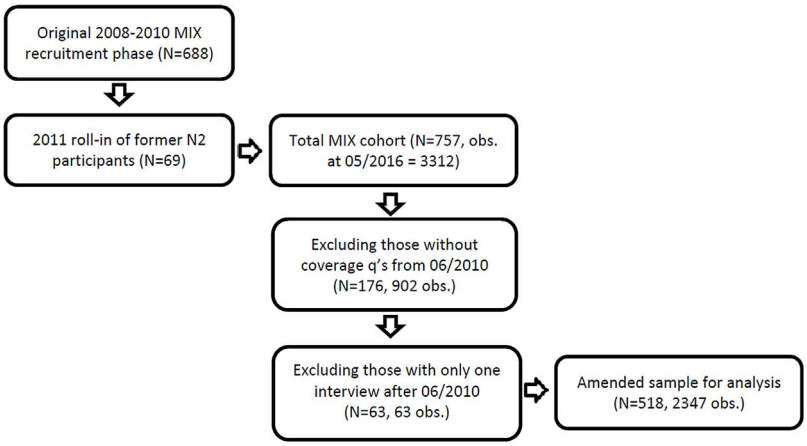

Fig. 1. The initial 2008–2010 MIX cohort recruitment phase (N = 688) and the additional roll-in of former N2 participants in 2011 (N = 69), gave a total of 757 participants. Our sample first excluded those without an interview after June 2010 (after introducing necessary coverage questions, N = 176), then excluded those with only one interview after June 2010 (inappropriate for longitudinal analysis, N = 63), leaving a final amended sample of 518 participants and 2347 longitudinal observations.

summed to create a total injecting frequency variable. Responses to each question were recorded as continuous variables.

2.3. Calculating coverage

As the questions regarding injecting frequency relate to the previous week, and coverage parameters relate to the previous two weeks, injecting frequency was multiplied by two to create a consistent time frame for coverage measurement. Injecting frequency was doubled rather than halving syringe acquisition, as initial inspection of the data showed less variance in injecting frequency, suggesting a more consistent practice.

We adapted the Bluthenthal et al. (Bluthenthal et al., 2007a) method of calculating individual-level syringe coverage. The number of syringes distributed was subtracted from the number of syringes acquired. The difference was divided by the past-two-week estimate of injecting frequency and then multiplied by 100, giving a percentage of injecting episodes utilising a sterile syringe. The coverage formula is presented below:

$$\frac{(syringes\ acquired - syringes\ distributed)}{(past\ week\ injecting\ frequency\ x\ 2)} x100$$

Though we calculated coverage as a continuous measure, we treated it as a dichotomous outcome, in line with much previous research (Allen et al., 2012; Bryant et al., 2012; Iversen et al., 2012; McCormack et al., 2016; Noroozi et al., 2015; O'Keefe et al., 2016; Palmateer et al., 2014). We considered recent individual coverage to be sufficient (≥100%) if every injecting episode was covered by at least one reported sterile syringe. Anything less than 100% coverage was considered insufficient. A dichotomous variable "recent coverage" (≥100% coverage/ < 100% coverage) was created and applied to each interview with valid data, classifying participants as either sufficiently or insufficiently covered for the two weeks prior to interview.

Coverage was only calculated for participants with valid data for each coverage parameter and those who reported both syringe acquisition and injecting within the two-week period (as the absence of injecting precluded calculation of coverage, whilst injecting with the complete absence of syringe acquisition was likely to be influenced by syringe stockpiling—see limitations). Forty-four per cent of all coverage responses (1029 observations) were missing. Of these missing data, most (735 observations, 71% of all missing responses) were due to injecting abstinence. A further 262 coverage observations were missing as a result of no syringe acquisition in the two weeks prior to interview reported by participants who nonetheless reported injecting (25% of all missing responses). The remaining 4% of missing coverage responses were due to missing/invalid data in any of the three coverage variables.

2.4. Defining successions in dichotomous coverage and exposure sub-groups

We explored the changes in dichotomous coverage and exposure sub-groups over time by what we termed "successions". We defined a succession of coverage observations, or a succession of exposure sub-group observations, as a pair of consecutive non-missing observations from the same participant. This definition was used even if the consecutive non-missing data were separated by one or more interviews (meaning that, if observation x occurred at interview one, whilst the next non-missing observation (observation x + 1) did not occur until interview four, this was still considered a valid succession). Individual participants were able to have more than one succession. We adopted this definition as it coincides with the workings of our fixed effects regression model described below.

The potential number of successions for the exposure sub-groups was greater than that for the dichotomous coverage successions as there was less missing data for the sub-group variables.

2.5. Statistical analysis

Predictors of change in recent coverage were estimated using logistic regression with fixed effects for each participant. The model estimates the odds of change in an outcome according to change in an exposure variable, and therefore focuses only on time-variant exposure variables (those variables that can change from one interview to another, as opposed to time-invariant variables, such as "country of birth") that have a logical association with syringe coverage or have been identified in previous research. Due to the longitudinal nature of the data, the model uses participants as their own controls and accounts for those time-invariant factors, both measured and unmeasured (Scott et al., 2016).

Moreover, as the model estimates the odds of change in an outcome according to change in an exposure variable, only those participants who experienced a change from sufficient to insufficient coverage (or vice versa) across interviews were included in the analysis (n = 179). Adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) were calculated, with change from sufficient to insufficient coverage being the outcome of interest. Significance was set at $p < 0.05$.

Time-variant exposure sub-groups included: " current employment status" (unemployed/employed), "current stable accommodation" (no/yes), "heroin injection (past month)" (no/yes), "methamphetamine injection (past month)" (no/yes), "current OST prescription" (no/yes), "NSP as usual source of syringe acquisition (past month)" (no/yes), "injecting more than usual (since last interview)" (no/yes), "injecting alone in the past month (≥80% of the time)" (no/yes), "receptive syringe sharing (past month)" (no/yes), "current HCV RNA status" (not detected/detected), and "recent arrest (since last interview)" (no/yes).

3. Results

3.1. Participant demographics

At first interview, the amended sample of 518 participants was predominantly male (64%), Australian-born (81%), non-Indigenous (95%), unemployed (78%) and living in stable accommodation (85%). Their average age was 30 years at first interview and, for those reporting any injecting in the month prior to interview (n = 429), 73% reported injecting predominantly heroin, followed by 11% reporting injecting predominantly methamphetamine.

3.2. Individual-level syringe coverage

Median continuous coverage at first and most recent interview was 162% (IQR: 88–350%) and 158% (IQR: 83–321%) respectively. Though levels of aggregate, continuous coverage were very high, when coverage was dichotomised, 27% and 26% of the sample were insufficiently covered at their first and most recent interview respectively.

Across all 2347 interviews, in the two weeks prior to interview, those participants who reported injecting collected a median 15 syringes (IQR: 5–70), distributed a median of zero syringes (IQR: 0–10), and collected syringes from any source a median of one time (IQR: 1–3). The median reported number of past-week injections was five (IQR: 2–12), a frequency in accordance with the Australian national PWID surveillance survey, the Illicit Drug Reporting System (Stafford and Burns, 2016). Coverage statistics for those reporting past month injecting at each interview wave are presented in Table 1.

Of those with at least two points of valid recent coverage data, 161 participants (45%) were consistently sufficiently covered (≥100% across all interviews), 14 participants (4%) were consistently insufficiently covered (< 100% across all interviews) and 179 participants (51%) fluctuated between states of sufficient and insufficient coverage across interviews. These percentages are comparable to results from our previous coverage article (O'Keefe et al., 2016) (which focused on an older and smaller dataset). The newer dataset, including more inter-

Table 1
Coverage parameter statistics across interview waves for those reporting injecting.

Int. wave	Total n	Median syringes acquired	Median syringes distributed	Median injections (past two weeks)	Insufficient coverage (%)[a]
1	518	20	0	10	27%
2	518	18	0	10	22%
3	455	14	0	8	29%
4	387	20	0	10	23%
5	289	20	2	10	31%
6	160	10	1	8	26%
7	20	20	2	8	25%

[a] Of those with valid coverage data.

views per participant, meant more participants were classified as fluctuating between states of coverage (45% of participants were previously classified as such).

3.3. Successions in longitudinal coverage

Table 2 presents the number of successions among the 179 participants who experienced at least one coverage fluctuation across the study period (i.e., the participants with the potential for regression model inclusion).

From a total of 483 successions of coverage observations, in 155 successions (32% of total successions) participants remained sufficiently covered from an initial state of sufficient coverage. In 48 successions (10%), participants remained insufficiently covered from an initial state of insufficient coverage.

Of the 280 successions (58%) in which participants changed coverage levels between interviews, approximately half (142) were from insufficient to sufficient coverage and half (138) were from sufficient to insufficient coverage. This highlights the fact that cross-sectional analyses can miss significant underlying individual variation.

3.4. Fixed effects regression

The fixed effects model comprised 530 observations from 152 unique individuals. The average number of observations per individual was 3.5. The mean days within the study of those experiencing transition in coverage over time was 1940 days (range: 308, 2607) or approximately 5.31 years of study time.

Several time-variant exposures were associated with a change in dichotomous recent coverage. A change in past month methamphetamine injection (from abstinence to injection) was associated with 2.16 (95% CIs: 1.28, 3.66) times the odds of experiencing change in recent coverage (from sufficient to insufficient coverage, see Table 3). Similarly, a new positive HCV RNA test result (following a negative HCV RNA result) was associated with increased odds of a recent coverage change (AOR: 4.93, 95% CIs: 1.96, 12.39).

Table 2
Successions of coverage observations between interviews.

		no. of successions, (% of total)		
		Subsequent state of coverage (observation x + 1)		
		< 100%	≥100%	Total
'Initial' state of coverage (observation x)	< 100%	48 (10%)	142 (29%)	190
	≥100%	138 (29%)	155 (32%)	293
	Total	186	297	483 (100%)

Table 3
Longitudinal sub-group successions and fixed effects regression testing associations with change to insufficient coverage.

Initial state of sub-group in succession (observation x)	Subsequent state of sub-group in succession (observation x + 1) Number (% of total successions)		Regression AOR (95% CI)	Regression AOR p-value
Current employment status				
	unemployed	*employed*		
unemployed	471 (67)	72 (10)	1	
employed	73 (10)	92 (13)	1.40 (0.78, 2.50)	0.260
Current stable accommodation				
	no	*yes*		
no	68 (9)	61 (9)	1	
yes	77 (11)	502 (71)	0.76 (0.42, 1.39)	0.379
Heroin injection (past month)				
	no	*yes*		
no	97 (14)	61 (9)	1	
yes	68 (9)	482 (68)	0.86 (0.41, 1.84)	0.704
Methamphetamine injection (past month)				
	no	*yes*		
no	276 (39)	118 (17)	1	
yes	98 (14)	216 (30)	2.16 (1.28, 3.66)	**0.004**
Current OST prescription				
	no	*yes*		
no	220 (31)	82 (11)	1	
yes	90 (13)	316 (45)	0.51 (0.30, 0.87)	**0.013**
NSP as usual source of syringe acquisition (past month)				
	no	*yes*		
no	37 (6)	72 (11)	1	
yes	81 (13)	438 (70)	0.41 (0.23, 0.73)	**0.003**
Injecting more than usual (since last interview)				
	no	*yes*		
no	351 (51)	122 (17)	1	
yes	132 (19)	89 (13)	1.18 (0.74, 1.88)	0.498
Injecting alone in the past month (≥80% of the time)				
	no	*yes*		
no	367 (57)	95 (15)	1	
yes	100 (15)	82 (13)	1.05 (0.64, 1.71)	0.859
Receptive syringe sharing (past month)				
	no	*yes*		
no	481 (76)	59 (9)	1	
yes	58 (9)	34 (6)	1.55 (0.82, 2.94)	0.176
Current HCV RNA status				
	not detected	*detected*		
not detected	192 (34)	24 (4)	1	
detected	21 (4)	334 (58)	4.93 (1.96, 12.39)	**0.001**
Recent arrest (since last interview)				
	no	*yes*		
no	254 (36)	111 (16)	1	
yes	128 (18)	214 (30)	1.46 (0.91, 2.35)	0.118

No. of observations in regression model: 530.
No. of groups in regression model: 152.
Average observations per group: 3.5 (min:2, max:7).
Regression model prob: < 0.0001.
Statistically significant regression results in bold.

Change to utilising NSPs as the primary source of syringe acquisition (previously acquiring syringes from pharmacies or friends/partners/dealers) reduced the odds of a change to insufficient coverage (AOR: 0.41, 95% CIs: 0.23, 0.73), as did OST enrolment (AOR: 0.51, 95% CIs: 0.30, 0.87).

4. Discussion

In this paper we tested a range of potential time-variant predictors of longitudinal change between states of sufficient and insufficient individual-level needle and syringe coverage. Although cross-sectional research has determined factors that identified groups of individuals who are more likely to experience insufficient coverage, we found that a transition to recent reporting of methamphetamine injection or HCV RNA infection were associated with increases in the odds of changing from sufficient to insufficient coverage, whilst enrolling in OST or NSPs becoming the most common source of syringe acquisition were associated with a decrease in the odds of changing from sufficient to insufficient coverage.

Individual-level syringe coverage is affected by injecting frequency. Whilst the potential exists for Australian PWID to sufficiently cover their injecting episodes no matter how frequently they may inject, higher injecting frequencies have been associated with lower coverage (Bryant et al., 2012). The efficacy of OST prescription in reducing injecting frequency amongst opioid users is well established (Amato et al., 2005), and the cross-sectional association between current OST prescription and sufficient coverage was supported in both our previous work (O'Keefe et al., 2016) and in the work of others (Iversen et al., 2012). Between 51% and 62% of our participants were being prescribed OST at any given interview. At most recent interview, 20% of those being prescribed OST were insufficiently covered, compared to 32% of those not being prescribed OST. Approximately 48,500 Australian PWID are prescribed OST (Department of Health and Human Services, 2016), representing half the country's estimated PWID population (IHRA, 2014). Though OST may not be suitable for or desired by many PWID (e.g., those primarily injecting stimulants), it represents an immediate means of improving individual-level syringe coverage via reduced injecting frequency.

Similarly, NSPs are an efficacious and cost-effective method of providing sterile injecting equipment to PWID and reducing BBV transmission (Kwon et al., 2012; Strathdee and Mailman, 2001; Wodak and Cooney, 2006). The reduced odds of change to insufficient coverage in our regression model validates NSPs as a harm reduction intervention and highlights the benefits of providing a free, low-threshold service. However, though most participants in our sample (84% of all those observations also reporting past month injecting) reported using NSPs as their main source of syringe acquisition, many participants reported acquiring syringes from pharmacies and informal sources. There are many reasons why PWID might not utilise formal, fixed-site NSPs (Aitken et al., 2002; Reid et al., 2001; Treloar et al., 2010), even if this means having to pay for their syringes or rely on potentially inconsistent sources (such as friends/partners/dealers). PWID should be provided with every opportunity to acquire sterile syringes and injecting equipment, whenever and wherever it may be needed, ideally via 24-hour NSP services. However, barring this, syringe vending machines (SVMs) are a cost-effective means of increasing syringe distribution, particularly outside of normal NSP operating hours (Islam et al., 2008; McDonald, 2009). Furthermore, research has suggested that SVMs service populations different from those accessing NSPs (Islam and Conigrave, 2007; Wodak and Cooney, 2006). At the time of writing, only five SVMs operate in Melbourne. Expanding the number of syringe outlets should assist in raising overall coverage.

The association between change to HCV positivity and change to insufficient coverage is potentially subject to temporal mismatches. Whilst our coverage variable measured coverage within the past two weeks, blood taken at the time of interview may be HCV positive as a result of a transmission incident at any time between interviews (in some instances, an interval of years). This makes identifying the direction of association between HCV positivity and coverage difficult. It may be that past two week insufficient coverage is indicative of long-term behaviour, involving relatively high injecting risk and increased cumulative hazard of BBV infection. However, an alternate interpretation is that some HCV-positive PWID do not adequately cover their injecting episodes. Whatever the direction of the association, it is important to acknowledge the consequences of this finding. The sharing of unsterile syringes is the main driver of BBV transmission amongst PWID (Palmateer et al., 2010; Wodak and McLeod, 2008), and low levels of syringe coverage promote this transmission route. Furthermore, injecting risk amongst those unaware of their BBV status is greater than amongst those who know their positive/negative BBV status (Kwiatkowski et al., 2002; Palmateer et al., 2008), which may be the case for those recently infected. Whilst the strong uptake (Kirby Institute, 2016) of new direct-acting antiviral treatment for HCV is likely to reduce the transmission and prevalence of HCV amongst Australian PWID, incidence and reinfection may persist in a contingent of the PWID population without parallel increases in coverage.

Finally, the transition to methamphetamine injection in the month prior to interview increased the odds of transitioning to insufficient coverage. The drug use transition, though not necessarily for all participants, may indicate a change in drug use patterns. From first to most recent interview, the percentage of participants within our sample who reported methamphetamine as the most commonly injected drug within the past month rose from 11% to 24%. If the adoption of methamphetamine injection leads to lower coverage levels, as suggested by our model, it would be prudent for harm reduction services to try to increase syringe distribution amongst this subgroup. Furthermore, recent Canadian research with street-involved youth showed an association between methamphetamine injection and phylogenetic clustering of HCV (Cunningham et al., 2015), supporting our finding that methamphetamine injectors display greater injecting risk, and therefore require interventional targeting.

4.1. Limitations

Measurement of syringe coverage relies on participant recall, which may introduce bias to our estimates. However, the reliability and validity of PWID recall has previously been demonstrated (Darke, 1998) and is likely to be small given the time frame in question was the past two weeks.

Unlimited NSP dispensation policy across much of Australia means many PWID may "stockpile" syringes (store additional sterile syringes for later use (McCormack et al., 2016)). The importance of stockpiling was highlighted in 2016, after construction of the MIX questionnaire, explaining the absence of syringe stockpiling as a parameter in our coverage formula. Whilst more recent iterations of the MIX questionnaire include a question about syringe stockpiling, this remains a limitation of the current study.

As previously noted, our outcome of syringe coverage was estimated for the two weeks prior to interview, whilst some of our exposure subgroups (arrest since last interview, injecting more than usual, HCV RNA detection) indicate longitudinal changes that potentially occurred long before this two-week period. Furthermore, our variables (including the coverage outcome) may indicate a change that occurred well before the captured timeframe and then persisted up until the point of interview. Because of these differences in temporality between the outcome and exposures the inference of a sequence of events is somewhat indefinite, and the model better thought of as indicating the association between change in one variable with change in another, regardless of the direction of association. An example of this is the association between the change in coverage and change in HCV status previously discussed.

Not all parameters in the coverage measure occur commensurately.

For example, PWID may inject daily, yet only acquire syringes (and then stockpile) once a month. Our two-week time period may therefore have missed instances of particular coverage behaviours. Future research needs to determine the most appropriate timeframe to both capture what may be relatively infrequent behaviours (such as syringe acquisition), whilst also lessening the impact of recall bias.

Finally, missing data was common. Forty-four per cent of all coverage responses were classified as missing (mostly due to injecting abstinence). However, the longitudinal regression model tests the transition to the next valid data point, meaning that the prevalence of missing data did not affect the model.

4.2. Conclusions

We statistically tested the transitions between time-variant exposure sub-groups and transitions in individual-level syringe coverage. The regression model showed that a transition to recent methamphetamine injection or a newly detected HCV infection increased the odds of a transition to insufficient syringe coverage, whilst enrolment in an OST program or NSPs becoming the main source of syringe acquisition decreased the odds of a similar transition. Whilst these results accord with findings from previous cross-sectional research, the longitudinal methodology adopted here controls for unmeasured characteristics over time, and therefore provides a more robust analysis.

Our results give important insights into means of improving coverage at the individual level. Targeting those who inject methamphetamine and increasing rates of OST prescription amongst suitable PWID should assist individuals to sufficiently cover their injecting episodes. Furthermore, our model validated formalised NSPs as the most effective means of syringe distribution. These services should be expanded both in quantity and quality in order to maximise coverage and to ensure that PWID can acquire sterile needles and syringes wherever and whenever they require them.

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Contributors

DO'K led the analysis and writing of the article. NS, CA and PD assisted with conceptualisation and provided essential input and support during analysis and writing. All authors have read the article and approve of its submission to Drug and Alcohol Dependence.

Conflict of interest

PD has received funding from Gilead Sciences Inc. and Reckitt Benckiser for work unrelated to this study. The other authors have nothing to declare.

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References

Aitken, C., Moore, D., Higgs, P., Kelsall, J., Kerger, M., 2002. The impact of a police crackdown on a street drug scene: evidence from the street. Int. J. Drug Policy 13, 193–202.
Allen, E.J., Palmateer, N.E., Hutchinson, S.J., Cameron, S., Goldberg, D.J., Taylor, A., 2012. Association between harm reduction intervention uptake and recent hepatitis C infection among people who inject drugs attending sites that provide sterile injecting equipment in Scotland. Int. J. Drug Policy 23, 346–352.
Amato, L., Davoli, M., Perucci, C.A., Ferri, M., Faggiano, F., Mattick, R.P., 2005. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. J. Subst. Abuse Treat. 28, 321–329.
Bluthenthal, R.N., Anderson, R., Flynn, N.M., Kral, A.H., 2007a. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. Drug Alcohol Depend. 89, 214–222.
Bluthenthal, R.N., Ridgeway, G., Schell, T., Anderson, R., Flynn, N.M., Kral, A.H., 2007b. Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. Addiction 102, 638–646.
Bryant, J., Paquette, D., Wilson, H., 2012. Syringe coverage in an Australian setting: does a high level of syringe coverage moderate syringe sharing behaviour? AIDS Behav. 16, 1156–1163.
Burrows, D., 2006a. Rethinking coverage of needle exchange programs. Subst. Use Misuse 41, 1045–1048.
Burrows, D., 2006b. Advocacy and coverage of needle exchange programs: results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. Cad. Saude Publica 22, 871–879.
Cooper, H., Moore, L., Gruskin, S., Krieger, N., 2005. The impact of a police drug crackdown on drug injectors' ability to practice harm reduction: a qualitative study. Soc. Sci. Med. 61, 673–684.
Cooper, H., Des Jarlais, D., Ross, Z., Tempalski, B., Bossak, B.H., Friedman, S.R., 2012. Spatial access to sterile syringes and the odds of injecting with an unsterile syringe among injectors: a longitudinal multilevel study. J. Urban Health 89, 678–696.
Cunningham, E.B., Jacka, B., DeBeck, K., Applegate, T.L., Harrigan, P.R., Krejden, M., Marshall, B.D.L., Montaner, J., Dias Lima, V., Olmstead, A.D., Milloy, M., Wood, E., Grebely, J., 2015. Methamphetamine injecting is associated with phylogenetic clustering of hepatitis C virus infection among street-involved youth in Vancouver, Candada. Drug Alcohol Depend. 152, 272–276.
Darke, S., 1998. Self report among injecting drug users: a review. Drug Alcohol Depend. 51, 253–263.
Department of Health and Human Services, 2016. Policy for Maintenance Pharmacotherapy for Opioid Dependence. Victoria, Australia.
Horyniak, D., Higgs, P., Jenkinson, R., Degenhardt, L., Stoove, M., Kerr, T., Hickman, M., Aitken, C., Dietze, P., 2013. Establishing the Melbourne injecting drug user cohort study (MIX): Rationale, methods, and baseline and twelve-month follow-up results. Harm Reduct. J. 10.
IHRA, 2014. Global State of Harm Reduction Report, 2014. London, United Kingdom.
Islam, M.M., Conigrave, K.M., 2007. Syringe vending machines as a form of needle syringe programme: advantages and disadvantages. J. Subst. Use 12, 203–212.
Islam, M., Wodak, A., Conigrave, K.M., 2008. The effectiveness and safety of syringe vending machines as a component of needle syringe programmes in community settings. Int. J. Drug Policy 19, 436–441.
Iversen, J., Topp, L., Wand, H., Maher, L., 2012. Individual-level syringe coverage among Needle and Syringe Program attendees in Australia. Drug Alcohol Depend. 122, 195–200.
Kirby Institute, 2016. Monitoring Hepatitis C Treatment Uptake in Australia (September 2016). Melbourne, Australia.
Kwiatkowski, C.F., Corsi, K.F., Booth, R.E., 2002. The association between knowledge of hepatitis C virus status and risk behaviours in injection drug users. Addiction 97, 1289–1294.
Kwon, J.A., Anderson, J., Kerr, C.C., Thein, H.H., Zhang, L., Iversen, J., Dore, G.J., Kaldor, J.M., Law, M.G., Maher, L., Wilson, D.P., 2012. Estimating the cost-effectiveness of needle-syringe programs in Australia. AIDS 26, 2201–2210.
McCormack, A., Aitken, C., Burns, L.A., Cogger, S., Dietze, P., 2016. Syringe stockpiling by people who inject drugs: an evaluation of current measures for needle and syringe program coverage. Am. J. Epidemiol. 183, 852–860.
McDonald, D., 2009. The evaluation of a trial of syringe vending machines in Canberra, Australia. Int. J. Drug Policy 20, 336–339.
Noroozi, M., Mirzazadeh, A., Noroozi, A., Mehrabi, Y., Hajebi, A., Zamani, S., Sharifi, H., Higgs, P., Soori, H., 2015. Client level coverage of needle and syringe program and high risk injection behaviours: a case study of people who inject drugs in Kermanshah, Iran. Addict. Health 7, 164–173.
O'Keefe, D., Scott, N., Aitken, C., Dietze, P., 2016. Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis. BMC Health Serv. Res. 16, 411.
Palmateer, N., Anderson, N., Wadd, S., Hutchinson, S., Taylor, A., Goldberg, D., 2008. Exploring associations between perceived HCV status and injecting risk behaviors among recent initiates to injecting drug use in Glasgow. Subst. Use Misuse 43, 375–388.
Palmateer, N., Kimber, J., Hickman, M., Hutchinson, S., Rhodes, T., Goldberg, D., 2010. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews. Addiction 105, 844–859.

Palmateer, N.E., Taylor, A., Goldberg, D.J., Munro, A., Aitken, C., Shepherd, S.J., McAllister, G., Gunson, R., Hutchinson, S.J., 2014. Rapid decline in HCV incidence among people who inject drugs associated with national scale-up in coverage of a combination of harm reduction interventions. PLoS One 9, e104515.

Reid, G., Crofts, N., Beyer, L., 2001. Drug treatment services for ethnic communities in Victoria, Australia: an examination of cultural and institutional barriers. Ethn. Health 6, 13–26.

Sacks-Davis, R., Daraganova, G., Aitken, C., Higgs, P., Tracy, L., Bowden, S., Jenkinson, R., Rolls, D., Pattison, P., Robins, G., Grebely, J., Barry, A., Hellard, M., 2012. Hepatitis C virus phylogenetic clustering is associated with the social-injecting network in a cohort of people who inject drugs. PLoS One 7, e47335.

Scott, N., Carrotte, E.R., Higgs, P., Cogger, S., Stoove, M.A., Aitken, C.K., Dietze, P.M., 2016. Longitudinal changes in psychological distress in a cohort of people who inject drugs in Melbourne, Australia. Drug Alcohol Depend. 168, 140–146.

Stafford, J., Burns, L., 2016. Illicit Drug Reporting System (IDRS) National Report 2015. National Drug and Alcohol Research Centre (NDARC), Sydney, Australia.

Strathdee, S.A., Mailman, J.L., 2001. The effectiveness of needle exchange programs: a review of the science and policy. AID Sci. 1.

Treloar, C., Hopwood, M., Bryant, J., 2010. 'Does anyone know where to get fits from around here? ' Policy implications for the provision of sterile injecting equipment through pharmacies in Sydney, Australia. Drugs Educ. Prev. Polic. 17, 72–83.

WHO, 2011. Global HIV/AIDS Response: Epidemic Update and Health Sector Progress Towards Universal Access. Geneva, Switzerland.

Wodak, A., Cooney, A., 2006. Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence. Subst. Use Misuse 41, 777–813.

Wodak, A., McLeod, L., 2008. The role of harm reduction in controlling HIV among injecting drug users. AIDS 22 (Suppl. 2), S81–S92.

Wood, E., Tyndall, M.W., Spittal, P., Li, K., Hogg, R.S., O'Shaughnessy, M.V., Schechter, M.T., 2002. Needle exchange and difficulty with needle access during an ongoing HIV epidemic. Int. J. Drug Policy 13, 95–102.

Wood, E., Kerr, T., Small, W., Jones, J., Schechter, M.T., Tyndall, M.W., 2003. The impact of police presence on access to needle exchange programs. J. Acquir. Immune Defic. Syndr. 34, 116–117.

3.3 Publication: Assessing individual-level needle and syringe coverage parameters and the measurement of coverage in Melbourne, Australia: methods and impacts

Assessing individual-level needle and syringe coverage parameters and the measurement of coverage in Melbourne, Australia: methods and impacts

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ABSTRACT

Background To assess the structure of individual-level needle and syringe coverage measurement formula, and to estimate the impact of coverage-related behaviours/parameters (instances of syringe acquisition, total syringes acquired, peer-to-peer syringe distribution, injecting frequency) on overall coverage.

Methods Data are drawn from the Melbourne (Australia) injecting drug user cohort study, 2010–16. Data from 518 participants were analysed. We used correlations to explore the relationships between coverage parameters; pooled multiple–linear regression to estimate the effect of each parameter on coverage over time; and exploratory factor analysis to assess the relevance of each parameter within the coverage formula.

Results A 1-unit increase in injecting frequency over time reduced coverage by 10.93 percentage points, almost twice as much as other coverage parameters. Factor analysis results indicated potential improvements to coverage formula structure.

Conclusions Our results suggest that reducing injecting frequency amongst people who inject drugs has the largest improvement in coverage levels, indicating harm reduction services should prioritize it. We also demonstrate that coverage measurement has been inconsistent to date. We sought to refine the method to assist in generating comparable research.

Keywords drug abuse, health services, measurement

Introduction

Needle and syringe program (NSP) coverage can be defined as the number of sterile needles and syringes (hereafter, 'syringe/s') acquired by people who inject drugs (PWID) relative to their injecting frequency. Multiple methods have been devised to estimate coverage according to this definition, the most prominent being Bluthenthal *et al.*'s measure.[1] Individual-level coverage measurements recognize that PWID have disparate injecting risk, while population-level measures assume homogeneity. For example, the WHO recommendation to distribute 200 syringes per PWID per annum[2] is inappropriate for PWID injecting at higher frequencies.

The coverage calculation formula includes several parameters, each corresponding to a particular PWID practice. Previous coverage measures have included instances of syringe acquisition,[1,3,4] peer-to-peer distribution[4–6] and stockpiling;[6] however, these parameters only supplement the central parameters of coverage: total syringes acquired and injecting frequency.

Bluthenthal *et al.*[1] showed that as individual-level coverage levels increased, the odds of reporting injecting risk behaviour decreased. This pattern continued even after coverage became sufficient (defined as 100% of injecting episodes

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covered by at least one sterile syringe), suggesting that having more syringes than actually required can further reduce risky injecting practices, illustrating the complex relationship between coverage, the behaviours that constitute its calculation, and injecting risk.

Whilst the research cited above tested associations between coverage as a categorical variable and various exposures, the effect each parameter has upon coverage as a continuous measure is uncertain. Whether change in syringe acquisition affects coverage more than (e.g.) change in injecting frequency is unknown. The effects of syringe access on injecting risk[7] and dispensation policy[8] on coverage have been well studied previously, but it remains uncertain which individual-level behavior is the more dominant driver of coverage. A nuanced understanding of these impacts is needed to improve coverage for PWID populations.

Finally, individual-level coverage has not been measured consistently, impairing the comparability of research. For example, O'Keefe *et al.*[5] and McCormack *et al.*[6] measured coverage by recording explicit responses to each parameter for a specified time period, whilst Bluthenthal *et al.*[1] extrapolated coverage by multiplying the number of syringes retained at the last instance of syringe acquisition by the number of syringe acquisitions per participant within 30 days. Differing methodologies have differing biases and weaknesses, highlighting the value of an exploration of measurement construction and optimal format.

In this article, we use data from a cohort of PWID in Melbourne, Australia, to analyse the change in each coverage parameter over time and their effect on coverage levels. Specifically, we:

(1) describe the longitudinal changes to individual-level coverage and determine correlations between parameters,
(2) compare the effect of change in each coverage parameter upon coverage as a continuous measure, and
(3) assess the appropriateness of parameters' inclusion in coverage formulae.

Methods

Data source

Our data are drawn from the Melbourne injecting drug user cohort study (MIX), described in detail elsewhere.[9] The 757 participants include those from the original MIX recruitment phase of 688 participants in 2008–10, and 69 participants from the Networks II cohort,[10] enroled in 2011. Both MIX and Networks II sought to recruit regular PWID. The cohorts' baseline characteristics are comparable.[11]

Eligibility criteria for the original MIX cohort were age 18–30 years and reporting injecting of heroin and/or methamphetamine regularly (at least monthly in the 6 months before recruitment). Informed written consent was obtained. The Victorian Department of Health Human Research Ethics Committee and the Monash University Human Research Ethics Committee approved the study.

Participant sample

At May 2016, MIX included 3312 interviews over nine interview waves. We used data after the introduction of coverage questions in June 2010 (excluding 902 interviews, and 176 participants). Due to our longitudinal focus, we also excluded 63 participants with only one interview after June 2010. The final dataset had 518 participants and 2347 interviews over a maximum of seven separate interview waves. Attrition was low, with 88% of included participants completing at least three interviews.

Coverage parameters

We compared four parameters for the 2 weeks prior to interview: instances of syringe acquisition (number of acquisitions of sterile syringes from any source), total syringes acquired, peer-to-peer syringe distribution and injecting frequency. Parameters came from the following questions:

> 'How many times in the last 2 weeks did you get (needles and) syringes?'

> 'In the last 2 weeks how many new (needles and) syringes in total did you get?'

> 'In the last 2 weeks how many new (needles and) syringes did you give away or sell to others?'

Past week injecting frequencies for 18 drug types were summed to create a total injecting frequency variable. To create an equitable timeframe for coverage calculation, past week injecting frequency was doubled to match the timeframe specified in the other coverage parameters. Injecting frequency was multiplied rather than total syringes acquired being divided because injecting frequency was less variable, suggesting more consistent practice.

Calculating coverage

We adapted Bluthenthal *et al.*'s[1] method to calculate individual-level syringe coverage. Our method utilizes only syringes acquired, syringe distribution and injecting frequency parameters. Syringes distributed is subtracted from total syringes acquired, divided by the past 2-week estimate of

injecting frequency, and multiplied by 100, giving a percentage of injecting episodes covered by a sterile syringe. The coverage formula is as follows:

$$\frac{(\textit{syringes acquired} - \textit{syringes distributed})}{(\textit{past week injecting frequency} \times 2)} \times 100$$

Coverage was only calculated for participants with valid data for each coverage parameter and who reported both syringe acquisition and injecting within the 2-week period (as no injecting precluded coverage calculation, whilst injecting without syringe acquisition was plausibly influenced by syringe stockpiling—see Limitations). Overall, 44% of coverage responses (1029 observations) were missing, most (735 observations, 71% of all missing responses) due to injecting abstinence. Another 262 coverage observations were missing due to no syringe acquisition by participants who reported injecting (25% of all missing responses). The remaining 4% of missing coverage responses were due to missing/invalid data in any of the coverage variables.

Calculating coverage change

To calculate longitudinal change in coverage and coverage parameters, the reported values of continuous coverage and each coverage parameter were subtracted from the same variable at the next immediately preceding, non-missing longitudinal observation.

To avoid the influence of stockpiling, each parameter change variable was classified as 'missing' if the participant reported 'zero' injecting at the succeeding interview and if there was zero change in the parameter change variable.

Treatment of outliers

We inspected the data for each change variable and noted extreme outliers that influenced the overall distributions. Several outlier treatments were tested using quantiles of normal distribution plots, whilst seeking to maximize data inclusion.

For each change variable we tested the following exclusion methods: exclusion of all values ±2 standard deviations from the mean; all data at the extreme 5% of either end of the distribution (10% of the overall distribution); all data at the extreme 2.5% of the distribution (5% overall); and the extreme 1% of the distribution (2% overall). The 2.5% method of exclusion accounted for outlier influence without excluding too many data points: 71 observations for 'change in total syringes acquired', 67 for 'change in syringe distribution', 73 for 'change in instances of syringe acquisition', 61 for 'change in injecting frequency' and 34 for the 'change in continuous coverage' variable.

Statistical analysis

The relationship between changes in the four coverage parameters was tested using Pearson's correlation. The relationship between change in continuous coverage as an outcome and change in the four coverage parameters was estimated using pooled multiple linear regression. To account for repeated measures bias, standard errors were clustered on individual participants.

Factor analysis assesses the correlational relationship between selected continuous variables and potential latent dimensions, or 'factors'.[12] It attempts to identify a common, hypothetical variable/s upon which the analysed variables are weighted, and assesses the strength of each weighting upon the factors. We used exploratory factor analysis to assess the weightings of each coverage parameter on four potential factors, using the raw coverage variables (those included in the coverage formula) as opposed to the transformed 'change' variables. We utilized promax rotation, due to the parameters being correlated, and report factor loadings for each variable.

All analysis was performed in STATA13 (StataCorp. 2013. College Station, TX).

Results

Demographics

At first interview, the amended sample was predominantly male (64%), Australian-born (81%), non-Indigenous (95%), unemployed (78%) and living in stable accommodation (85%). Average age was 30 years, and those reporting injecting ($n = 429$) mainly injected heroin in the month before interview (73%), followed by methamphetamine (11%).

Change in coverage and coverage parameters

Median continuous coverage values at first and most recent interview were 162% (IQR: 88–350%) and 158% (IQR: 83–321%), respectively. Though coverage as an aggregate continuous outcome was sufficient, when dichotomized, 27 and 26% of the sample were insufficiently covered at their first and most recent interview, respectively.

In the 2 weeks before interview, participants who reported injecting collected a median 15 syringes (IQR: 5–70), distributed a median of zero syringes (IQR: 0–10), collected syringes from any sources a median of one time (IQR: 1–3) and reported a median of five injections (IQR: 2–12).[13]

Table 1 presents the mean and range of the change in tested variables between the first and the second interview and between the second-last and the last interview.

Table 1 Descriptive statistics of change in coverage parameters and continuous coverage

Parameter	*Change from first to second interview* *Mean (range)*	*Change from second last to last interview* *Mean (range)*
Total syringes acquired	−0.52 (−180, +180)	+4.21 (−180, +190)
Syringe distribution	+0.41 (−75, +90)	+1.62 (−60, +95)
Instances of syringe acquisition	−0.09 (−10, +11)	+0.33 (−10, +11)
Injecting frequency	+1.54 (−40, +54)	+3.09 (−42, +52)
Continuous coverage	−20.37 (−1542, +1625)	+54.86 (−1271, +1606)

Relationship between parameter change and coverage

The four coverage change parameters were low to moderately correlated. Of the seven tested relationships (Fig. 1), change in total syringes acquired and change in syringe distribution had the strongest correlation (0.497), followed by change in total syringes acquired and change in injecting frequency (0.302).

The pooled multiple linear regression model showed that the increase in 2-week injecting frequency was associated with the largest effect on continuous coverage change, reducing coverage by 10.93 percentage points for every additional injecting episode between interviews (Table 2). Unit increases in syringe distribution and instances of syringe acquisition were associated with reductions in coverage of 5.34 and 5.77 percentage points, respectively (although the association with syringe acquisition was not significant). Only an increase in syringes acquired was associated with increased continuous coverage (a unit increase in total syringes acquired predicting a 5.99 percentage point increase in coverage).

Factor analysis

The factor analysis included 2299 observations. From a potential four-factor solution, positive eigenvalues existed for only the first two factors (factor 1: 1.4552 and factor 2: 0.0059), meaning only these two factors were considered. Before and after promax rotation, all tested parameters loaded most strongly upon factor 1 (Table 3—presenting results after rotation), suggesting that all parameters correlate with a common dimension. 'Total syringes acquired' and 'syringe distribution' had the strongest factor loading, whilst 'instances of syringe acquisition' had the weakest.

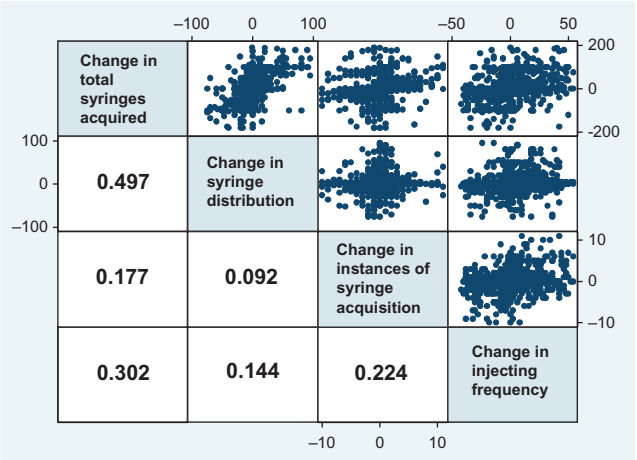

Fig. 1 Matrix of correlations between coverage change parameters.

The correlations between the four change parameters were weak to moderate. Only two pairs showed any real strength of (positive) association: change in total syringes acquired and change in syringe distribution, and change in total syringes acquired and change in injecting frequency.

Multiple linear regression showed that only an increase in total syringes acquired was associated with increased overall coverage, further validating Australia's mostly unlimited syringe dispensation policies, in contrast to more restrictive policies elsewhere.[8] Increases in all other parameters were associated with decreases in coverage.

Factor analysis suggested that the four parameters loaded most strongly upon a single factor, presumably the latent dimension of 'coverage'.

Discussion

Main findings of this study

In this study, we explored the dynamics of individual-level coverage parameters by assessing their relationships with one another and upon coverage as a continuous outcome.

What is already known on this topic

Daily or more injecting frequencies and inconsistent or non-use of NSPs[1,3,5] have previously been associated with insufficient coverage in regression analysis.[3,5] and the behaviours that constitute the coverage parameters have previously been explored in isolation in relation to coverage. Bluthenthal *et al.*[1] found evidence that PWID who have

Table 2 Multiple linear regression of coverage parameters

Change variable	*Bivariable coefficient (95% CIs)*	P-*value*	*Multivariable coefficient (95% CIs)*	P-*value*
Change in total syringes acquired	2.70 (1.98, 3.41)	<0.01	5.99 (5.03, 6.94)	<0.01
Change in syringe distribution	1.19 (−0.47, 2.85)	0.16	−5.34 (−7.11, −3.58)	<0.01
Change in instances of syringe acquisition	−9.14 (−19.02, 0.74)	0.07	−5.77 (−13.07, 1.53)	0.12
Change in injecting frequency	−3.91 (−5.71, −2.11)	<0.01	−10.93 (−12.85, −9.02)	<0.01

Number of obs. in multivariable regression: 553, P <0.001, R^2: 0.45.

Table 3 Factor weightings of coverage parameters

	Factor 1	*Factor 2*
Total syringes acquired	0.7254	0.0710
Syringe distribution	0.7449	−0.0467
Instances of syringe acquisition	0.2797	0.0106
Injecting frequency	0.3284	0.1918

more instances of syringe acquisition, who acquire fewer syringes, who do not distribute syringes and who have higher injecting frequencies have lower coverage levels. However, these studies did not investigate the correlations between individual coverage parameters, or their relative importance in predicting a change in coverage over time.

What this study adds

The correlation between syringe distribution and total syringes acquired suggests that many PWID are purposely acquiring additional syringes to distribute to peers, and is consistent with previous findings that PWID acquire syringes for others, such as friends and family members.[14]

Whilst it may be concerning that increased injecting frequency and syringe acquisition are not more strongly correlated, many participants had more than sufficient coverage. Strike *et al.*[15] categorized PWID by syringe acquisition habits: those stockpiling syringes for personal and others' use; those routinely keeping several days' supply available; and those obtaining syringes only when about to inject. It may be that our PWID stockpiled syringes to cover any increase in injecting frequency.

Our regression results show that as PWID distribute syringes, their reserves diminish, thereby reducing overall coverage. This does not necessarily represent risk, if the distributing individuals account for it in their acquisition. We explored this risk by recalculating the coverage formula. With the peer-to-peer distribution parameter included, 26% of participants were insufficiently covered (<100% coverage); after excluding it, 19% were insufficiently covered, suggesting some PWID do not account for distribution in their syringe acquisition. Peer-to-peer syringe distribution has been characterized as an important adjunct to formalized services, with 32–40% of PWID reporting it.[14] The non-use of NSPs has also been associated with insufficient coverage;[5] peer-to-peer distribution can increase coverage for PWID who eschew formal services, but it is important that this does not decrease the coverage of those distributing.

Increasing instances of syringe acquisition decreased coverage. This finding may appear counterintuitive, and is at odds with Bluthenthal *et al.*'s[1] findings, but is probably explained by differences between Australia's syringe dispensation policy and the relatively restrictive policies in the United States. At most recent interview, 56% of injectors acquired syringes on one or two occasions over the preceding 2 weeks, but as syringe acquisitions increased, median injecting frequency increased only marginally, suggesting many participants were acquiring syringes for immediate use. Strike *et al.*[15] showed that such PWID were at greater injecting risk than those who plan acquisition; plausibly, they are at greater risk of reduced coverage.

The associations between the two central parameters (total syringes acquired and injecting frequency) and coverage best indicate how to maximize coverage at the individual level. A one unit increase in injecting frequency was associated with a 10.93 percentage point decrease in continuous coverage, an effect size nearly double that of any other parameter. This effect is particularly salient when comparing the variable range for change in injecting frequency (range: −42 to +54) versus change in total syringes acquired (range: −180 to +190). Extrapolating the regression results suggests that reducing injecting frequency by 10 episodes per fortnight would increase coverage by 110 percentage points, whilst providing PWID with another 10 syringes would only increase their coverage by 60 percentage points. The maximum injecting frequency of PWID over a fortnight is small compared with the number of syringes they can acquire, suggesting that interventions to reduce injecting frequency would have the greatest effect upon individual-level coverage.

Reducing injecting frequency carries additional benefits. High-frequency injecting has been associated with BBV infection,[16,17] injection-related infection,[18] overdose[19] and other

injecting-related risk.[20] High-frequency injecting has also been associated with insufficient coverage.[1,3] Reducing injecting frequency via drug treatment, particularly via OST prescription is efficacious and cost-effective.[21] Furthermore, the association between OST prescription and higher coverage has been demonstrated in our previous work[5,13] and in that of others.[4]

For PWID who do not inject opiates (meaning OST prescription is inappropriate), other methods of reducing injecting frequency are needed. Some work has been done on medication-based replacement therapies for meth/amphetamine-dependent PWID[22,23] with varying results. However, more work is needed to validate non-OST treatments.

The differential effect sizes we report do not mean we recommend one intervention over another. Maximizing coverage comes from a coordinated approach, whereby multiple methods of syringe delivery, both formal and informal, complement the idiosyncratic needs of PWID—a diverse population with different levels of service utilization. Whilst some interventions have greater impact than others, each helps ensure that PWID can acquire sufficient syringes when and where required. For example, increasing syringe acquisition via increased dispensation may prove more cost-effective and easier to implement (and would target all PWID, rather than only opioid injectors); however, we only highlight here the different impacts based upon the results of analysis. It must also be remembered that the behaviours observed in our sample may not correspond to behaviours of other PWID populations, as shown in Bluthenthal *et al.*'s findings.[1] The PWID in our sample inject less often than many other populations,[24,25] which has an effect upon coverage.[1] Consequently, other PWID samples may not experience the effect sizes seen here.

Finally, our factor analysis supports the assertion that numerous behaviours/practices affect coverage, beyond the bipartite relationship between syringe acquisition and injecting frequency. A consistent method of measuring individual-level coverage is important for future research and evaluation. For example, McCormack *et al.* produced strong evidence for including a syringe stockpiling parameter (see Limitations). Of the parameters tested, 'instances of syringe acquisition' had least weight upon the latent factor; although excluded from our coverage formula, it was part of Bluthenthal *et al.*'s[1] original formula construction, and appears in other research.[3,4] Our analysis suggests its omission is warranted.

Limitations of this study

Each parameter within the coverage formula is open to recall bias, which is compounded by each additional measure. We believe the 2-week period used in our analysis reduced the bias in recall.

McCormack *et al.*'s[6] finding that many Australian PWID stockpile syringes was published after construction of the MIX questionnaire, so stockpiling was not included in our coverage measure or analysis. However, in accordance with Bluthenthal *et al.*'s[1] finding that higher coverage reduces injecting risk, we hypothesized that PWID who stockpile syringes have the highest levels of coverage. If true, stockpiling has a large effect upon continuous coverage. We have since included stockpiling in a recent MIX questionnaire update, so can explore this hypothesis in future research.

Not all parameters in the coverage measure occur commensurately. For example, PWID may inject daily, yet only acquire syringes (and stockpile) monthly. Our 2-week time period may therefore miss some coverage behaviours. Future research should determine the most appropriate timeframe to capture infrequent behaviours, whilst minimizing recall bias.

Finally, 44% of all coverage responses were missing. Though most (71%) were due to injecting abstinence, invalid coverage parameter responses precluded analysis of otherwise valid data. Also, because we calculated change between succeeding interviews, missing data complicated analysis as it relied upon sequential ordering of valid coverage/parameter data, meaning many change outcomes were excluded.

Conclusions

Measurement of individual-level needle and syringe coverage is based on parameters corresponding to particular behaviours. Changes in these behaviours affect individuals' ability to 'cover' their injection episodes with sterile syringes. Our analysis suggests that decreased injecting frequency would improve coverage nearly twice as much as an equivalent increase in syringe acquisition. Improving the quantity and quality of NSP service delivery is vitally important to ongoing harm reduction efforts, but interventions to reduce injecting frequency (such as OST prescription) may have greater impact for particular PWID, notably primary opioid injectors.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

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Conflicts of interest

PD has received funding from Gilead Sciences Inc. for work unrelated to this study. Other authors have nothing to declare.

References

1 Bluthenthal RN, Anderson R, Flynn NM *et al*. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. *Drug Alcohol Depend* 2007;**89**(**2–3**):214–22.

2 WHO. *Technical Guide for Countries to Set Targets for Universal HIV Services for Injecting Drug Users*. Geneva, Switzerland: World Health Organisation, 2012.

3 Bryant J, Paquette D, Wilson H. Syringe coverage in an Australian setting: does a high level of syringe coverage moderate syringe sharing behaviour? *AIDS Behav* 2012;**16**(**5**):1156–63.

4 Iversen J, Topp L, Wand H *et al*. Individual-level syringe coverage among Needle and Syringe Program attendees in Australia. *Drug Alcohol Depend* 2012;**122**(**3**):195–200.

5 O'Keefe D, Scott N, Aitken C *et al*. Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis. *BMC Health Serv Res* 2016;**16**(**1**):411.

6 McCormack AR, Aitken CK, Burns LA *et al*. Syringe stockpiling by persons who inject drugs: an evaluation of current measures for Needle and Syringe Program Coverage. *Am J Epidemiol* 2016;**183**(**9**): 852–60.

7 Bluthenthal RN, Malik MR, Grau LE *et al*. Sterile syringe access conditions and variations in HIV risk among drug injectors in three cities. *Addition* 2004;**99**(**9**):1136–46.

8 Bluthenthal RN, Ridgeway G, Schell T *et al*. Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. *Addiction* 2007;**102**(**4**):638–46.

9 Horyniak D, Higgs P, Jenkinson R *et al*. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. *Harm Reduct J* 2013;**10**:11.

10 Sacks-Davis R, Daraganova G, Aitken C *et al*. Hepatitis C virus phylogenetic clustering is associated with the social-injecting network in a cohort of people who inject drugs. *PLoS One* 2012;**7**(**10**): e47335.

11 Scott N, Carrotte ER, Higgs P *et al*. Longitudinal changes in psychological distress in a cohort of people who inject drugs in Melbourne, Australia. *Drug Alcohol Depend* 2016;**168**:140–6.

12 Bryant FB, Yarnold PR. Principal-components analysis and exploratory and confirmatory factor analysis. In: Grimm LG, Yarnold PR (eds). *Reading and Understanding Multivariate Statistics*. Washington, DC: American Psychological Association, 1995, 99–136.

13 O'Keefe D, Scott N, Aitken C *et al*. Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people how inject drugs in Melbourne, Australia. *Drug Alcohol Depend* 2017;**176**:7–13.

14 Newland J, Newman C, Treloar C. 'We get by with a little help from our friends': small-scale informal and large-scale formal peer distribution networks of sterile injecting equipment in Australia. *Int J Drug Policy* 2016;**34**:65–71.

15 Strike C, Cavalieri W, Bright R *et al*. Syringe acquisition, peer exchange and HIV risk. *Contemp Drug Probl* 2005;**32**:319–40.

16 Strathdee SA, Patrick DM, Currie S *et al*. Needle exchange is not enough: lessons from the Vancouver injecting drug use study. *AIDS* 1997;**11**:F59–65.

17 Castro-Sanchez A, Shkedy Z, Hens N *et al*. Estimating the force of infection for HCV in injecting drug users using interval-censored data. *Epidemiol Infect* 2012;**140**:1064–74.

18 Stein ES, Anderson B. Injection frequency mediates health service use among persons with a history of drug injection. *Drug Alcohol Depend* 2003;**70**(**2**):159–68.

19 Brugal MT, Barrio G, La Fuente LD *et al*. Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration. *Addiction* 2002;**97**(**3**):319–27.

20 Loewinger G, Sharma B, Karki DK *et al*. Low knowledge and perceived hepatitis C risk despite high risk behaviour among injection drug users in Kathmandu, Nepal. *Int J Drug Policy* 2016;**33**:75–82.

21 Amato L, Davoli M, Perucci CA *et al*. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treat* 2005;**28**:321–9.

22 Rose ME, Grant JE. Pharmacotherapy for methamphetamine dependence: a review of the pathophysiology of methamphetamine addiction and the theoretical basis and efficacy of pharmacotherapeutic interventions. *Ann Clin Psychiatry* 2011;**20**(**3**):145–55.

23 Stoops WW, Rush CR. Agonist replacement for stimulant dependence: a review of clinical research. *Curr Pharm Des* 2013;**19**(**40**):7026–35.

24 Swe LA, Nyo KK, Rashid AK. Risk behaviours among HIV positive injecting drug users in Myanmar: a case control study. *Harm Reduct J* 2010;**7**:12.

25 Eckhardt B, Winkelstein ER, Shu MA *et al*. Risk factors for hepatitis C seropositivity among young people who inject drugs in New York City: implications for prevention. *PLoS One* 2017;**12**(**5**):e0177341.

3.4 Summary of Chapter Three

This chapter builds upon the initial descriptive findings in Chapter Two, exploring factors that influence change in individual-level syringe coverage change and elements of individual-level syringe coverage measurement. In Paper Two, I demonstrated a number of time-varying associations with changes in individual-level syringe coverage. A shift to past-month methamphetamine injecting from not injecting methamphetamine in the past month (at the previous interview) and newly acquired HCV-positivity were associated with increased odds of a change from sufficient to insufficient individual-level syringe coverage. In contrast, changes in fixed-site NSP utilisation and initiating OST decreased the odds of a change from sufficient to insufficient individual-level syringe coverage. More so than the cross-sectional associations with insufficient individual-level syringe coverage in Paper One, these results show that syringe coverage is not solely determined by service-level influences but also person-level factors. This finding suggests the need for targeted interventions, such as increasing syringe distribution amongst needle and syringe program clients known to inject methamphetamine, or facilitating retention in OST for opioid dependent PWID. These targeted measures may avert decreases in individual-level syringe coverage amongst PWID who would otherwise be sufficiently covered.

Paper Three had two aims: 1) assessing the differential impacts the individual parameters have upon the measurement of individual-level syringe coverage, and 2) assessing the appropriateness of the inclusion of each parameter within the individual-level syringe coverage formula. In regression analysis, changes to *peer-to-peer syringe distribution* and *instances of syringe acquisition* had the least effect on individual-level syringe coverage. This was expected, as both parameters are secondary to the essential relationship between *total syringes acquired* and *injecting frequency*. Changes in injecting frequency had almost twice the effect size on syringe individual-level coverage levels compared to the four other tested parameters, suggesting that a focus on injecting frequencies would be appropriate for interventions. This finding complements the results in Papers One and Two, in which reduced odds of insufficient individual-level syringe coverage was observed among those on OST. OST has been shown to reduce injecting frequencies and drug use more generally (13), in addition to reductions in

other injecting risk behaviours (such as receptive syringe sharing (13)). If syringe acquisition were to remain stable for those on OST, individual-level syringe coverage will improve for these particular, opioid-dependent, PWID. For other PWID, such as methamphetamine injectors, other interventions have been tested (such as alternate substitution therapies), with varying results (162, 163).

To meet the second aim of Paper Three, the inclusion of different parameters in the individual-level syringe coverage formula was assessed via factor analysis. In factor analysis, all four parameters loaded upon a single latent factor, presumably syringe coverage. However, it was *instances of syringe acquisition* that loaded with the least weight, warranting its omission from the individual-level syringe coverage formula. Importantly, this parameter was essential to Bluthenthal et al.'s extrapolation method of calculating individual-level syringe coverage (5), and not subsequently used in McCormack et al.'s enumeration method. The weakness of the parameter's loading within the factor analysis, and the subsequent recommendation of its omission from future individual-level syringe coverage formulas, may represent indirect support for McCormack et al.'s adapted enumeration method (146).

This initial work to improve the individual-level syringe coverage formula showed that some parameters do not share an equal correlation with individual-level syringe coverage. Additional, currently unidentified parameters may exist that have important influence on syringe coverage, such as McCormack et al. showed in relation to syringe stockpiling. One potential parameter is the use of multiple sterile syringes per injecting episode. I explore this parameter in Chapter Four, and the appropriateness of its inclusion within the individual-level syringe coverage formula.

Chapter Four: Improving the individual-level needle and syringe coverage measure

4.1 Overview of Chapter Four

Both the way in which individual-level syringe coverage is calculated, and the parameters included within the individual-level syringe coverage formula, have been adapted, altered and refined. Whilst Bluthenthal et al.'s extrapolation method has been used in multiple studies, its use was not examined prior to McCormack et al.'s work, which proposed an alternate enumeration method, whereby the numerical value of each parameter is explicitly recorded (146). In their study, McCormack et al. also provided strong evidence for the inclusion of a syringe stockpiling parameter. Seventy-five percent of their sample reported syringe stockpiling. When information on syringe stockpiling was included within an adaptation of the Bluthenthal et al. measure, insufficient individual-level syringe coverage was reduced by 8 percentage points (from 24% to 16%), its inclusion therefore reducing bias and improving the accuracy of the individual-level syringe coverage estimate (146). Further, the new measure proved superior at discriminating some key injecting risk behaviours (specifically receptive syringe sharing, syringe re-use and receptive injecting equipment sharing) in receiver operating characteristic curve analysis (164), compared to a measure without syringe stockpiling. This work suggests there may be other, as yet, unidentified and unmeasured behaviours that may impact syringe coverage. The omission of these behaviours as individual-level syringe coverage formula parameters may result in inaccurate individual-level syringe coverage estimates.

Because the re-use of unsterile syringes increases the risk of bacterial infection and vein trauma via the blunting of needles (14, 36), it's a discouraged practice. However, many PWID report difficulty injecting, due either to naturally small veins or prior vein damage (15). Consequently, PWID may require multiple sterile syringes for a single episode of drug use, if they need to make multiple attempts at injecting. If the practice of using

multiple sterile syringes is unaccounted for, individual-level syringe coverage may be overestimated for these individuals.

Paper Four replicates the methodology employed by McCormack et al., to test the appropriateness of a parameter representing the use of multiple sterile syringes per injecting episode. This chapter makes progress towards a standardised individual-level syringe coverage measure, by potentially identifying a behaviour that may have relevance to individual-level syringe coverage calculation, and therefore should be included within the individual-level syringe coverage formula.

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Research paper

How does the use of multiple needles/syringes per injecting episode impact on the measurement of individual level needle and syringe program coverage?

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ABSTRACT

Background: Recent work by McCormack et al. (2016) showed that the inclusion of syringe stockpiling improves the measurement of individual-level syringe coverage. We explored whether including the use of a new parameter, multiple sterile syringes per injecting episode, further improves coverage measures.
Methods: Data comes from 838 people who inject drugs, interviewed as part of the 2015 Illicit Drug Reporting System. Along with syringe coverage questions, the survey recorded the number of sterile syringes used on average per injecting episode. We constructed three measures of coverage: one adapted from Bluthenthal et al. (2007), the McCormack et al. measure, and a new coverage measure that included use of multiple syringes. Predictors of multiple syringe use and insufficient coverage (<100% of injecting episodes using a sterile syringe) using the new measure, were tested in logistic regression and the ability of the measures to discriminate key risk behaviours was compared using ROC curve analysis.
Results: 134 (16%) participants reported needing multiple syringes per injecting episode. Women showed significantly increased odds of multiple syringe use, as did those reporting injection related injuries/diseases and injecting of opioid substitution drugs or pharmaceutical opioids. Levels of insufficient coverage across the three measures were substantial (20%–28%). ROC curve analysis suggested that our new measure was no better at discriminating injecting risk behaviours than the existing measures.
Conclusion: Based on our findings, there appears to be little need for adding a multiple syringe use parameter to existing coverage formulae. Hence, we recommend that multiple syringe use is not included in the measurement of individual-level syringe coverage.

Introduction

Needle and syringe programs (NSPs) are a cost-effective, low-threshold intervention that reduces the transmission of blood-borne viruses (BBVs) via the provision of sterile injecting equipment to people who inject drugs (PWID) (Laufer, 2001; Strathdee & Mailman, 2001). NSP coverage can be measured at both the population-level and at the individual-level and both methods have advantages and disadvantages. Population-level coverage measurements (often defined as the proportion of PWID utilising a service within a given geographic area (Burrows, 2006), or the average number of syringes distributed across an estimated PWID population (WHO, 2012)), are more commonly utilised as they are relatively easier to calculate in comparison to individual-level measures, but their reliance on population estimates leads to wide margins of error, and the practice of aggregating data means that poor coverage among the most at-risk individuals can be masked by the coverage of less risky individuals. For example, the WHO recommends that an average of 200 sterile syringes be

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distributed per PWID per annum to curtail HIV transmission (WHO, 2012). Though conceived as a method of evaluating service delivery, in practical terms, there may be PWID who far exceed this benchmark and may therefore overshadow those who fail to meet it. These shortcomings have previously been identified (Wiessing et al., 2001). In response, individual-level measures have been developed. Whilst these measures are more difficult to calculate, they better capture injecting risk for individual PWID and potentially provide a more accurate picture of programmatic shortfalls and better identify target populations. Most widely used is the Bluthenthal, Anderson, Flynn, and Kral (2007) "one-shot-for-one-syringe" method. This method defines coverage as the percentage of an individual's injecting episodes (the single injection of a drug, including drug preparation) that utilise a sterile needle and syringe (hereafter referred to as "syringe/s"). Less than 100% coverage suggests individuals have insufficient sterile syringes to cover their injections and are therefore risking harm (such as BBV infection through sharing injecting equipment). It is a method that, in contrast to population-level measures, accounts for individual variation and sets a benchmark that PWID should be facilitated to meet.

However, Bluthenthal et al.'s measure relies upon limited parameters (occasions of syringe acquisition, number of syringes acquired and injecting frequency). McCormack, Aitken, Burns, Cogger, and Dietze (2016) explored the addition of syringe stockpiling. Unlike in many countries, NSP policy across much of Australia effectively allows for unlimited syringe acquisition without the corresponding exchange of used syringes (Bluthenthal, Ridgeway et al., 2007). McCormack et al. showed that many PWID utilise this unlimited policy; three quarters of their sample reported stockpiling at least one sterile syringe within the month preceding interview and, on average, participants reported stockpiling 56 syringes (interquartile range (IQR): 6–51). When this parameter was included within their variant of the Bluthenthal et al. measure, the proportion of PWID sufficiently covered increased from 76% to 84% (McCormack et al., 2016) due to the higher number of syringes compared to injecting episodes. This research showed how extending the basis of coverage measurement can affect coverage levels and hence assessment of intervention efficacy.

McCormack et al.'s findings nevertheless accord with previous Australian research suggesting that, despite comprehensive levels of service, insufficient individual-level syringe coverage remains substantial. An estimated 16–37% (Bryant, Paquette, & Wilson, 2012; Iversen, Topp, Wand, & Maher, 2012; McCormack et al., 2016; O'Keefe, Scott, Aitken, & Dietze, 2016) of Australian PWID do not acquire sufficient syringes to cover their injecting episodes. In Australia and elsewhere, this insufficiency has been associated with high-frequency injecting, failure to utilise primary PWID services, hepatitis C virus (HCV) infection, and injecting risk practices such as syringe reuse and receptive syringe sharing (Allen et al., 2012; Bluthenthal, Anderson et al., 2007; Bryant et al., 2012; Iversen et al., 2012). In this paper, we explore the effect of adding a fourth parameter to McCormack et al.'s coverage measure: the use of multiple sterile syringes per injecting episode.

PWID may require more than one syringe per successful injection due to poor venous access, as a consequence of either small surface veins or injection-related vein damage (Koester, 2012). The reuse of unsterile syringes increases the risk of skin and soft tissue infections (Brett, Hood, Brazier, Duerden, & HahnÉ, 2005; Dahlman, Hakansson, Bjorkman, Blome, & Kral, 2015), sepsis development (Dahlman et al., 2015), scarring and bruising (Dolinar, 2009), painful injections via needle blunting (Harris & Rhodes, 2012), and the use of veins (femoral, jugular) that pose greater risk of harm (Harris & Rhodes, 2012). Research among Australian PWID found 43% reported difficulty with injecting (Dwyer et al., 2009; Topp, Iversen, Conroy, Salmon, & Maher, 2008), and this difficulty impels many PWID to use multiple sterile syringes during their injecting episodes. For these individuals, the relationship between syringe acquisition and injecting frequency is distorted, resulting in an overestimation of aggregate coverage. Excluding multiple syringe use may therefore weaken coverage measurement, as does the exclusion of syringe stockpiling.

In this paper, we utilised cross-sectional data from the 2015 Illicit Drug Reporting System (IDRS) survey and replicate the methodology of McCormack et al. to assess the effect of inclusion of multiple syringes per injecting episode in measuring syringe coverage. Our primary aims were to:

1) describe the prevalence and frequency of multiple syringe use among a sample of PWID,
2) construct a measure of individual syringe coverage that includes both stockpiling and use of multiple syringes and compare coverage levels against the Bluthenthal et al. and the McCormack et al. measures,
3) test predictors of multiple syringe use and insufficient coverage under the new measure, and
4) test the discriminative ability of the new coverage measure compared to existing coverage measures using receiver operating characteristic (ROC) curve analysis.

Methods

The IDRS is an Australian nationwide annual surveillance survey. Conducted since 1999, the survey monitors emerging trends among Australian PWID (Stafford & Burns, 2016). The questionnaire covers drug use, service utilisation, drug purchasing characteristics, injecting risk practices and criminal activity. Eligibility criteria are at least 18 years of age, injecting at least once a month in the six months prior to interview, residing in the city of survey administration for at least 12 months prior to interview, and ability to provide informed consent. Interviews typically take 45–60 min and participants are compensated for their time. The survey methodology has been described in detail elsewhere (Hando, Darke, O'Brien, Maher, & Hall, 1998). This study uses data from the 2015 IDRS, conducted between June/July 2015.

Ethics approval was obtained from the University of New South Wales Research Ethics Committee and local equivalents as required.

Sample

The IDRS recruits approximately 100 active PWID from all Australian capital cities (except Melbourne and Sydney where, due to larger PWID populations, 150 participants are recruited) via convenience sampling at NSPs and community health centres. The final sample size in 2015 was 888 participants. Fifty participants who reported no injecting within the month prior to interview were excluded, resulting in an amended sample of 838 participants for analysis.

Measures

To measure individual levels of syringe coverage in the month prior to interview, the following questions were asked:

"In the LAST MONTH how many new (needles and) syringes in total did you get?"

"In the LAST MONTH how many (needles and) syringes did you give away or sell to others?"

"Thinking about it overall, about how many times did you inject in the LAST MONTH?"

Bluthenthal et al. measure of coverage

To calculate the adapted Bluthenthal, Anderson et al. (2007) coverage measure (hereafter the Bluthenthal et al. measure), the number of syringes sold or given away was subtracted from the number of syringes acquired. Retained syringes were then divided by participants' past month injecting frequency and multiplied by 100 to obtain an estimated percentage of injecting episodes that utilised a sterile syringe. The equation for the Bluthenthal et al. measure is therefore:

$$\frac{(syringes\ acquired - syringes\ distributed)}{injecting\ frequency} \times 100$$

McCormack et al. measure of coverage

To replicate the work of McCormack et al. (2016) we included the stockpiling question:

"How many (needles and) syringes do you have stored away at the MOMENT? (at home, in car etc.)"

The number of syringes stockpiled was added to the number retained. The equation for the McCormack et al. measure is therefore:

$$\frac{(syringes\ acquired - syringes\ distributed + syringes\ stock\ piled)}{injecting\ frequency} \times 100$$

New measure of coverage

Finally, the use of multiple syringes per injecting episode was captured by the question:

"How many needles on average have you needed to successfully inject each 'hit' during the LAST MONTH?"

The term "hit", whilst slang, is widely used and understood amongst Australian PWID to mean a single injection of a drug.

The average number of syringes was multiplied by participants' past month injecting frequency, creating the new coverage measure equation:

$$\frac{(syringes\ acquired - syringes\ distributed + syringes\ stock\ piled)}{(injecting\ frequency \times average\ number\ of\ syringes)} \times 100$$

All coverage parameters were recorded and analysed as continuous data. Responses from three participants who reported needing an average of "zero" syringes per injecting episode were recoded as missing.

Exposure variables

We analysed exposure variables identified as related to coverage in the literature, and those used by McCormack et al. Exposure variables were in demographic, drug use, drug treatment utilisation, mental health, injecting risk and injecting-related injuries and diseases (IRIDs) domains (see Table 3 for full list).

Participants were asked if they experienced a number of separate IRIDs within the past month, including abscesses/infections (n = 49, 6%), prominent scarring/bruising (n = 385, 46%), difficulty injecting (n = 322, 38%), a "dirty hit" (n = 84, 10%) and thrombosis/blood clots (n = 44, 5%). Each of these variables was individually tested against the use of multiple syringes in bivariable regression analysis and found to have a significant association. Consequently, we collapsed the five variables into one dichotomous "IRID (past month)" exposure.

Analysis

We created dichotomised variables for use of multiple syringes (one syringe per episode/more than one syringe per episode) and coverage using the new measure (<100%/≥100% coverage). Descriptive proportions for both outcomes across exposure variables were explored. Separate multivariable logistic regression models tested the associations between the two outcome variables and the exposure variables with adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) reported.

The discriminative ability of the new coverage measure was separately compared with that of the Bluthenthal et al. and McCormack et al. coverage measures and tested using ROC curve analysis (Metz, 1978). Logistic regression models separately tested the association between the three coverage measures as continuous independent exposures, and four key injecting risk practices (receptive syringe sharing, distributive syringe sharing, personal syringe reuse, receptive injecting equipment sharing) as binary, dependent outcomes, selected as potential consequences of insufficient coverage. ROC curves were plotted to assess the fit of each model, and the areas under the curves (AUC) were tested for equality (Hanley & McNeil, 1982).

Results

Participant demographics

Most participants were male (66%), Australian-born (89%), non-Indigenous (80%), single (58%), unemployed (84%) and living in stable accommodation (76%). Mean age was 42 years (range 17–71). Forty-seven per cent of participants received treatment for their drug use, predominantly methadone (n = 263, 31%). Heroin was the most commonly injected drug in the previous month (42%), followed by methamphetamine (34%).

Use of multiple syringes per injecting episode

One hundred and thirty-four participants (16%) reported needing more than one syringe on average (range 2–13) per successful injecting episode. Eighty-three participants (10%) needed an average of two syringes, and 51 participants (6%) needed three or more syringes.

Median injecting frequency within the previous month was 25 (IQR: 10, 60). Multiplying injecting frequency by the average number of syringes utilised gave an amended median injecting frequency of 28 (IQR: 10, 60).

Coverage

Seven hundred and eighty-seven participants (94%) reported acquiring syringes from NSPs within the six months prior to interview (this does not preclude syringe acquisition from other sources). One hundred and thirty-eight (16%) reported syringe acquisition from pharmacies, 77 (9%) from friends and 124 (15%) from syringe vending machines. Participants reported acquiring syringes (from any source) a median of three times, acquiring a median 50 syringes, selling or giving away a median of five syringes, and currently stockpiling a median of seven syringes (Table 1).

Comparing measures of coverage

The Bluthenthal et al. measure (without stockpiling and without multiple syringes) produced the highest percentage of insufficiently covered participants (Table 2). The inclusion of stockpiling (McCormack et al.) reduced the percentage of

Table 1
Coverage statistics (month prior to interview).

Coverage statistics	Median (IQR)
Injecting frequency	25 (10, 60)
Amended injecting frequency (incl. multiple syringes)	28 (10, 60)
Occasions of syringe acquisition	3 (1, 4)
Total syringes acquired	50 (20, 120)
No. of syringes sold or given away	5 (0, 25)
No. of syringes stockpiled	7 (0, 30)

insufficient coverage by eight percentage points. Including the new multiple syringes parameter raised the proportion of insufficient coverage a further four percentage points.

Regardless of the measure utilised, the percentages of participants with insufficient coverage remained substantial: a fifth to approximately a quarter of participants were insufficiently covered within the month prior to interview (Table 2).

Correlates of multiple syringe usage per injecting episode

Women had significantly increased odds of reporting the use of multiple syringes (AOR = 2.56, 95% CIs: 1.56, 4.19 (Table 3)). Those with an injecting career 16–25 years in length (compared to those with careers ≤15 years) were similarly at significantly increased odds (AOR = 3.73, 95% CIs: 1.90, 7.31). Those with injecting careers ≥26 years were not significantly different from the reference group. Those self-reporting mental health problems within the past six months had decreased odds of reporting using multiple syringes (AOR = 0.53, 95% CIs: 0.32, 0.86). Reported use of multiple syringes was significantly associated with past month experience of IRIDs (AOR = 3.60, 95% CIs: 2.02, 6.40).

When testing the drug most injected within the past month, two drug subgroups showed increased odds of reporting multiple syringe use in comparison with heroin injection. The injection of prescription opioids (predominantly morphine and oxycodone) was associated with a threefold increase in odds (AOR = 3.21, 95% CIs: 1.62, 6.36), while OST injection (methadone/buprenorphine-naloxone/buprenorphine) showed a sevenfold increase (AOR = 7.60, 95% CIs: 3.76, 15.39). No significant difference in multiple syringe use was detected for people who reported predominately injecting methamphetamine.

Correlates of insufficient coverage using the new coverage measure

Participants of Indigenous background had increased odds of <100% coverage (AOR = 1.60, 95% CIs: 1.01, 2.52) (Table 3). A significant association between insufficient coverage and personal syringe reuse was also found (AOR = 1.82, 95% CIs: 1.22, 2.72). Similar to the multiple syringes model, past month OST injection showed an increase in odds of insufficient coverage compared with heroin injection (AOR = 2.82, 95% CIs: 1.55, 5.12).

ROC curve analysis

Prior to comparing the discriminative abilities of the three coverage measures, significant associations were found between the coverage levels derived using each measure and the key injecting risk practices. For every one percentage point increase in continuous coverage using either the Bluthenthal et al. or the McCormack et al. measure, the odds of distributive sharing (a participant providing their previously used syringe to another PWID) were significantly reduced (Table 4). Distributive sharing was not significantly associated with the new measure. A one unit increase in coverage in all three coverage measures significantly reduced the odds of personal syringe re-use.

Comparison of ROC curves for the new coverage measure and, first, the Bluthenthal et al. measure, then the McCormack et al. measure showed only one significant difference in AUC. The AUC for the new measure was significantly greater for syringe reuse than for the Bluthenthal et al. measure (difference in AUC = 0.0325 (Table 4)), and therefore, the new measure was better at discriminating cases and non-cases of syringe reuse than the Bluthenthal et al. measure alone. Across all other risk practices, the new measure showed no significant improvement in discriminative ability.

Discussion

In this paper, we describe the use of multiple sterile syringes per injecting episode and test the effect of its inclusion in the measurement of individual-level syringe coverage.

Multiple syringe use

We found that a minority of PWID report using multiple syringes per injecting episode. This practice is preferable to syringe reuse in terms of injecting risk. Of the 134 participants who reported multiple syringe use, most (62%) reported no syringe reuse within the month prior to interview. Though the reasons why PWID reuse unsterile syringes or use multiple syringes are often the same (i.e., difficulty with injecting, as reflected by the reporting of past month IRIDs), it is a validation of Australia's unlimited dispensation policy that many PWID acquire extra syringes, rather than invite additional risk by reusing unsterile syringes.

The increased odds of female PWID using multiple syringes is potentially linked to two factors: having naturally less prominent surface veins than men (Darke, Topp, & Ross, 2002), and power disparities with male injecting partners (MacRae & Aalto, 2000). Male PWID often control the injecting practices of their female injecting partners, either by leaving women with used, blunted syringes, or may perform a woman's injection, both increasing the likelihood of vein damage (Topp et al., 2008). That women are more likely to have difficulty injecting (Topp et al., 2008) or to reuse their own syringes (Maher et al., 2001) has been demonstrated in previous research and the same factors may plausibly influence the use of multiple sterile syringes.

We assume that the reporting of the drug most commonly injected within the month prior to survey is an indication of an ongoing practice. The injection of both OST and prescription opioids has previously been associated with vein damage (Darke et al., 2002; Horyniak, Armstrong, Higgs, Wain, & Aitken, 2007; Jenkinson, Clark, Fry, & Dobbin, 2005), which may in turn lead to the need for multiple syringes. The injection of large volume OST

Table 2
Coverage levels across differing coverage measures.

Coverage measure	Median coverage (IQR)	≥100%, n (%)	<100%, n (%)
Bluthenthal et al. (without stockpiling, without multiple syringes)	167% (85–320)	605 (72)	233 (28)
McCormack et al. (with stockpiling, without multiple syringes)	222% (100–467)	670 (80)	168 (20)
New coverage measure (with stockpiling, with multiple syringes)[a]	200% (100–400)	631 (75)	199 (24)

[a] Eight missing data points.

Table 3
Descriptive and regression analyses for use of multiple syringes and insufficient coverage.

	n (%)	Use of multiple syringes n (%)	AOR (95% CI) for multiple syringes regression	Insufficient coverage (<100%) n (%)	AOR (95% CI) for insufficient coverage (<100%) regression
Sex					
Male	559 (66)	63 (47)	1	127 (64)	1
Female	278 (33)	71 (53)	2.56 (1.56, 4.19)***	72 (36)	0.95 (0.63, 1.44)
Transgender	1 (1)	0	NA	0	NA
Age					
≤35	188 (22)	33 (25)	1	50 (25)	1
36–45	350 (42)	46 (34)	0.61 (0.32, 1.18)	85 (43)	0.97 (0.59, 1.62)
≥46	300 (36)	55 (41)	1.75 (0.77, 3.95)	64 (32)	1.13 (0.59, 2.18)
Missing	1	0		0	
Country of birth					
Australia	742 (89)	114 (85)	1	178 (89)	1
Other	95 (11)	20 (15)	1.69 (0.88, 3.25)	21 (11)	1.25 (0.70, 2.25)
Missing	1	0		0	
Indigenous status					
Non-Indigenous	673 (80)	106 (79)	1	144 (72)	1
Indigenous	164 (20)	28 (21)	1.01 (0.56, 1.82)	55 (28)	1.60 (1.01, 2.52)*
Missing	1	0		0	
Relationship status					
Married/de facto/regular partner	301 (36)	52 (39)	1	63 (32)	1
Single	480 (58)	70 (52)	0.90 (0.55, 1.47)	119 (60)	1.06 (0.71, 1.59)
Separated/divorced/widowed	50 (6)	12 (9)	1.64 (0.65, 4.10)	16 (8)	1.33 (0.59, 2.97)
Missing	7	0		1	
Accommodation					
Stable	620 (76)	102 (78)	1	139 (71)	1
Unstable	194 (24)	28 (22)	1.17 (0.67, 2.04)	58 (29)	1.43 (0.94, 2.19)
Missing	24	4		2	
Self-reported mental health problems (past six months)					
No	440 (55)	75 (57)	1	98 (51)	1
Yes	365 (45)	56 (43)	0.53 (0.32, 0.86)**	96 (49)	1.20 (0.82, 1.76)
Missing	33	3		5	
Employment status					
Employed	128 (16)	18 (14)	1	29 (15)	1
Unemployed	695 (84)	115 (86)	0.98 (0.50, 1.92)	164 (85)	0.94 (0.55, 1.61)
Missing	15	1		6	
Weekly income					
≤$398	473 (57)	80 (61)	1	107 (55)	1
>$378	353 (43)	51 (39)	0.69 (0.42, 1.12)	89 (45)	1.29 (0.88, 1.91)
Missing	12	3		3	
Injecting career					
≤15 years	210 (25)	24 (18)	1	54 (27)	1
16–25 years	328 (39)	62 (46)	3.73 (1.90, 7.31)***	86 (43)	1.11 (0.69, 1.79)
≥26 years	298 (36)	48 (36)	1.88 (0.81, 4.34)	59 (30)	0.66 (0.36, 1.21)
Missing	2	0		0	
Drug most injecting (past month)					
Heroin	342 (42)	43 (34)	1	71 (38)	1
Methamphetamine	281 (34)	33 (26)	1.61 (0.90, 2.85)	56 (30)	0.92 (0.59, 1.45)
OST injection	72 (9)	27 (22)	7.60 (3.76, 15.39)***	28 (15)	2.82 (1.55, 5.12)**
Prescription opiates	119 (15)	22 (18)	3.21 (1.62, 6.36)**	33 (17)	1.67 (0.95, 2.95)
Missing	24	9		11	
Current drug treatment					
No current treatment	442 (53)	58 (43)	1	108 (55)	1
Current OST prescription	365 (44)	74 (55)	1.61 (0.99, 2.60)	82 (42)	0.87 (0.59, 1.28)
Other treatment	22 (3)	2 (2)	0.46 (0.05, 3.83)	6 (3)	1.08 (0.35, 3.29)
Missing	9	0		3	
Injecting related injury and disease (past month)					
No	307 (37)	22 (16)	1	71 (36)	1
Yes	519 (63)	112 (84)	3.60 (2.02, 6.40)***	124 (64)	0.84 (0.56, 1.25)
Missing	12	0		4	
Receptive syringe sharing (past month)					
No	783 (93)	127 (95)	1	184 (92)	1
Yes	55 (7)	7 (5)	0.63 (0.22, 1.86)	15 (8)	0.78 (0.35, 1.74)

Table 3 (*Continued*)

	n (%)	Use of multiple syringes n (%)	AOR (95% CI) for multiple syringes regression	Insufficient coverage (<100%) n (%)	AOR (95% CI) for insufficient coverage (<100%) regression
Distributive syringe sharing (past month)					
No	742 (89)	121 (90)	1	162 (82)	1
Yes	91 (11)	13 (10)	0.70 (0.31, 1.60)	35 (18)	1.63 (0.91, 2.90)
Missing	5	0		2	
Re-use of own syringe (past month)					
No	506 (61)	83 (62)	1	97 (49)	1
Yes	329 (39)	51 (38)	1.08 (0.66, 1.77)	102 (51)	1.82 (1.22, 2.72)**
Missing	3	0		0	
Receptive sharing of injecting equipment (past month)					
No	652 (78)	95 (71)	1	151 (76)	1
Yes	186 (22)	39 (29)	1.25 (0.71, 2.18)	48 (24)	1.09 (0.68, 1.75)

Multiple syringes regression model, number of observations: 698; Prob(chi^2): <0.001; Pseudo R^2: 0.17.
Coverage measure regression model, number of observations: 698; Prob(chi^2): 0.002; Pseudo R^2: 0.06.
* p-Value = < 0.05.
** p-Value = < 0.01.
*** p-Value = < 0.001.

Table 4
Association between coverage measures, risk behaviour and ROC curve analysis.

Risk behaviour	OR (95% CIs)	AUC (95% CIs)	Difference in AUC	p-Value
Receptive syringe sharing				
Bluthenthal et al.	0.9993 (0.9982, 1.0003)	0.5407 (0.4639, 0.6175)	0.0119	0.5242
McCormack et al.	0.9992 (0.9984, 1.0001)	0.5672 (0.4937, 0.6408)	−0.0146	0.1511
New measure	0.9993 (0.9984, 1.0001)	0.5526 (0.4791, 0.6261)		
Distributive syringe sharing				
Bluthenthal et al.	**0.9992 (0.9983, 0.9999)**	0.5618 (0.4990, 0.6246)	0.0119	0.3597
McCormack et al.	**0.9993 (0.9987, 0.9999)**	0.5878 (0.5263, 0.6493)	−0.0141	0.0740
New measure	0.9995 (0.9989, 1.0000)	0.5737 (0.5104, 0.6371)		
Personal syringe reuse				
Bluthenthal et al.	**0.9992 (0.9987, 0.9996)**	0.5733 (0.5341, 0.6124)	0.0325	**0.0046**
McCormack et al.	**0.9992 (0.9988, 0.9995)**	0.6116 (0.5731, 0.6502)	−0.0058	0.3821
New measure	**0.9991 (0.9987, 0.9995)**	0.6058 (0.5671, 0.6445)		
Receptive equipment reuse				
Bluthenthal et al.	1.0000 (0.9996, 1.0004)	0.5053 (0.4570, 0.5536)	0.0079	0.8667
McCormack et al.	1.0000 (0.9998, 1.0002)	0.5018 (0.4534, 0.5502)	0.0114	0.1634
New measure	0.9999 (0.9996, 1.0001)	0.5132 (0.4651, 0.5614)		

Bluthenthal et al.: without stockpiling, without multiple syringes.
McCormack et al.: with stockpiling, without multiple syringes.
New measure: with stockpiling, with multiple syringes.

(i.e. methadone) may also be associated. It is possible that multiple syringes may be used in the preparation of drugs for injection (particularly for prescription opioids), without each syringe actually being used to penetrate the skin. Whilst we are confident participants correctly understood the meaning of our question related to needles/syringes, this interpretation cannot be ruled out entirely (see limitations).

Participants reporting recent mental health problems had significantly reduced likelihood of using multiple syringes. This finding is not necessarily indicative of risk, as this subgroup reported less frequent past month injecting and was no more likely to engage in injecting risk practices than the overall sample. Further research may be needed to clarify this association.

Finally, it may be expected that those with longer injecting careers would have greater vein damage and therefore more need for multiple syringes, but those with very long careers (>25 years) did not show significantly increased odds of multiple syringe use compared to the reference group (≤15 years). Between career subgroups, there was no substantial difference in injecting frequency or IRID prevalence. However, those with the longest careers were much more likely to report heroin as their most commonly injected drug within the past month than the other two career subgroups (52% vs. 33–39%) and less likely to report the injection of OST (6% vs. 10–11%) or prescription opioids than the ≤15 year career group (13% vs. 21%). It may be that PWID towards the furthest ends of injecting careers are less likely to inject drugs that may exacerbate vein damage or increase difficulty with injections, and thereby, increase the need for multiple syringes.

Insufficient coverage using the new measure

The regression models showed significant associations between insufficient coverage and Indigenous status, OST injection and syringe reuse. Past research has shown Indigenous Australians

experience numerous barriers to accessing services (Kratzmann et al., 2011). Whilst insufficient coverage can lead to increases in risk practices (Bluthenthal, Anderson et al., 2007; Iversen et al., 2012), this is particularly compounded for Indigenous Australian PWID, who often have higher rates of injecting risk (Paquette, McEwan, & Bryant, 2013; Ward et al., 2011), potentially due to longstanding societal drivers of poor health. The association between insufficient coverage and OST injection is almost certainly a product of the OST association seen in the multiple syringes regression model.

The regression model was re-run separately using the insufficient coverage outcome under the Bluthenthal et al. and McCormack et al. measures, with only the syringe reuse association consistent across all three models. This association replicates other research (Iversen et al., 2012). In this regard, it is probable that individuals who experience insufficient coverage are more likely to reuse their syringes, rather than syringe reuse predicting insufficient coverage.

Most important is that, regardless of the measure used, the percentage of PWID experiencing insufficient coverage remains substantial, and consistent with previous work. Across the sample, 12% of participants reported difficulty accessing syringes within the past month, suggesting that structural barriers exist for syringe acquisition. To raise coverage levels, it is important that PWID are afforded every opportunity to cover their injecting episodes via the upscaling of services, such as longer NSP opening hours and alternate forms of syringe delivery (such as syringe vending machines, which are not available in all Australian jurisdictions) (O'Keefe et al., 2016). It should also be remembered that individual-level syringe coverage measures seek only to calculate a pool of "potential" sterile syringes an individual PWID can draw from, without necessarily guaranteeing that the person will actually inject with any of them. The measure seeks to evaluate the sufficiency of NSP syringe distribution for individual PWID needs. However, there are many reasons why PWID may acquire sufficient sterile syringes, yet not always make use of them, and further research, potentially qualitative in nature, should explore how many injecting episodes *actually* utilise a sterile syringe and the reasons for any short falls.

Discriminative ability of the new coverage measure

For those PWID who report the use of multiple syringes, asking about injecting frequency alone may underestimate their need for syringes and create inaccuracies in coverage measurement. However, whilst McCormack et al. (2016) showed that 75% of their sample reported stockpiling syringes, only 16% of our participants reported the use of multiple syringes. To include any new parameter within existing coverage measures introduces corresponding recall bias. Each parameter within the coverage calculation requires participants to remember and report a specific number of syringes or injecting episodes, all prone to bias, which is then compounded as the number of parameters increases. If a large proportion of PWID reported a particular behaviour, this would justify its potential bias when including it as a parameter within coverage measures. However, though 16% represents a reasonable number of people needing multiple syringes for their injecting episodes, and this finding has practical importance, it remains a small number.

Furthermore, the ability of the new coverage measure to discriminate the key injecting risk practices was no better than existing measures. Across all tested injecting risk practices, the magnitude of each AUC was moderate and most differences non-significant. Only syringe reuse could be better discriminated using the new measure compared to the Bluthenthal et al. measure. However, we further tested the discriminative ability of the Bluthenthal et al. and the McCormack et al. measures for syringe reuse and found that the difference of the AUC was greater (AUC = 0.0378), suggesting that it was the inclusion of syringe stockpiling that better discriminated syringe reuse, not multiple syringes in the new measure.

Limitations

The measurement of syringe coverage has inherent bias. Each parameter requires the recall of a specific number of syringes or injecting frequency over a particular time period. Such bias is an unavoidable element in the measurement of coverage based on self-report.

The question we used to measure multiple syringe use means it is possible that some participants misinterpreted our intended meaning. For example, participants may have interpreted our question as including situations involving the use of multiple syringes for drug preparation (and not injecting with each syringe), such as using separate needles/syringes to draw up dissolved drug solutions. Alternatively, participants may have believed the question meant "number of skin penetrations per successful 'hit'". Both interpretations of the question would introduce bias into the measure. Our interviewers believed participants understood the intent of the question, as a small number sought clarification if uncertain. However, future researchers should explicitly ask about the use of multiple *sterile* syringes that *penetrated the skin* per injecting episode.

In order to record the use of multiple syringes, we asked for the "average" number required per injecting episode. Of course, many participants will at times require more or fewer syringes than their reported average, but the specification of an "average" number should account for these difference across episodes.

Conclusion

As an injecting practice, the use of multiple syringes by PWID shows the benefits of Australia's unlimited syringe dispensation policy. From a harm reduction perspective, it is preferable that PWID use multiple sterile syringes rather than reuse unsterile syringes, and this may not occur in locations with restricted syringe distribution. However, the use of multiple syringes, just like syringe reuse, is an indicator of injecting difficulty. In this regard, our findings suggest the need for further intervention for those at-risk groups highlighted in analysis, potentially through programs that demonstrate how to inject safely (for example, reducing the harms of particulate contamination through filtration when injecting pills), which have previously shown positive results (Wood et al., 2008). Whilst our results accord with past Australian research, we believe further research (such as qualitative interviewing) in this area is warranted to explore questions about multiple syringe use and the best methods to improve injecting practices and vein health amongst PWID.

Based on our findings, there is no need to add a multiple syringe parameter to existing coverage formulae. The inclusion of a new parameter must justify the introduction of its inherent recall bias. The minority of participants reporting multiple syringe use and the inferior discriminative ability of our new measure did not justify the parameter's inclusion. Hence, we recommend that multiple syringe use is not included in future measurement of individual-level syringe coverage.

Contributors

DO'K led the development, analysis and writing of the paper. AMc and CA provided indispensable assistance with analysis and writing. SC, LB, RB, JS, KB, CB and PD supervised field activities and

provided substantial assistance with paper writing. All authors have read the article and approve of its submission to the International Journal of Drug Policy.

Conflict of interest

PD has received funding from Gilead Sciences Inc. and Reckitt Benckiser for work unrelated to this study. Other authors have nothing to declare.

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References

Allen, E. J., Palmateer, N. E., Hutchinson, S. J., Cameron, S., Goldberg, D. J., & Taylor, A. (2012). Association between harm reduction intervention uptake and recent hepatitis C infection among people who inject drugs attending sites that provide sterile injecting equipment in Scotland. *International Journal of Drug Policy*, *23*, 346–352.

Bluthenthal, R. N., Anderson, R., Flynn, N. M., & Kral, A. H. (2007). Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. *Drug and Alcohol Dependence*, *89*, 214–222.

Bluthenthal, R. N., Ridgeway, G., Schell, T., Anderson, R., Flynn, N. M., & Kral, A. H. (2007). Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. *Addiction*, *102*, 638–646.

Brett, M. M., Hood, J., Brazier, J. S., Duerden, B. I., & HahnÉ, S. J. M. (2005). Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. *Epidemiology and Infection*, *133*, 575–582.

Bryant, J., Paquette, D., & Wilson, H. (2012). Syringe coverage in an Australian setting: Does a high level of syringe coverage moderate syringe sharing behaviour? *AIDS and Behavior*, *16*, 1156–1163.

Burrows, D. (2006). Advocacy and coverage of needle exchange programs: Results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. *Cadernos de Saúde Publica*, *22*, 871–879.

Dahlman, D., Hakansson, A., Bjorkman, P., Blome, M. A., & Kral, A. H. (2015). Correlates of skin and soft tissue infections in injection drug users in a syringe-exchange program in Malmo, Sweden. *Substance Use and Misuse*, *50*, 1529–1535.

Darke, S., Topp, L., & Ross, J. (2002). The injection of methadone and benzodiazepines among Sydney injecting drug users 1996–2000: 5-year monitoring of trends from the illicit drug reporting system. *Drug and Alcohol Review*, *21*, 27–32.

Dolinar, R. (2009). The importance of good insulin injection practices in diabetes management. *US Endocrinology*, *5*, 49–52.

Dwyer, R., Topp, L., Maher, L., Power, R., Hellard, M., Walsh, N., et al. (2009). Prevalences and correlates of non-viral injecting-related injuries and diseases in a convenience sample of Australian injecting drug users. *Drug and Alcohol Dependence*, *100*, 9–16.

Hando, J., Darke, S., O'Brien, S., Maher, L., & Hall, W. (1998). The development of an early warning system to detect trends in illicit drug use in Australia: The illicit drug reporting system. *Addiction Research & Theory*, *6*, 99–113.

Hanley, J. A., & McNeil, B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*, *143*, 29–36.

Harris, M., & Rhodes, T. (2012). Venous access and care: Harnessing pragmatics in harm reduction for people who inject drugs. *Addiction*, *107*, 1090–1096.

Horyniak, D., Armstrong, S., Higgs, P., Wain, D., & Aitken, C. (2007). Poor man's smack: A qualitative study of buprenorphine injecting in Melbourne, Australia. *Contemporary Drug Problems*, *34*, 525–548.

Iversen, J., Topp, L., Wand, H., & Maher, L. (2012). Individual-level syringe coverage among needle and syringe program attendees in Australia. *Drug and Alcohol Dependence*, *122*, 195–200.

Jenkinson, R. A., Clark, N. C., Fry, C. L., & Dobbin, M. (2005). Buprenorphine diversion and injection in Melbourne, Australia: An emerging issue? *Addiction*, *100*, 197–205.

Koester, S. (2012). Commentary on Harris & Rhodes (2012): Discouraging syringe re-use by addressing drug injectors' everyday suffering. *Addiction*, *107*, 1097–1098.

Kratzmann, M., Mitchell, E., Ware, J., Banach, L., Ward, J., & Ryan, J. (2011). *Injecting drug use and associated harms among Aboriginal Australians*. ACT, Australia: Australian National Council on Drugs.

Laufer, F. N. (2001). Cost-effectiveness of syringe exchange as an HIV prevention strategy. *Journal of Acquired Immune Deficiency Syndromes*, *28*, 272–278.

MacRae, R., & Aalto, E. (2000). Gendered power dynamics and HIV risk in drug-using sexual relationships. *AIDS Care*, *12*, 505–515.

Maher, L., Sargent, P. L., Higgs, P., Crofts, N., Kelsall, J., & Le, T. T. (2001). Risk behaviours of young Indo–Chinese injecting drug users in Sydney and Melbourne. *Australian and New Zealand Journal of Public Health*, *25*, 50–54.

McCormack, A., Aitken, C., Burns, L. A., Cogger, S., & Dietze, P. (2016). Syringe stockpiling by people who inject drugs: An evaluation of current measures for needle and syringe program coverage. *American Journal of Epidemiology*, *183*, 852–860.

Metz, C. E. (1978). Basic principles of ROC analysis. *Seminars in Nuclear Medicine*, *8*, 283–298.

O'Keefe, D., Scott, N., Aitken, C., & Dietze, P. (2016). Individual-level needle and syringe coverage in Melbourne, Australia: A longitudinal, descriptive analysis. *BMC Health Services Research*, *16*, 411.

Paquette, D., McEwan, M., & Bryant, J. (2013). Risk practices among aboriginal people who inject drugs in New South Wales, Australia. *AIDS and Behavior*, *17*, 2467–2473.

Stafford, J., & Burns, L. (2016). *Illicit drug reporting system (IDRS) national report 2015*. Sydney, Australia: National Drug and Alcohol Research Centre (NDARC).

Strathdee, S. A., & Mailman, J. L. (2001). The effectiveness of needle exchange programs: A review of the science and policy. *AIDScience*, *1*.

Topp, L., Iversen, J., Conroy, A., Salmon, A. M., & Maher, L. (2008). Prevalence and predictors of injecting-related injury and disease among clients of Australia's needle and syringe programs. *Australian and New Zealand Journal of Public Health*, *32*, 34–37.

Ward, J., Topp, L., Iversen, J., Wand, H., Akre, S., Kaldor, J., et al. (2011). Higher HCV antibody prevalence among Indigenous clients of needle and syringe programs. *Australian and New Zealand Journal of Public Health*, *35*, 421–426.

WHO (2012). *Technical guide for countries to set targets for universal HIV services for injecting drug users*. Geneva, Switzerland: World Health Organisation.

Wiessing, L., Denis, B., Guttormsson, U., Haas, S., Hamouda, O., Hariga, F., Hoch, E., Imbert, E., De Maere, W., Nociar, A., Origer, A., Partanen, A., Rajniaková, T., Rhodes, T., Rodés, A., Šejda, J., Terzidou, M., Kraus, L., Kümmler, P., Burkhart, G., & Hartnoll, R. (2001). The global research network on HIV prevention in drug-using populations (GRN) 1998-2000: estimating coverage of harm-reduction measures for injection drug users in Europe. *National Institute on Drug Abuse. Global Research Network Meeting on HIV Prevention in Drug-Using Populations, Third Annual Meeting Report* (pp. 1–8).

Wood, R. A., Wood, E., Lai, C., Tyndall, M. W., Montaner, J., & Kerr, T. (2008). Nurse-delivered safer injection eduction among a cohort of injection drug users: Evidence from the evaluation of Vancouver's supervised injection facility. *International Journal of Drug Policy*, *19*, 183–188.

4.3 Summary of Chapter Four

Sixteen percent of the sample reported requiring, on average, more than one sterile syringe per injecting episode. This finding shows that many PWID experience difficulty injecting. This practice was significantly associated with the injection of pharmaceutical opioids, the injection of OST (e.g. methadone or burprenorphine), the experience of injection related injuries and diseases (such as scarring/bruising and injection-related infections) and female gender. These associations suggest this behaviour may result from difficulties with injecting that may be related to particularly risky injecting practices, such as injecting substances known to cause vein damage (pharmaceutical opioids and OST (165, 166)) and the experience of consequent injecting-related injuries. Whilst the use of multiple sterile syringes is preferable to syringe re-use, the promotion of safe injecting techniques, particularly the proper filtration of drug contaminants for those injecting pharmaceutical opioids or OST medications, needs to be emphasised by harm reduction services.

I constructed a new individual-level syringe coverage measure, inclusive of multiple sterile syringe use. The use of this measure estimated an insufficient individual-level syringe coverage prevalence of 24%, four percentage points lower than a formula without the parameter. Insufficient individual-level syringe coverage under this measure was associated with syringe re-use, past month injection of OST medications, and self-reported Australian Aboriginal or Torres Strait Islander (ATSI) background. However, I re-ran this analysis using more established individual-level syringe coverage formulas: the adapted Bluthenthal et al. measure and the McCormack et al. measure. The associations between the injection of OST medications, ATSI-background and insufficient individual-level syringe coverage was not reproduced in these models. Moreover, the only consistent association across the three regression models was between syringe re-use and insufficient individual-level syringe coverage, a finding previously replicated in other independent research (5, 37, 148).

The new individual-level syringe coverage measure was compared against the adapted Bluthenthal et al. and the McCormack et al. measures, exploring the abilities of each measure to detect cases and non-cases of injecting risk behaviours. The results suggested the newly constructed measure was no better at this discrimination than the

two existing measures. This finding, coupled with the relatively low percentage of the sample reporting the use of multiple sterile syringes, suggested the parameter need not be included within the individual-level syringe coverage formula.

Chapter Five: Harm reduction in low and middle income countries

5.1 Overview of Chapter Five

Global harm reduction response is inadequate (8). This shortfall is a result of insufficient funding, competing public health priorities, political inaction and the ongoing marginalisation of PWID (82, 99). Whilst IDU has been reported in 179 countries, needle and syringe programs have only been implemented in 93, and OST is prescribed in only 86 (8), meaning that PWID in those countries without these harm reduction responses are at significant risk of BBV infection and other IDU-related harms (84). The issues described above are particularly prevalent in LMICs (99).

Paper Five presents a review for the Journal of Viral Hepatitis of IDU and harm reduction in LMICs. The review discusses the level of harm reduction implementation, the causes and consequences of its shortfalls, those countries that have successfully instituted effective response and key priorities looking towards the future.

The absence of high-quality public health data in LMICs is a particular problem (143). IDU has now been reported in 87% of the world's countries and territories, covering 99% of the global population (9). Yet PWID prevalence estimates exist for only 83 countries (9), again most of the countries for which estimates are not available are LMICs (9). If most PWID research originates from high-income countries, findings may bare little relevance or applicability to many LMICs. Furthermore, without the capacity for even basic descriptive demographic studies in LMICs, the potential for more complex research is limited, hampering the understanding of local PWID populations and the planning/monitoring of public health interventions.

Similarly, most individual-level syringe coverage research has been conducted in high-income settings. Noroozi et al. previously published work measuring individual-level syringe coverage amongst Iranian PWID, reporting an insufficient individual-level syringe coverage prevalence of 53%, and that this insufficiency was associated with injecting risk behaviours, such as receptive syringe sharing and syringe re-use (148).

Their work provided important research on individual-level syringe coverage in an LMIC, however, it shouldn't be presumed that the barriers to sufficient syringe coverage are similar across countries.

Like many other South-East Asian countries, Myanmar's HIV epidemic is driven mainly by IDU (127, 167) (rather than via sexual transmission). In recent years, Myanmar has sought to reduce the high prevalence of PWID-specific HIV via a concerted expansion of their national harm reduction program. As a result, HIV prevalence in the PWID population decreased from over 70% in the 1990s, to 28.5% in 2016 (168, 169). However, syringe coverage measurement in Myanmar remains at the population level. In 2016, an estimated 168 syringes were distributed per PWID, a figure below WHO recommendations, but high compared to other countries in the region (8, 82). Levels of insufficient syringe coverage at the individual-level remain unknown. Furthermore, whilst some past Myanmar-based research exists, it has been restricted mostly to border areas with China where drug production is high and government control is low (127, 167). PWID research in Myanmar's urban centres is minimal.

In Paper Six I measure syringe coverage at the individual-level across three characteristically different urban locations in Myanmar. This research has two purposes: providing a more complete estimate of syringe coverage in Myanmar, and expanding syringe coverage research outside high-income settings. To better understand the barriers to sufficient individual-level syringe coverage, research needs to be performed in diverse contexts.

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5.2 Publication: Injecting drug use in low and middle-income countries: opportunities to improve care and prevent harm

COMMISSIONED REVIEW

WILEY JOURNAL OF VIRAL HEPATITIS JVH

Injecting drug use in low and middle-income countries: Opportunities to improve care and prevent harm

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Summary

Inadequate response to injecting drug use (IDU) is a significant problem the world over. Low levels of funding, political inaction, poor levels of health service coverage, high prevalence and incidence of IDU-related blood-borne viruses (BBVs) and ongoing stigmatization/marginalization affect people who inject drugs (PWID) regardless of the income status of the country they reside in. These barriers and system failings are, however, exacerbated in low and middle-income countries (LMICs), meaning that the potential consequences of inaction are more pressing. In this narrative review, we describe the levels of IDU and IDU-specific BBV prevalence in LMICs; levels of harm reduction implementation; the consequences of late or insufficient response, the shortcomings of data collection and dissemination; and the barriers to effective LMIC harm reduction implementation. We also exemplify cases where IDU-related harms and BBV epidemics have been successfully curtailed in LMICs, showing that effective response, despite the barriers, is possible. In conclusion, we suggest four key priorities on the basis of the review: confirming the presence or absence of IDU in LMICs, improving the collection and dissemination of national IDU-specific data, increasing the level of harm reduction programme implementation in LMICs, and increasing both national and international advocacy for PWID and attendant public health interventions.

KEYWORDS
harm reduction, hepatitis C, injecting drug use, low and middle income countries, people who inject drugs

1 | INTRODUCTION

Injecting drug use (IDU) is a global public health concern, with an estimated 12 million current people who inject drugs (PWID) worldwide.[1] IDU is associated with a range of health and social harms, including blood-borne viral infections (BBVs),[2] injecting-related injuries, stigma,[3] involvement with criminal justice systems[4] and premature death from many causes, including those as a direct consequence of IDU.[5]

Once considered a public health issue predominantly affecting high-income countries, IDU has now been reported across numerous low- and middle-income countries (LMICs), such that the majority of the world's PWID are now estimated to live in LMICs.[6] The social and environmental realities of many LMICs—rapid urbanization, high intracountry migration, high unemployment and poverty, overcrowded and polluted environments, high levels of violence and low social support—create fertile conditions for the presence and expansion of IDU.[7] International experience has shown that emergent IDU requires swift, comprehensive and sustained intervention to minimize the long-term health and social harms associated with IDU.[7] Competing public health priorities, political intransigence, disproportionate burden of disease, insufficient resources and poor health infrastructure mean that few LMICs are equipped to adequately tackle an emergent epidemic amongst a new at-risk population, amplifying the negative outcomes.

This article provides an overview of IDU in LMICs, describing the population prevalence of IDU and the associated epidemiology of BBVs amongst PWID in these countries. We also highlight how harms

associated with IDU can be amplified in LMICs, identify interventions aimed at reducing these harms (including the current implementation across LMICs) and provide examples of successful programmes in LMICs.

2 | INJECTING DRUG USE ACROSS LMICS

The World Bank categorizes LMICs according to gross national income per capita (low income: ≤US$1,025; lower-middle income: US$1026-US$4035; upper-middle income: US$4036-$12 475).[8] According to World Bank categorization, 31 countries are classified as "low income," 52 as "lower-middle income" and 56 as "upper-middle income"; a combined 139 countries and territories. Country-by-country data on evidence of IDU and population prevalence of IDU are listed in Table 1.

IDU has been documented in 158 of the world's countries and territories.[9] Evidence of IDU has been reported in 10 (32%) of the 31 countries classified as "low income," compared to 45 (87%) of those classified as "lower-middle income" and 41 (73%) of those classified as "upper-middle income".[9,10] Estimated population prevalence of IDU amongst 15- to 64-year-olds ranges from 0.01% (Cambodia) to 4.20% (Dominican Republic) ‡.[9] Although LMICs account for 64% of all countries and territories, an estimated 80% of the world's PWID live in LMICs, predominately in Eastern Europe (approximately 3.5 million PWID) and East/South-East Asia (approximately 4 million PWID).[10-12]

3 | BLOOD-BORNE VIRUSES

Injecting drug use is a key driver of BBV transmission. Globally, it is estimated that three million PWID are HIV positive,[10] ten million are hepatitis C virus (HCV) antibody positive* and 1.2 million are hepatitis B virus (HBV) surface antigen positive†. [13] Much of this IDU-related infection burden is concentrated in Eastern Europe and East/South-East Asia,[13] with half of all HIV and HCV-positive PWID in these two regions.[10,13] It is estimated that nearly half (47%) of all PWID infected with HIV in LMICs live in just five countries—China, Vietnam, Russia, Ukraine and Malaysia.[14] Table 1 shows the estimated prevalence of HIV amongst PWID in LMICs ranging from 0% (Kosovo) to 50-73% (Mozambique); of HCV, from 3.4% (Dominican Republic) to 96.5% (Mauritius); and of HBV, from 0% (Montenegro) to 60.5% (Syria).[9] However, the variability in quality of country data demands caution of such estimates.

In recent years, IDU has replaced sexual transmission as the leading cause of HIV infection in a number of LMICs. IDU is now the primary mode of HIV transmission in many North African, Middle Eastern, Asian and South American countries, a development particularly concerning given the higher potential for BBV transmission via parenteral compared to sexual exposure.[15] Of additional concern is the identification of PWID as a bridging population for HIV and other BBVs when onward transmission occurs to sexual partners of PWID and from mother to child.[15] For example, a study of male PWID and their (non-drug-using) wives in Manipur, India, where HIV prevalence amongst PWID is 80%, found that 45% of wives were HIV positive.[16]

Many PWID in LMICs are not receiving treatment for their BBV infections. Reasons for the denial or delay of antiretroviral therapy (ART) for HIV-positive PWID include clinician's concern about nonadherence and resultant ART resistance and comorbidity-related complications.[14] Other factors impacting on treatment uptake include systemic and structural barriers such as user fees, bans on treatment for active injectors and other eligibility requirements that disproportionately affect PWID, police use of drug-user registries (thus discouraging treatment seeking), detention of drug users in compulsory drug rehabilitation centres and ongoing stigmatization.[14] As a consequence, HIV-positive PWID are more likely to be poorly engaged in care and experience increased risk of death, even in countries with well-established ART programmes.[14]

Whilst strengthening of HIV treatment and prevention is a key target in reducing global burden of disease and supported by many international agencies and strategies, a focus on HIV has often meant the neglect of viral hepatitis.[13] Until recently, this neglect has been compounded by a reliance on low efficacy interferon-based treatments with significant side effects that require treatment through relatively high-cost specialist care services. In most countries reporting IDU, the prevalence of HCV in PWID is far in excess of HIV, even in countries with comprehensive harm reduction programmes (such as Australia).[17] Therefore, emerging populations of PWID in unprepared and under-resourced LMICs need monitoring, especially those with a high prevalence of HCV (Africa, the Middle East and South-East Asia) and HBV (East and South-East Asia) in the general population.[13] BBV co-infection, leading to accelerated disease progression, is a distinct issue.[18] However, the new era of HCV treatment via direct-acting antivirals provides new hope for disease elimination.[19] The key challenge is reaching individuals in LMICs with these new treatments.[20] Improving detection amongst infected individuals and ensuring affordable access to treatments (especially in middle-income countries, many of which are becoming important markets for pharmaceutical companies, which price their products accordingly) is paramount.[20] Regarding HBV, the WHO recommends expedited vaccination schedules and incentives to complete vaccination for PWID and must be prioritized amongst susceptible individuals,[13,21] whilst barriers to the detection and treatment of currently infected individuals [13] need to be identified and reduced across LMICs.

4 | HARM REDUCTION IN LMICS

Needle and syringe programmes (NSPs) and opioid substitute therapy (OST) are key harm reduction interventions that are effective at reducing unsafe injecting practices,[22] opioid overdose [23] and BBV transmission.[24,25] UN organizations include both NSPs and OST amongst their list of "essential" interventions in response to HIV amongst PWID.[26]

Reuse of needles and syringes (whether by a single individual or sharing between individuals) is a key driver of IDU-related harms, and the removal of used injecting equipment reduces the circulation of

TABLE 1 Evidence of IDU, PWID prevalence (amongst 15- to 64-year-olds), BBV prevalence (amongst PWID) and harm reduction implementation in LMICs

	Evidence of IDU	PWID prev. amongst 15-64-year-olds (%)	HIV prev. amongst PWID (%)	HCV (Ab+) prev. amongst PWID (%)	HBV (Sag+) prev. amongst PWID (%)	NSP	OST
Low income							
Benin	NA						
Burkina Faso	NA						
Burundi	NA						
Central African Republic	NA						
Chad	NA						
Comoros	NA						
Democratic Republic of the Congo	NA						
Eritrea	NA						
Ethiopia	NA						
Gambia, The	NA						
Guinea	NA						
Guinea-Bissau	NA						
Madagascar	NA						
Mali	NA						
Niger	NA						
Rwanda	NA						
Sierra Leone	NA						
Somalia	NA						
South Sudan	NA						
Togo	NA						
Zimbabwe	NA						
Afghanistan	Yes	0.25	4.4	31.2	6.6	Y	Y
Mozambique	Yes	0.02	50-73	62-77	32-36		
Nepal	Yes	0.30	6.3	87.3	5.8	Y	Y
Senegal	Yes	0.02	9.1	38.9	NA	Y	Y
Tanzania	Yes	0.12	35	28	3.8	Y	Y
Haiti	Yes	NA					
Korea, Democratic People's Republic	Yes	NA					
Liberia	Yes	NA					
Malawi	Yes	NA					
Uganda	Yes	NA					
Lower-middle income							
Cameroon	NA						
Cape Verde	NA						
Congo, Republic	NA						
Lesotho	NA						
Mauritania	NA						
Sao Tome and Principe	NA						
Swaziland	NA						
Armenia	Yes	0.60	6.3	NA	NA	Y	Y
Bangladesh	Yes	0.02	1.1	39.6	9.4	Y	Y

TABLE 1 (Continued)

	Evidence of IDU	PWID prev. amongst 15-64-year-olds (%)	HIV prev. amongst PWID (%)	HCV (Ab+) prev. amongst PWID (%)	HBV (Sag+) prev. amongst PWID (%)	NSP	OST
Cambodia	Yes	0.01	24.8	NA	NA	Y	Y
Egypt, Arab Republic	Yes	0.06	6.5-6.8	49.4	13.5	Y	
Ghana	Yes	0.04	NA	40.1	NA		
India	Yes	0.21	9.9	41	10.2	Y	Y
Indonesia	Yes	0.04	36.4	63.5	2.9	Y	Y
Kenya	Yes	0.08	18.3	51.4	6.4	Y	Y
Kosovo	Yes	1.01	0	26.6	4.1	Y	Y
Kyrgyz Republic	Yes	0.70	12-15	50	NA	Y	Y
Lao PDR	Yes	0.03	0.1	NA	NA	Y	
Moldova	Yes	1.15	7.9	70-73	3.4-14.2	Y	Y
Mongolia	Yes	0.03	NA	NA	NA	Y	
Morocco	Yes	0.08	11.4	57	NA	Y	Y
Myanmar	Yes	0.23	28.5	79.2	9.1	Y	Y
Nigeria	Yes	0.02	3.4	NA	NA		
Pakistan	Yes	0.10	37.8	93	6.8	Y	
Philippines	Yes	0.03	41.6	70	NA	Y	
Syria	Yes	0.07	NA	60.5	NA		
Tajikistan	Yes	0.49	13.5	36.2	NA	Y	Y
Tunisia	Yes	0.12	3	NA	NA	Y	
Ukraine	Yes	0.97	22	27.1	4.5	Y	Y
Uzbekistan	Yes	0.39	7.3	21.8	NA	Y	
Vietnam	Yes	0.43	40	74.1	19.5	Y	Y
Bhutan	Yes	NA					
Bolivia	Yes	NA					
Cote d'Ivoire	Yes	NA					
Djibouti	Yes	NA					
El Salvador	Yes	NA					
Guatemala	Yes	NA					
Honduras	Yes	NA					
Kiribati	Yes	NA					
Micronesia, Federated States	Yes	NA					
Nicaragua	Yes	NA					
Papua New Guinea	Yes	NA					
Samoa	Yes	NA					
Solomon Islands	Yes	NA					
Sri Lanka	Yes	NA					
Sudan	Yes	NA					
Timor-Leste	Yes	NA					
Tonga	Yes	NA					
Vanuatu	Yes	NA					
West Bank and Gaza	Yes	NA				Y	
Yemen, Republic	Yes	NA					
Zambia	Yes	NA					

TABLE 1 (Continued)

	Evidence of IDU	PWID prev. amongst 15-64-year-olds (%)	HIV prev. amongst PWID (%)	HCV (Ab+) prev. amongst PWID (%)	HBV (Sag+) prev. amongst PWID (%)	NSP	OST
Upper-middle income							
American Samoa	NA						
Angola	NA						
Belize	NA						
Botswana	NA						
Cuba	NA						
Dominica	NA						
Equatorial Guinea	NA						
Grenada	NA						
Guyana	NA						
Marshall Islands	NA						
Namibia	NA						
Palau	NA						
Saint Lucia	NA						
Saint Vincent and the Grenadines	NA						
Tuvalu	NA						
Albania	Yes	0.26	0.5	28.8	11.5	Y	Y
Argentina	Yes	0.25	3.5	4.8	1.6	Y	
Azerbaijan	Yes	1.05	9.5	57.9	7.4	Y	Y
Belarus	Yes	1.13	25.1	65.4	6.9	Y	Y
Bosnia and Herzegovina	Yes	0.46	0.3	12-43	2.3	Y	Y
Brazil	Yes	0.39	5.9	63.9	2.3	Y	
Bulgaria	Yes	0.40	10.6	67.8	5.7	Y	Y
China	Yes	0.26	6	67	9.6	Y	Y
Dominican Republic	Yes	4.20	11	3.4	3.1	Y	
Georgia	Yes	1.59	2.2	66	7.2	Y	Y
Iran, Islamic Republic	Yes	0.36	13.8	50.2	17.3	Y	Y
Iraq	Yes	0.19	NA	NA	NA		
Kazakhstan	Yes	1.02	7.9	60.3	7.9	Y	Y
Lebanon	Yes	0.10	1	52.8	2.5	Y	Y
Libya	Yes	0.18	87	94	5		
Macedonia, FYR	Yes	1.17	0.12	64.5	NA	Y	Y
Malaysia	Yes	0.83	16.3	67.1	NA	Y	Y
Mauritius	Yes	1.27	44.3	96.5	6.7	Y	Y
Mexico	Yes	0.20	2.5	96	NA	Y	Y
Romania	Yes	0.14	24.9	79	5	Y	Y
Russian Federation	Yes	1.79	18-31	72.5	2.6-7.1	Y	
Serbia	Yes	0.63	<5	61	69	Y	Y
South Africa	Yes	0.21	14	NA	NA	Y	Y
Thailand	Yes	0.15	21	89.8	NA	Y	Y
Algeria	Yes	NA					
Colombia	Yes	NA				Y	Y
Costa Rica	Yes	NA					

TABLE 1 (Continued)

	Evidence of IDU	PWID prev. amongst 15-64-year-olds (%)	HIV prev. amongst PWID (%)	HCV (Ab+) prev. amongst PWID (%)	HBV (Sag+) prev. amongst PWID (%)	NSP	OST
Ecuador	Yes	NA					
Fiji	Yes	NA					
Gabon	Yes	NA					
Jamaica	Yes	NA					
Jordan	Yes	NA				Y	
Maldives	Yes	NA					Y
Montenegro	Yes	NA	1.1	53.6	0	Y	Y
Panama	Yes	NA					
Paraguay	Yes	NA	9.3	9.8	NA	Y	
Peru	Yes	NA	1	NA	NA		
Suriname	Yes	NA					
Turkey	Yes	NA	0.2	42.8	4.2		Y
Turkmenistan	Yes	NA				Y	
Venezuela, RB	Yes	NA					

Evidence of in-country IDU was primarily derived from previous systematic reviews,[10,13] and the 2016 Global State of Harm Reduction report, prepared by Harm Reduction International.[9] PWID population numbers were drawn from the latter and transformed to population prevalence of national 15- to 64-year-olds via population figures derived from the World Bank. Where a range of PWID population numbers were provided, the midpoint of the range was used. BBV prevalence estimates were drived from the Global State of Harm Reduction report.

potentially contaminated needles and syringes.[27] However, only 90 countries (57% of those countries with reported IDU) worldwide have implemented NSPs,[9] 53 of which are classified as LMICs. NSPs are absent in many LMICs where IDU is known to occur—across East, South-East and South Asia, in the majority of Latin American and Caribbean countries, across the Middle East and North Africa, and in nearly all countries in sub-Saharan Africa.[28] In some of these countries, needles and syringes are available through pharmacies, at varying cost to PWID.[28]

OST has been demonstrated to be effective at reducing injecting frequency, injecting risk behaviours, BBV transmission, death from overdose and criminal activity, and enhancing ART adherence amongst opioid-injecting PWID.[29-32] However, only 80 countries (49% of countries with reported IDU) worldwide have OST programmes,[9] 40 of which are classified as LMICs.

Other harm reduction interventions, such as supervised injecting facilities (SIFs) and medically prescribed heroin, are supported by empirical evidence,[33-35] but have not been implemented in any LMICs.

The mere presence of harm reduction interventions is a relatively crude indicator of a country's BBV prevention capacity, with coverage of harm reduction across key populations a key driver of population-level prevention.[36] There is considerable variability in harm reduction coverage both within and between countries.[27] Even in countries with existing harm reduction programmes, most operate well below the levels required to reduce BBV transmission.[9] For example, Vietnam, Ukraine and Taiwan have each implemented over 1000 NSP services nationally, whilst Russia services an estimated PWID population of 1.8 million (1.72% population prevalence) with just four NSPs whilst maintaining a blanket ban on OST prescription;[9] consequently, over 80% of the region's new HIV infections occur in Russia.[9] Consistently low (<10% of the PWID population) access to NSP is recorded across most LMICs,[28] and syringe distribution in Latin America, the Caribbean, the Middle East, North Africa and sub-Saharan Africa averages less than one syringe per PWID per year.[28] Fifty-five LMICs in Table 1 have implemented some form of harm reduction, meaning 41 countries with evidence of IDU are without a response.

For programmatic coverage to have impact, programmes need to dispense sufficient injecting equipment to prevent syringe reuse (ideally, one sterile syringe for every injecting episode), and OST at a therapeutic dose for as long as is necessary.[37] The WHO recommends a syringe distribution rate of 200 and 300 sterile needles/syringes per PWID per annum to curb HIV and HCV spread, respectively,[38,39] and "high" coverage of OST considered as 40% of people who inject opioids under prescription.[38] Although these seem to be modest targets, most countries, regardless of setting, fail to reach these benchmarks. It is estimated that globally, only 22 needles/syringes are distributed per PWID per year and that only 8% of global PWID access formal NSPs annually.[28,39] It is estimated that only eight per 100 PWID are in receipt of OST.[28]

5 | THE CONSEQUENCES OF INADEQUATE RESPONSE

Government endorsement is central to the success of harm reduction programmes,[40] yet political support in many LMICs is absent, with explicit support for harm reduction in national policy documents evident in only a minority of these countries.[9] Public health interventions for PWID are politically and socially unpalatable meaning the climate in which harm reduction usually operates is particularly difficult. Even

in high-income countries, these interventions are often hard fought for and lacking in public support. More than this, many governments are openly hostile towards harm reduction and the population it seeks to assist with negative consequences for PWID. For example, 43% of Vietnamese out-of-treatment PWID reported experiencing one or more drug overdoses.[41] Between a third to a half of global drug-related deaths are as a result of overdose (mainly attributable to opioids),[1] yet access to naloxone (an opioid antagonist) is often unavailable.[42] Without access to harm reduction programmes, HIV prevalence can rise to 40% within one to 2 years of virus introduction[37] and HCV, with a greater transmission potential, can spread even more rapidly.[43] For example, in Manipur, India, HIV spread quickly through the PWID population, taking estimated population prevalence from 0% in 1989 to over 50% within 6 months.[44] One of the highest recorded incidence rates of HCV, 37.6 per 100 person-years, (at the time of publication) was recorded amongst young southern Chinese PWID.[45] In both examples, the absence of an adequate harm reduction programme was cited as a key reason for the epidemics. Despite the cost-effectiveness and low cost of harm reduction programmes, many LMICs do not have sufficient resources to implement and maintain them. However, modelling has suggested that modest levels of harm reduction coverage can have significant impacts. Vickerman et al.[46] showed that with a coordinated and holistic harm reduction programme in Eastern Europe and Central Asia, a coverage target of only 14% for NSP, OST and ART (working in combination) can reduce HIV incidence by 30%, over ten years.

6 | BARRIERS TO EFFECTIVE RESPONSE

Access to health care is dependent upon geographic accessibility, availability, financial accessibility and acceptability.[47] Harm reduction services in LMICs often fail to meet these criteria. Des Jarlais et al.[6] listed the four reasons why harm reduction services in LMICs may not be as effective as those in high-income countries: low financial resources; services in often tenuous states of operation due to finite, short-term nongovernmental funding options; greater levels of stigmatization faced by PWID; and greater interference by law enforcement.

7 | BARRIERS TO EFFECTIVE RESPONSE: FUNDING

Even for governments funding their own HIV prevention expenditure, PWID are rarely prioritized, with only 3.3% of reported funds directed towards PWID.[9] Harm reduction programmes typically receive much less funding than other drug-related initiatives such as law enforcement. An estimated $100 billion is spent annually on global drug supply and demand reduction efforts,[48] but only an estimated $160 million on harm reduction (7% of the estimated total required for adequate coverage)[48,49]. Furthermore, global harm reduction funding from both governmental and donor sources (such as the Global Fund) is currently declining, resulting in the closure of services in some countries.[9] This funding decrease is felt hardest in LMICs, where harm reduction is traditionally supported by NGOs and international donors. Donor contributions for harm reduction-based HIV prevention initiatives in LMICs dropped 7% between 2014 and 2015.[9]

The majority of harm reduction programmes in LMICs are funded by nongovernmental sources.[50] These programmes often operate under "pilot" status, with funding both tenuous and unsustainable, and are restricted in their reach and ability to expand. The imminent defunding of programmes operating in many middle-income countries is a case in point. Between 2017 and 2019, up to 24 countries will become ineligible for Global Fund support, the assumption being that national governments will fill this shortfall.[9] This funding withdrawal will particularly affect countries in South and South-East Asia and Eastern Europe, countries with minimal domestic support for harm reduction, and in some of which, the closure of NSPs has already been reported as a direct consequence.[9] Sudden reductions in harm reduction services have previously been shown to increase injecting risk behaviour;[51] to function appropriately, services need not only comprehensive implementation, but sustained and dependable funding.

8 | BARRIERS TO EFFECTIVE RESPONSE: STIGMA AND DISCRIMINATION

The widespread negative, marginalizing and often inaccurate beliefs about PWID that underpin stigmatizing attitudes towards this population are pervasive and multilayered. Stigma effects the standing of PWID, including their ability to participate fully as equal members of society and to advocate on behalf of themselves to receive appropriate health care. Importantly, there are multiple stigmatizing facets to the lives of many PWID that compound the discrimination and consequent marginalization they face. Aside from their status as users of illicit drugs, the prevalence of comorbid mental illness, the high rates of criminal behaviours, co-occurring participation in other marginalized activities such as sex work, and a generally lower socio-economic status have a cumulative stigmatizing impact. Stigma related to IDU is also intertwined with BBV-related stigma.[52] Such stigma has been implicated in poor HIV testing uptake amongst PWID in sub-Saharan Africa[53] and the reluctance to receive health care due to the threat of disclosure by health officials in Vietnam, where PWID reported far greater stigma towards their IDU, compared to their HIV status.[50] Whilst programmes to reduce stigma from health staff can and should be implemented,[54] the entrenched stigma experienced by PWID is generally society-wide and tacitly endorsed by authoritarian drug control policies.[55]

9 | BARRIERS TO EFFECTIVE RESPONSE: LAW ENFORCEMENT

Most drug control policies involve criminalization of drugs and the people who use them.[56] Reflecting this criminalization, PWID

are often exposed to saturation policing including arrest and harassment for possession of injecting equipment, even in countries where such possession is legal.[57] These policies have led to the mass imprisonment of PWID in China and Vietnam,[11] the extrajudicial killing of drug users in the Philippines and Thailand[58,59] and the establishment of compulsory detention centres across Asia, particularly in Cambodia, China, Laos, Malaysia, Myanmar, Thailand, Turkmenistan and Vietnam, where forced labour and violence occur (in the name of "treatment") in violation of human rights norms.[50] Some Latin American countries (Peru, Guatemala, Ecuador, Mexico) adopt similar forms of intervention, whilst others (Brazil, Uruguay) are said to be considering these approaches.[50,60] Not only do such approaches lead to human rights violations, recent evidence suggests such approaches fail to reduce relapse amongst opioid-dependent individuals (often PWID), compared with evidence-based treatments.[61]

10 | SUCCESSFUL RESPONSES TO IDU

There are many examples of successful harm reduction programme implementation and consequent positive health outcomes for PWID in LMICs. Vietnam, Ukraine and Taiwan have demonstrated that high population coverage is possible.[9,28] Nearly half a million Iranian drug users received OST via nearly 6000 prescribing outlets.[62] The effective administration of naloxone by PWID peers has been demonstrated in LMICs such as Kyrgyzstan and Tajikistan.[63] Nepal's harm reduction programme delayed its HIV epidemic by several years;[40,64] Bangladesh has maintained an HIV population prevalence comparable to countries with far greater resources, such as Australia and Hong Kong;[40] several Brazilian cities have seen HIV prevalence amongst PWID fall due to expanded harm reduction;[9,40] and high-coverage NSPs have been established in Belarus and Thailand.[6,40] Myanmar, with the fourth-highest PWID population in the Asia region, recognized PWID as a priority population for HIV prevention efforts and called for a considerable expansion of its national harm reduction programme in its National HIV Strategic Plan on HIV and AIDS.[65] The plan includes increased access to NSPs via a combination of fixed and outreach services, the distribution of 30 million sterile syringes per annum (from a baseline level of 6.9 million) and OST for 12 000 PWID (compared to a baseline level of 1121)[65] and an emphasis on a peer approach to health education and outreach.[66] Recent HIV prevalence amongst Myanmar's PWID was estimated at 28.5%, a substantial decline from the >70% prevalence reported in the 1990s.[66,67]

A comparison of HIV prevalence in 103 global cities found that those who had introduced NSPs decreased prevalence by an average of 19% annually, whilst the prevalence in cites without NSPs increased by an average of 8% annually.[68,69] Reduction in HIV prevalence following an expansion of national harm reduction programmes has been demonstrated in multiple LMICs,[6] suggesting that with appropriate funding and motivation, the barriers previously identified can be overcome, producing outcomes just as effective as those in high-income countries.[6]

11 | DATA QUALITY ISSUES

Accurate data on IDU are scarce,[26] and available data are often of poor quality, meaning valid population IDU and BBV prevalence estimation is difficult. Gender, age and drug type information are often missing, and data are largely restricted to metropolitan areas.[26]

Wodak et al.[70] claimed that "the orderly division of the planet into developing countries which produce drugs and developed countries which consume these drugs ceased to exist long ago". Indeed, whilst 80 (largely developed) countries reported IDU in 1992, 121 did so in 1995 and 158 countries and territories as of 2008.[9] Although the substantial increase in national reporting is probably due to the diffusion of IDU to new countries, it is also likely to derive from improved reporting systems detecting pre-existing IDU.[9,71] Many LMICs that do not report IDU have neighbours with well-established PWID populations (eg Somalia and Ethiopia border Kenya; Niger and Chad border Libya); others, including some that acknowledge IDU amongst their populations but who have limited data, are situated along key global drug supply routes where heroin and cocaine is transported from the major production hubs of Afghanistan, Myanmar, Mexico and Colombia.[1] It is unlikely that IDU has not diffused to countries along these routes where it currently goes unreported.

The absence of quality data and routine data collection, limited by poor capacity and the "hidden" nature of IDU, mean that the aggregation, reporting and evaluation of public health outcomes and indicators linked to IDU across LMICs are limited. For example, half of all countries listed in Table 1 with evidence of IDU are without prevalence estimates.[9,10]

12 | CONCLUSION

From this review, we suggest four key priorities in looking ahead: confirming the presence or absence of IDU in LMICs, improving the collection and dissemination of national IDU-specific data, increasing the level of harm reduction programme implementation in LMICs, and increasing both national and international advocacy for PWID and attendant public health interventions.

IDU goes unreported in many LMICs; and LMICs with the lowest levels of income and therefore the least capacity for comprehensive data collection are also the least likely to have reported IDU. Rapid assessments[72] need to be conducted in these LMICs to assess the existence and potential extent of the problem.

Quality IDU-specific data are needed—the lack of these data has been described as the main obstacle to the implementation of relevant interventions.[73] Detailed data on population characteristics, risk behaviours, BBV prevalence and subpopulations at highest risk of harm are essential for appropriately tailoring and targeting interventions.[71] Moreover, little public health intervention research has been conducted on IDU in LMICs: in a recent review of the effectiveness of harm reduction services, 144 of 152 included studies focused on high-income countries.[6,74] This lack of research means potentially novel and innovative LMIC interventions and strategies go unreported.

The significant scale-up of existing harm reduction programmes and their introduction into LMICs without current harm reduction implementation should be considered a priority. The consequences of delayed or insufficient response have been detailed above. Such scale-up will not occur without an increase in global funding for harm reduction, and such support is unlikely without an increase in advocacy for PWID. The recent adoption of the Sustainability Development Goals (SDGs) may provide the impetus for much of this target setting. The SDGs, for the first time, acknowledge the prevention and treatment of harmful drug use under a global framework.[1] Reaching the targets set in the SDGs requires the expansion of coverage and quality of "a range of evidence-based and gender-responsive interventions for the prevention of drug use, as well as the care, treatment and rehabilitation of drug use disorders".[1] Further SDG targets (such as reductions in BBVs or reducing inequality) cannot be met without directly considering the lives of PWID.[1]

Inadequate IDU response is a significant problem the world over. Low levels of funding, political inaction, poor levels of health service coverage, high prevalence and incidence of IDU-related BBVs, and ongoing stigmatization/marginalization affect PWID regardless of the income status of the country they reside in. These barriers and system failings are exacerbated in LMICs, meaning that the potential consequences of inaction are more pressing. However, services and systems in many of these countries show effective response is possible and should be prioritized in other LMICs.

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CONFLICT OF INTERESTS

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ENDNOTES

* Denoting current or previous infection.

† Denoting current infection.

‡ The quality of the Dominican Republic prevalence estimate requires validation.

REFERENCES

1. UNODC. *World Drug Report*. Vienna: United Nations; 2016.
2. Aceijas C, Hickman M, Donoghoe MC, Burrows D, Stuikyte R. Access and coverage of needle and syringe programmes (NSP) in Central and Eastern Europe and Central Asia. *Addiction*. 2007;102:1244-1250.
3. Sarang A, Stuikyte R, Bykov R. Implementation of harm reduction in Central and Eastern Europe and Central Asia. *Int J Drug Policy*. 2007;18:129-135.
4. Dolan K, Moazen B, Noori A, Rahimzadeh S, Farzadfar F, Hariga F. People who inject drugs in prison: HIV prevalence, transmission and prevention. *Int J Drug Policy*. 2015;26(Suppl 1):S12-S15.
5. Mathers BM, Degenhardt L, Bucello C, Lemon J, Wiessing L, Hickman M. Mortality among people who inject drugs: a systematic review and meta-analysis. *Bull World Health Organ*. 2013;91:102-123.
6. Des Jarlais D, Feelemyer JP, Modi SN, Abdul-Quader A, Hagan H. High coverage needle/syringe programs for people who inject drugs in low and middle income countries: a systematic review. *BMC Public Health*. 2013;13:1-13.
7. Uchtenhagen A. Substance use problems in developing countries. *Bull World Health Organ*. 2004;82:641-642.
8. World Bank. World Bank Country and Lending Groups 2017. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. Accessed February 23, 2017.
9. HRI. *Global State of Harm Reduction*. London: Harm Reduction International; 2016.
10. Mathers BM, Degenhardt L, Phillips B, et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. *Lancet*. 2008;372:1733-1745.
11. Hammett TM, Wu Z, Duc TT, et al. 'Social evils' and harm reduction: the evolving policy environment for human immunodeficiency virus prevention among injection drug users in China and Vietnam. *Addiction*. 2007;103:137-145.
12. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet*. 2012;379:55-70.
13. Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet*. 2011;378:571-583.
14. Wolfe D, Carrieri MP, Shepard D. Treatment and care for injecting drug users with HIV infection: a review of barriers and ways forward. *Lancet*. 2010;376:355-366.
15. Dewing S, Pluddemann A, Myers B, Parry C. Review of injection drug use in six African countries: Egypt, Kenya, Mauritius, Nigeria, South Africa and Tanzania. *Drugs*. 2006;13:121-137.
16. Panda S, Chatterjee A, Bhattacharya SK, et al. Transmission of HIV from injecting drug users to their wives in India. *Int J STD AIDS*. 2000;11:469-473.
17. Hellard M, Sacks-Davis R, Doyle JS. Hepatitis C elimination by 2030 through treatment and prevention: think global, act in local networks. *J Epidemiol Community Health*. 2016;70:1151-1154.
18. Bowring A, Luhmann N, Pont S, et al. An urgent need to scale-up injecting drug harm reduction services in Tanzania: prevalence of blood-borne viruses among drug users in Temeke District, Dar-es-Salaam, 2011. *Int J Drug Policy*. 2013;24:78-81.
19. Scott N, McBryde ES, Thompson AJ, Doyle JS, Hellard M. Treatment scale-up to achieve global HCV incidence and mortality elimination targets: a cost-effectiveness model. *Gut*. 2016. Accessed February 04, 2016.
20. Graham CS, Swan T. A path to eradication of hepatitis C in low- and middle-income countries. *Antiviral Res*. 2015;119:89-96.
21. WHO. *Guidance on Prevention of Viral Hepatitis B and C Among People Who Inject Drugs*. Geneva: World Health Organisation; 2012.
22. Gibson DR, Flynn NM, Perales D. Effectiveness of syringe exchange programs in reducing HIV risk behaviour and HIV seroconversion among injecting drug users. *AIDS*. 2001;15:1329-1341.

23. Walley A, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ*. 2013;206:326-329. Epub 31 January 2013.
24. White B, Dore GJ, Lloyd AR, Rawlinson WD, Maher L. Opioid substitution therapy protects against hepatitis C virus acquisition in people who inject drugs: the HITS-c study. *Med J Aust*. 2014;201:326-329.
25. Wodak A, Cooney A. Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence. *Subst Use Misuse*. 2006;41:777-813.
26. Mathers BM, Cook C, Degenhardt L. Improving the data to strengthen the global response to HIV among people who inject drugs. *Int J Drug Policy*. 2010;21:100-102.
27. Strathdee SA, Mailman JL. The effectiveness of needle exchange programs: a review of the science and policy. *AIDScience*. 2001;1.
28. Mathers BM, Degenhardt L, Hammad A, et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. *Lancet*. 2010;365:1014-1028.
29. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treat*. 2005;28:321-329.
30. Lawrinson P, Ali R, Bauvirat A, et al. Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. *Addiction*. 2008;103:1484-1492.
31. Weber R, Huber M, Rickenbach M, et al. Uptake of and virological response to antiretroviral therapy among HIV-infected former and current injecting drug users and persons in an opiate substitution treatment programme: the Swiss HIV Cohort Study. *HIV Med*. 2009;10:407-416.
32. Gowing L, Ferrell M, Bornemann R, Sullivan L, Ali R. Substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst Rev*. 2008;(2):CD004145.
33. Wood E, Tyndall MW, Montaner JS, Kerr T. Summary of findings from the evaluation of a pilot medically supervised safer injecting facility. *Can Med Assoc J*. 2006;175:1399-1404.
34. Strang J, Metrebian N, Lintzeris N, et al. Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *Lancet*. 2010;375:1885-1895.
35. Fischer B, Oviedo-Joekes E, Blanken P, et al. Heroin-assisted treatment (HAT) a decade later: a brief update on science and politics. *J Urban Health*. 2007;84:552-562.
36. Vickerman P, Hickman M, Rhodes T, Watts C. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. *J Acquir Immune Defic Syndr*. 2006;42:355-361.
37. Sharma M, Oppenheimer E, Saidel T, Loo V, Garg R. A situation update on HIV epidemics among people who inject drugs and national responses in South-East Asia Region. *AIDS*. 2009;23:1405-1413.
38. WHO. *Technical Guide for Countries to Set Targets for Universal HIV Services for Injecting Drug Users*. Geneva: World Health Organisation; 2012.
39. WHO. *Global Health Sector Strategy on Viral Hepatitis 2016-2021*. Geneva: World Health Organisation; 2016.
40. Burrows D. Advocacy and coverage of needle exchange programs: results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. *Cad Saude Publica*. 2006;22:871-879.
41. Quan VM, Minh NL, Ha TV, et al. Mortality and HIV transmission among male Vietnamese injection drug users. *Addiction*. 2010;106:583-589.
42. UNODC. Joint UNODC/WHO initiative addresses public health impact of community management of opioid overdose 2017. https://www.unodc.org/unodc/en/frontpage/2017/March/joint-unodc-who-initiative-addresses-public-health-impact-of-community-management-of-opioid-overdose.html?ref=fs6. Accessed April 5, 2017.
43. Hagan H, Des Jarlais D. HIV and HCV infection among injecting drug users. *Mt Sinai J Med*. 2000;67:423-428.
44. Sarkar S, Das N, Panda S, et al. Rapid spread of HIV among injecting drug users in north-eastern states of India. *Bull Narc*. 1993;45:91-105.
45. Garten RJ, Lai S, Zhang J, et al. Rapid transmission of hepatitis C virus among young injecting heroin users in Southern China. *Int J Epidemiol*. 2004;33:182-188.
46. Vickerman P, Platt L, Jolley E, Rhodes T, Kazatchkine MD, Latypov A. Controlling HIV among people who inject drugs in Eastern Europe and Central Asia: insights from modeling. *Int J Drug Policy*. 2014;25:1163-1173.
47. Peters DH, Garg A, Bloom G, Walker DG, Brieger WR, Rahman MH. Poverty and access to health care in developing countries. *Ann N Y Acad Sci*. 2008;1136:161-171.
48. HRI. *The Funding Crisis for Harm Reduction: Donor Retreat, Government Neglect and the Way Forward*. London: Harm Reduction International; 2014.
49. UNAIDS. *A New Investment Framework for the Global HIV Response*. Geneva: United Nations Programme on HIV/AIDS; 2011.
50. UNAIDS. *The Gap Report 2014: People Who Inject Drugs*. Geneva: United Nations Programme on HIV/AIDS; 2014.
51. Broadhead RS, van Hulst Y, Heckathron DD. The impact of a needle exchange's closure. *Public Health Rep*. 1999;114:439-447.
52. Chan K-Y, Yang Y, Zi-rong L, Stoove MA, Reidpath DD. Interrelationships between HIV/AIDS and risk behaviour prejudice among medical students' in Southern China. *Curr HIV Res*. 2009;7:606-611.
53. Asher AK, Hahn JA, Couture M, Maher K, Page K. People who inject drugs, HIV risk, and HIV testing uptake in Sub-Saharan Africa. *J Assoc Nurses AIDS Care*. 2013;24:e35-e44.
54. Mahendra V, Gilborn L, Bharat B, et al. Understanding and measuring AIDS-related stigma in health care settings: A developing country perspective. *SAHARA J*. 2007;4:616-625.
55. Gupta GR, Parkhurst JO, Ogden JA, Aggleton P, Mahal A. Structural approaches to HIV prevention. *Lancet*. 2008;372:764-775.
56. Csete J, Kamarulzaman A, Kazatchkine M, et al. Public health and international drug policy. *Lancet*. 2016;387:1427-1480.
57. Rhodes T, Mikhailova L, Sarang A, et al. Situational factors influencing drug injecting, risk reduction and syringe exchange in Togliatti City, Russian Federation: a qualitative study of micro risk environment. *Soc Sci Med*. 2003;57:39-54.
58. Berehulak D. *They are Slaughtering Us Like Animals*. New York, USA: The New York Times; 2016.
59. Bionat M. *Gains from Thailand's Bloody War on Drugs Proves Fleeting*. New Hampshire, USA: Inquirer; 2016.
60. Consortium. IDP. *IDPC Advocacy Note: Compulsory Rehabilitation in Latin America: An Unethical, Inhumane and Ineffective Practice*. London: International Drug Policy Consortium; 2014.
61. Wegman MP, Altice FL, Kaur S, et al. Relapse to opioid use in opioid-dependent individuals released from compulsory drug detention centres compared with those from voluntary methadone treatment centres in Malaysia: a two-arm prospective observational study. *Lancet Glob Health*. 2017;5:e198-e207.
62. National AIDS Committee Secretariat. *Islamic Republic of Iran AIDS Progress Report*. Tehran: Ministry of Health and Medical Education; 2015.
63. Kan M, Gall JA, Latypov A, et al. Effective use of naloxone among people who inject drugs in Kyrgyzstan and Tajikistan using pharmacy- and community- based distribution approaches. *Int J Drug Policy*. 2014;25:1221-1226.

64. Poudel KC, Tandukar KP, Yasuoka J, Joshi AB, Jimba M. Correlates of sharing injection equipment among male injecting drug users in Kathmandu, Nepal. *Int J Drug Policy*. 2010;21:507-510.
65. Ministry of Health and Sports. *Myanmar National Strategic Plan on HIV and AIDS (2011-2016)*. Myanmar: Ministry of Health and Sports; 2014.
66. Ministry of Health and Sports. *Myanmar National Strategic Plan on HIV and AIDS (2016-2020)*. Myanmar: Ministry of Health and Sports; 2016.
67. UNODC. *Myanmar Country Advocacy Brief: Injecting Drug Use and HIV*. Myanmar: United Nations; 2010.
68. Department of Health and Ageing. *Return on Investment 2: Evaluating the Cost-Effectiveness of Needle and Syringe Programs in Australia*. Sydney: Australia; 2009.
69. Dolan K, MacDonald M, Silins E, Topp L. *Needle and Syringe Programs: A Review of the Evidence*. Canberra: Australian Government Department of Health and Ageing; 2005.
70. Wodak A, Sarkar S, Mesquita F. The globalisation of drug injecting. *Addiction*. 2004;99:799-801.
71. Aceijas C, Friedman SR, Cooper H, Wiessing L, Stimson GV, Hickman M. Estimates of injecting drug users at the national and local level in developing and transitional countries and gender and age distribution. *Sex Transm Infect* 2006;3:iii10-iii17.
72. Stimson GV, Fitch C, Des Jarlais D, et al. Rapid assessment and response studies of injection drug use: knowledge gain, capacity building, and intervention development in a multisite study. *Am J Public Health*. 2006;96:288-295.
73. McCoy CB, Rodriguez F. Global overview of injecting drug use and HIV infection. *Lancet*. 2005;365:1008-1009.
74. Palmateer N, Kimber J, Hickman M, Hutchinson S, Rhodes T, Goldberg D. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews. *Addiction*. 2010;105:844-859.

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5.3 Prepared manuscript: Measuring individual-level needle and syringe coverage among people who inject drugs in Myanmar

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Abstract

Background:

Myanmar has prioritised people who inject drugs (PWID) as a key population for HIV mitigation efforts, with targets for needle and syringe distribution set at a population level. However, individual-level coverage, defined as the percentage of an individual's injecting episodes covered by a sterile syringe, is a more sensitive measure of intervention coverage. We sought to examine individual-level coverage in a sample of PWID in Myanmar.

Methods:

We recruited 512 PWID through urban drop-in-centres in Yangon, Mandalay and Pyin Oo Lwin. Participants were administered a quantitative questionnaire covering five domains: demographics, drug use, treatment and coverage, and injecting risk behaviour.

We calculated past fortnight individual-level syringe coverage, estimating levels of sufficient (≥100% of injecting episodes covered by a sterile syringe) and insufficient

(<100%) coverage, and examined associations between key variables and insufficient coverage via logistic regression.

Results:

Our sample was predominately male (97%), employed (76%), and living in stable accommodation (96%), with a median age of 27. All participants reported heroin as the drug most frequently injected, and injected a median of 27 times in the past two weeks.

Nineteen per cent of participants had insufficient coverage in the two weeks before interview. Insufficient coverage was positively associated with syringe re-use (AOR: 5.19, 95% CIs: 2.57, 10.48) and acquiring sterile syringes from a location other than a formal drop-in-centre (AOR: 2.04, 95% CIs: 1.08, 3.82). Participants recruited in Mandalay (AOR: 0.30, 95% CIs: 0.11, 0.80) and Pyin Oo Lwin (AOR: 0.39, 95% CIs: 0.18, 0.87) had lower odds of insufficient coverage than those recruited in Yangon.

Conclusion:

Our study shows coverage in selected areas of Myanmar was comparable with studies in other countries. Our results inform the delivery of harm reduction services for PWID, specifically by encouraging the use of formal drop-in-centres, over other sources of syringe distribution, such as pharmacies.

Introduction

The Government of Myanmar estimates there are 83,000 people who inject drugs (PWID) within the country (0.23% of the population aged between 15-64 years) (1, 2), although other sources estimate a PWID population size of 90,000-150,000 (3). Myanmar has historically seen high levels of HIV among its PWID population and has previously identified PWID as a priority population for HIV mitigation efforts (4, 5). Recent targeted responses have dramatically increased harm reduction services across the country. Myanmar's National Strategic Plan for HIV specified increased access to needle and syringe programs (NSPs) via drop-in centres and outreach programs, and a significant increase in national sterile syringe distribution (to 360 sterile needles and syringes per PWID per year) and methadone OST treatment (to 32,000 PWID receiving methadone) (1). In 2014, PWID-specific HIV prevalence was reported at 28.5% (1) (though HIV prevalence differs greatly across national regions (6)), representing a substantial decline from its 1990s peak of over 70% (5), but still a prevalence typical of the highly endemic Asia region (7).

Minimal descriptive research has been performed amongst PWID in Myanmar. Both Yu Mon Saw et al. (2013) and Lin Aung Swe et al. (2010) described samples of predominately (>96%) male, young (<35 years old), single and employed PWID (3, 8). Most participants reported primarily injecting heroin and injecting at least daily (3, 8). Approximately half of participants in the Yu Mon Saw et al. study reported recent unsafe injecting practices (3). These samples were, however, drawn from border areas in the remote parts of Shan state, outside of central government control, reflecting the importance border areas play in blood-borne virus (BBV) transmission (9). Similar work on both sides of the Myanmar-Chinese border has also been conducted (9-11). These studies highlight the differential geographical risk in areas of heroin production and little governmental control (10), but also exemplify the lack of PWID research in Myanmar's urban centres.

The World Health Organization (WHO) has previously set population-level targets for sterile needle and syringe distribution to PWID. To reduce HIV transmission, it recommends that nationwide programs distribute 200 needles and syringes per PWID per annum (12). A distribution rate of 300 needle and syringes per PWID per annum is

recommended to eliminate hepatitis C virus (HCV) (13), which has a higher transmission potential than HIV (14). These targets are deemed "effective" or "high coverage" at the population level with respect to their targeted BBV (12, 13).

Population-level coverage measurements are important for evaluating and comparing public health programs within and between countries. However, even in countries with high population-level coverage, substantial coverage shortfalls are experienced at the individual level (15, 16). Population-level measures assume a PWID population with homogenous coverage behaviours, yet these behaviours are highly variable (15). For example, some PWID may need many more or fewer sterile syringes than the WHO recommended 200–300 per year, and it is known that coverage is influenced by many context-specific factors, such as drug use preferences (17), policy (18, 19) and geographic access to services (20). Research measuring coverage at the individual level, broadly defined as the percentage of an individual's injecting episodes that are "covered" by a sterile syringe (21), has shown that PWID without current opioid substitution therapy (OST) (17), low engagement with NSPs (17, 22, 23), higher injecting frequencies (21, 22) and HCV positivity (17) have greater odds of reporting experiencing insufficient coverage. Insufficient individual-level coverage has also been associated with injecting risk behaviours, such as receptive syringe sharing and syringe reuse (21, 24-26). These coverage variations in PWID subgroups can only be understood by measuring coverage at the individual level.

To date, only population-level NSP coverage has been reported for Myanmar. The proposed increases in population-level coverage are promising, but the proportion of PWID experiencing insufficient coverage at an individual level has not been estimated. It is important to determine individual-level coverage, because it is logically associated with risk of transmission and acquisition of serious blood-borne virus infections. Previous research has characterised HIV-positive and HIV-negative PWID in Myanmar (8): Lin Aung Swe et al. (2010) showed that PWID living rurally (compared to those living in urban locations) had increased odds of HIV positivity (8), and similar differences between individuals may impact upon the ability to sufficiently cover one's injecting episodes, thereby increasing the likelihood of BBV transmission. Furthermore, a greater understanding of the barriers to sufficient coverage is needed for countries

such as Myanmar, as findings from high-income countries may not be relevant to low and middle income contexts.

We estimated individual-level needle and syringe coverage in a cross-sectional sample of PWID across three urban locations. Specifically, we aimed to:

1. Describe demographic, service utilisation and risk profiles of PWID in major urban centres in Myanmar,
2. Measure individual-level needle and syringe coverage amongst PWID across qualitatively different areas of Myanmar, and
3. Explore associations between demographic, drug use, risk behaviour and service use, and insufficient coverage.

Methods

Setting:

Data were collected through the Burnet Institute (BI)-operated harm reduction program in Myanmar, which deliver services to PWID via community-based drop-in-centres (DICs) and outreach at five harm reduction services across three urban locations: two in Yangon (Yangon East and Yangon West), two in Mandalay (Mandalay city and Sagaing city) and one in Pyin Oo Lwin. The Yangon East, Mandalay city and Pyin Oo Lwin services are fixed site DICs that, along with distribution of sterile injecting equipment, offer BBV counselling and testing, STI screening and treatment, condom distribution, health education and referral to ART, OST and other drug treatment services. Yangon West and Sagaing city are basic services, offering minimal intervention beyond sterile injecting equipment distribution via a small outpost and peer outreach, and referral to more expanded services. The BI program was initiated in 2014 and funded by the Global Fund to Fight AIDS, Malaria and Tuberculosis and the 3 Millennium Development Goals fund.

Ethical approval was obtained from the Alfred Ethics Committee (Australia) and the Department of Medical Research Ethics Committee (Myanmar).

Participant sample:

Recruitment was initiated in March 2017 and completed in July 2017. Five hundred and thirteen self-identified PWID were recruited via convenience and snowball sampling. Recruitment was intended to be spread evenly across the five program sites (100 participants at each site), but differences in numbers eventuated (see Table 1).

Study eligibility criteria were: ≥18 years of age; regularly injecting drugs (defined as injecting at least once a month for the six months prior to interview); able and willing to provide informed consent. Due to the cross-sectional nature of the research, and the vulnerability of the study population, only verbal informed consent was required and recorded on data collection devices, with one participant excluded from analysis due to incomplete consent data. To protect participant confidentiality further, no identifying information was collected. Participants were reimbursed 3200 Kyats (approximately USD$3) for their time and expenses.

Questionnaire construction and administration:

A short-form quantitative, researcher-administered questionnaire was developed. Using non-identifying features, the questionnaire included five general domains: "demographics" (e.g. recruitment site, sex, age, employment status, accommodation status); "drug use characteristics" (e.g. types of drugs used/injected, drug preferences, injecting frequency); "treatment utilisation and coverage" (e.g. past and present drug treatment, coverage measurement variables); "injecting risk behaviours" (e.g. syringe sharing, BBV self-report and testing history); and "sexual risk" (number of sexual partners, condom use, potential sex work involvement). The questionnaire was originally constructed in English, then translated by bilingual Myanmar national investigators. Translations were verified by other bilingual staff for errors and translational appropriateness. Questionnaires were administered on electronic tablets using RedCap V7.5.1 (Vanderbilt University, TN, USA), and required, including informed consent, approximately 20-25 minutes to complete.

Participant recruitment and questionnaire administration were conducted by existing DIC staff, who were trained in research ethics and methods for the purposes of this research. Interviews were conducted either in DICs or external venues – acceptable to both researchers and participants – where privacy was assured

Measuring individual-level needle and syringe coverage:

Individual-level needle and syringe coverage was calculated using an adapted method previously devised by Bluthenthal et al. (2007) (21) and expanded by McCormack et al. (2016) (16). The measure calculates the percentage of a person's injecting episodes that are "covered" by a sterile syringe across a specified time period. The measure accounts for behaviours related to coverage other than syringe acquisition and injecting frequency (e.g. peer-to-peer syringe distribution) (15). We collected coverage data for the two weeks prior to interview.

The following questions collected the parameter data necessary to calculate coverage:

*"How many sterile syringes have you gotten in total in the **past two weeks**?"*

*"How many sterile syringes have you given away (to friends/partners/acquaintances) in the **past two weeks**?"*

"How many sterile syringes do you have stored away at the moment (at home, for example?)"

*"How many times have you injected in the **past two weeks**?"*

Responses to each question were recorded as continuous data. The total number of sterile syringes acquired (from any source), *minus* the number of sterile syringes distributed to injecting peers/partners, *plus* the number of sterile syringes currently stockpiled for later use, was divided by the past-two-week injecting frequency. The resultant figure was multiplied by 100 to create a percentage of past-two-week injecting episodes covered by at least one sterile syringe. The formula for the individual-level coverage calculation is presented below:

$$\frac{(syringes\ acquired - syringes\ distributed + syringes\ stockpiled)}{injecting\ frequency}\ x\ 100$$

Whilst the formula produces a continuous coverage percentage, the outcome is commonly dichotomised to classify participants as either sufficiently (≥100% coverage) or insufficiently (<100%) covered (22, 24, 26). Coverage calculation was only possible

for participants with valid data for each parameter and those reporting injecting within the previous month. The set of parameters needed to calculate coverage was incomplete for three per cent of cases, who were classified as missing for the purposes of analysis.

Analysis strategy:

Descriptive statistics were generated for a variety of demographic, drug use, service utilisation and risk variables. Descriptive statistics were stratified across recruitment sites to assess any geographical differences.

We used multivariable logistic regression to test the associations between demographic, drug use, risk behaviour and service use exposure sub-groups and insufficient coverage (<100%) as the outcome of interest. Exposure sub-groups were selected by past research and a priori, with some otherwise relevant sub-groups excluded (such as sex) or collapsed either due to sparse outcome data or to avoid model overfit. The most parsimonious model was reached by assessing variance inflation factors for collinearity between exposures, finding that factors for recruitment site and location of injection (e.g. public toilet or private home) were >10, higher than the proposed cut-off for collinearity (27). Consequently, we removed the location of injection variable from the model.

All analysis was performed in Stata 13.1 (StataCorp LP, TX, USA).

Results

Participant sample

The final sample of 512 participants was predominately male (97%), employed (76%), not currently married or in a relationship with a regular partner (70%) and living in stable accommodation (96%) (Table 1). The median age was 27 years. There were no substantial differences in participants' demographic characteristics between recruitment sites, although participants at Pyin Oo Lwin were older than average and Yangon participants had a greater percentage of unemployment compared to participants at the other recruitment sites.

Table 1. Descriptive characteristics stratified by recruitment site

Variable (missing obs.)	Total, n (%)	Mandalay city (n=104)	Sagaing city (n=98)	Pyin Oo Lwin (n=100)	Yangon East (n=109)	Yangon West (n=101)
Survey location (n=1)						
DIC	248 (49%)	57 (55%)	37 (38%)	29 (29%)	93 (85%)	32 (32%)
Outreach	263 (51%)	47 (45%)	61 (62%)	71 (71%)	16 (15%)	68 (68%)
Sex (n=2)						
Male	496 (97%)	100 (96%)	96 (99%)	99 (99%)	106 (97%)	95 (95%)
Female	14 (3%)	4 (4%)	1 (1%)	1 (1%)	3 (3%)	5 (5%)
Age						
Mean (range)	27 (18-67)	27 (18-48)	26 (18-47)	34 (18-67)	29 (18-54)	29 (18-49)
Current relationship (n=6)						
Single/separated/widowed	352 (70%)	77 (75%)	65 (67%)	64 (64%)	82 (75%)	64 (66%)
Married/regular partner	154 (30%)	26 (25%)	32 (33%)	36 (36%)	27 (25%)	33 (34%)
Accommodation						
Stable	491 (96%)	97 (93%)	96 (98%)	95 (95%)	108 (99%)	95 (94%)
Unstable	21 (4%)	7 (7%)	2 (2%)	5 (5%)	1 (1%)	6 (6%)
Employment (n=1)						
Employed	383 (75%)	90 (87%)	81 (83%)	90 (90%)	64 (59%)	58 (58%)
Unemployed	128 (25%)	14 (13%)	17 (17%)	10 (10%)	45 (41%)	42 (42%)
Past week income (MMK) (n=1)						
Median (IQR)	50k (30-80)	45k (30-70)	58k (35-90)	40k (30-70)	50k (30-85)	60k (30-100)
Past week drug expenditure (MMK)						
Median (IQR)	40k (25-70)	37k (21-55)	32k (21-55)	30k (20-50)	50k (30-80)	70k (30-100)
Drug most injected (heroin)						
n (%)	512 (100%)	104 (100%)	98 (100%)	100 (100%)	109 (100%)	101 (100%)
Main drug injection location (n=5)						
Private	212 (42%)	0	1 (1%)	69 (70%)	72 (67%)	70 (70%)
Public	88 (17%)	0	0	23 (23%)	35 (33%)	30 (30%)
Shooting gallery	207 (41%)	104 (100%)	96 (99%)	7 (7%)	0	0
Mainly injecting completely alone (n=2)						
Yes	173 (34%)	2 (2%)	1 (1%)	72 (72%)	52 (48%)	46 (46%)
Current drug treatment (n=5)						
None	321 (63%)	82 (80%)	49 (51%)	81 (81%)	61 (56%)	48 (48%)
*Current drug treatment**	186 (37%)	21 (20%)	47 (49%)	19 (19%)	47 (44%)	52 (52%)
Main source of syringe acquisition (past month)						
DIC/outreach	202 (39%)	1 (1%)	26 (27%)	81 (81%)	38 (35%)	56 (55%)
Other injectors	14 (3%)	0	0	9 (9%)	1 (1%)	4 (4%)
Pharmacy	119 (23%)	0	0	8 (8%)	70 (64%)	41 (41%)
Shooting gallery	177 (35%)	103 (99%)	72 (73%)	2 (2%)	0	0
HIV testing history (n=5)						
<6 months	342 (67%)	88 (85%)	65 (69%)	60 (60%)	63 (58%)	66 (66%)
6-≥12 months	121 (24%)	12 (11%)	9 (10%)	28 (28%)	39 (36%)	33 (33%)
Never had a test	44 (9%)	4 (4%)	20 (21%)	12 (12%)	7 (6%)	1 (1%)
HIV positivity (self-report) (n=63)						
Positive	64 (14%)	4 (4%)	9 (12%)	25 (29%)	18 (19%)	8 (8%)
HIV positive participants receiving ART (% of HIV positive participants) (n=443)						
Receiving ART	36 (56%)	2 (50%)	9 (100%)	8 (32%)	12 (67%)	6 (75%)
HCV testing history (n=10)						
<6 months	229 (46%)	43 (41%)	16 (18%)	54 (54%)	57 (53%)	59 (58%)
6-≥12 months	183 (36%)	23 (22%)	56 (63%)	31 (31%)	38 (35%)	35 (35%)
Never had a test	90 (18%)	38 (37%)	17 (19%)	15 (15%)	13 (12%)	7 (7%)
HCV positivity (self-report) (n=113)						
Positive (Antibody+)	202 (51%)	17 (26%)	21 (28%)	40 (48%)	66 (77%)	58 (64%)
HBV testing history (n=8)						
<6 months	213 (42%)	41 (39%)	13 (14%)	41 (41%)	57 (52%)	61 (62%)
6-≥12 months	216 (43%)	34 (33%)	68 (74%)	42 (42%)	36 (33%)	36 (36%)
Never had a test	75 (15%)	29 (28%)	11 (12%)	17 (17%)	16 (15%)	2 (2%)

HBV positivity/vaccination (self-report) (n=93)						
Positive	28 (7%)	6 (8%)	9 (11%)	6 (7%)	4 (5%)	3 (3%)
Vaccinated	74 (17%)	1 (1%)	4 (5%)	69 (83%)	0	0

* Current drug treatment represented 99% methadone treatment and 1% "other" treatment.

Drug use characteristics

All participants reported heroin as the drug most injected in the month prior to interview (Table 1). Forty-one per cent of participants reported their main location of injecting as a shooting gallery (illegally run locations where PWID can both acquire and inject drugs), although the presence of shooting galleries was isolated to Mandalay and resulted in clear geographical differences between recruitment sites. Forty-two per cent of participants reported injecting in other private locations, such as their homes, or the homes of another person. Seventeen per cent reported mainly injecting in public locations, such as public toilets or in streets. In total, 173 participants (34%) reported usually injecting completely alone, though the percentages of solitary injecting were different across sites, with 46–72% of participants at the Yangon sites and Pyin Oo Lwin reporting mainly injecting alone, and only 1-2% at the Mandalay city and Sagaing city sites.

Service utilisation characteristics

One hundred and eighty-six participants (37%) reported currently receiving drug treatment (typically methadone maintenance therapy (MMT) - 99% of those reporting current drug treatment were receiving MMT) (Table 1). Of those participants currently receiving MMT, 43% had been in receipt of their prescription for 12 months or less.

Nearly 40% of participants reported DICs as their main source of syringe acquisition, and 35% reported mainly acquiring syringes from shooting galleries. No participants in Yangon reported either injecting or acquiring syringes from a shooting gallery, and nearly all participants in both Mandalay sites reported shooting galleries as their main location of injecting and syringe acquisition.

BBV testing/prevalence and injecting risk behaviours

Most participants reported receiving a blood test for HIV, HCV and/or hepatitis B virus (HBV) within the twelve months prior to interview, but 44 (9%) reported never having received a HIV test, and 90 (18%) participants and 75 (15%) participants reported

never having received an HCV and HBV test respectively. Of those ever tested for BBVs, 64 participants (14%) self-reported HIV positivity based on their most recent blood test (Table 1). Two hundred and two participants (51%) and 28 (7%) participants self-reported HCV (antibody) and HBV (antigen) positivity respectively. Seventy-four participants (17%) reported HBV vaccination. Of participants testing positive for HIV, many were not receiving antiretroviral therapy (ART). At Pyin Oo Lwin, only eight of 25 HIV-positive participants (32%) were receiving ART.

Forty-eight participants (9%) reported receptive syringe sharing (re-using another PWID's unsterile syringe) (Table 2). Fifty-six (11%) reported distributive syringe sharing (providing an unsterile syringe to another PWID). One hundred and seventy-nine participants (35%) reported syringe re-use (re-using one's own unsterile syringe). Again, clear differences between sites exist. Few participants recruited from the two Mandalay sites reported any syringe sharing or syringe re-use. The majority of participants at the two Yangon sites reported reusing their own syringes within the month prior to interview.

The prevalence of participants reporting either injecting another person (33%) or being injected by another person (41%) was high. Reports of being injected by another person were particularly frequent at the Mandalay city site (83% of participants), where shooting galleries often have "professional injectors" on site to perform injections for customers. This is evidenced by the number of injections reported to be performed by another person, which for Mandalay participants, very closely matched the overall injecting frequency.

Table 2. Injecting risk behaviours by recruitment site (past two weeks)

Injecting risk behaviour	Total, n (%)	Mandalay city, n (%)	Sagaing city, n (%)	Pyin Oo Lwin, n (%)	Yangon East, n (%)	Yangon West, n (%)
Receptive sharing	48 (9%)	0	1 (1%)	7 (7%)	26 (24%)	14 (14%)
Distributive sharing	56 (11%)	0	0	11 (11%)	31 (28%)	14 (14%)
Syringe re-use	179 (35%)	2 (2%)	2 (2%)	45 (45%)	68 (62%)	62 (61%)
Injected another person	170 (33%)	36 (35%)	16 (16%)	31 (31%)	44 (40%)	43 (43%)
Injected by another person	210 (41%)	86 (83%)	47 (48%)	17 (17%)	36 (33%)	24 (24%)

Coverage calculation and associations with insufficient coverage

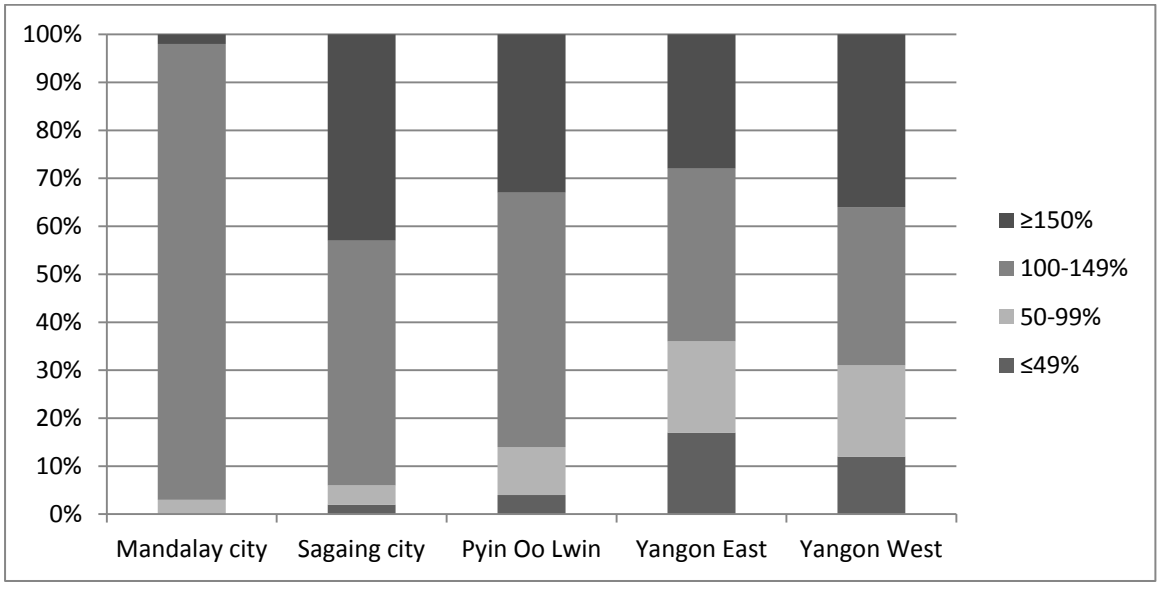
Participants reported acquiring a median 28 sterile syringes and injecting a median 27 times in the two weeks prior to interview (Table 3). Median total coverage, as a continuous measure, was 100% (IQR: 100–157%), but once dichotomised, 94 (19%) participants were insufficiently covered. Insufficient coverage was much more common in the two Yangon sites, as Table 3 shows.

Table 3. Syringe coverage parameters by recruitment site (past two weeks)

Coverage parameter	Total (median, IQR)	Mandalay city (median, IQR)	Sagaing city (median, IQR)	Pyin Oo Lwin (median, IQR)	Yangon East (median, IQR)	Yangon West (median, IQR)
Instances of syringe acquisition	10, 4-17	28, 20-42	12, 7-14	4, 2-8	7, 4-14	8, 3-14
Total syringes acquired	28, 14-45	28, 28-42	18, 10-34	53, 42-100	14, 8-28	16, 10-40
Peer-to-peer distribution	0, 0-5	0, 0-0	0, 0-10	3, 0-18	0, 0-5	1, 0-6
Syringes stockpiled	0, 0-2	0, 0-0	0, 0-6	2, 0-10	0, 0-0	0, 0-1
Injecting frequency	27, 10-42	28, 25-42	14, 8-15	42, 28-42	20, 8-28	15, 5-28
Insufficient coverage, n (%)*	94 (19%)	3 (3%)	6 (6%)	14 (14%)	40 (40%)	31 (31%)

* 14(3%) missing observations

Figure 1. Coverage categories by recruitment site



After accounting for potentially confounding variables in the multivariable regression model, three exposure sub-groups displayed significant associations with insufficient coverage (Table 4). Participants from the Mandalay sites or Pyin Oo Lwin site

(compared to the Yangon sites) had reduced odds of insufficient coverage (AOR: 0.30, 95% CIs: 0.11, 0.80), (AOR: 0.39, 95% CIs: 0.18, 0.87). Participants who reported mainly acquiring their sterile syringes from sources other than the DIC, such as pharmacies or shooting galleries, had over twice the odds of experiencing insufficient coverage (AOR: 2.04, 95% CIs: 1.08, 3.82). Whilst our collapsed variable included syringe acquisition at shooting galleries as a "location other than DIC", in expanded testing, the significant result was driven mainly by those acquiring syringes from pharmacies. Those reporting the re-use of their own unsterile syringes had over five times the odds of insufficient coverage (AOR: 5.19, 95% CIs: 2.57, 10.48).

Table 4. Multivariable logistic regression associations with insufficient coverage

Variable	Total, n (%)	Insufficient coverage (<100%), n (%)	Regression AOR (95% CI)	Regression AOR p-value
Recruitment site				
Yangon east/west	210 (41%)	71 (75%)	1	
Mandalay city/Sagaing city	202 (39%)	9 (10%)	**0.30 (0.11, 0.80)**	**0.02**
Pyin Oo Lwin	100 (20%)	14 (15%)	**0.39 (0.18, 0.87)**	**0.02**
Recruitment type				
Outreach	248 (49%)	39 (42%)	1	
DIC	263 (51%)	54 (58%)	1.18 (0.66, 2.12)	0.57
Age				
≤24 years	184 (36%)	34 (36%)	1	
>24 years	328 (64%)	60 (64%)	1.30 (0.69, 2.45)	0.42
Current relationship				
Single/separated/widowed	352 (70%)	69 (73%)	1	
Married/regular partner	154 (30%)	25 (27%)	0.84 (0.46, 1.53)	0.56
Employment				
Unemployed	383 (75%)	63 (67%)	1	
Employed	128 (25%)	31 (33%)	1.23 (0.66, 2.27)	0.52
Current drug treatment				
None	321 (63%)	64 (69%)	1	
*Current drug treatment**	186 (37%)	29 (31%)	0.74 (0.39, 1.38)	0.34
Main source of syringe acquisition (past month)				
DIC	202 (39%)	29 (31%)	1	
Location other than DIC	310 (61%)	65 (69%)	**2.04 (1.08, 3.82)**	**0.03**
Receptive syringe sharing (past month)				
No	463 (91%)	70 (75%)	1	
Yes	48 (9%)	23 (25%)	1.49 (0.62, 3.59)	0.38
Distributive syringe sharing (past month)				
No	456 (89%)	68 (72%)	1	
Yes	56 (11%)	26 (28%)	1.61 (0.69, 3.72)	0.27
Syringe re-use				
No	333 (65%)	21 (22%)	1	
Yes	179 (35%)	73 (78%)	**5.19 (2.57, 10.48)**	**<0.001**
HIV testing history				
Recent test (<6 months)	342 (67%)	59 (63%)		
No recent test	165 (33%)	35 (37%)	1.50 (0.61, 3.69)	0.38
HCV testing history				
Recent test (<6 months)	229 (46%)	53 (56%)		
No recent test	273 (54%)	41 (44%)	0.53 (0.22, 1.27)	0.15

Number of obs in multivariable regression: 477, Prob: <0.001, R^2: 0.26.

* Current drug treatment represented 99% methadone treatment and 1% "other" treatment.

Discussion

We measured individual-level needle and syringe coverage in a sample of PWID in Myanmar. Our results showed that approximately one in five participants reported not acquiring sufficient sterile syringes to cover their injecting episodes in the two weeks prior to interview. We described PWID samples in Yangon, Mandalay and Pyin Oo Lwin. The demographics of our sample were largely consistent with the rural samples described by Yu Mon Saw et al. and Lin Aung Swe et al. (3, 8). Insufficient coverage was significantly associated with recruitment site, mainly acquiring syringes from locations other than DICs and syringe re-use. Importantly, we noted substantial individual and service use/implementation differences across recruitment sites, particularly in Mandalay, where the dominance of shooting galleries as locations to simultaneously acquire illicit drugs and sterile syringes influenced injecting risk.

The overall level of insufficient coverage seen here is comparable to that in other countries, even high-income countries with greater capacity for harm reduction response (16, 23). Current global needle and syringe coverage is inadequate. Only 93 countries worldwide have implemented NSPs (7) and an estimated 33 sterile syringes are distributed per PWID per year (28), well below WHO recommendations (29). UNAIDS estimated in 2014 that 168 needles and syringes were distributed per PWID per year within Myanmar (30). Whilst our findings showed that further work is needed to increase the utilisation of DICs, our participants reportedly acquired a total of 19,352 sterile syringes – 38 per PWID for the two week period, or approximately 988 per PWID per annum, a figure far higher than the estimate for Myanmar more broadly (28). Inadequate distribution of sterile injecting equipment may, therefore, not be the driver of insufficient coverage and injecting risk, at least among our sample. Instead, the inability to covers one's injecting episodes may be the result of varied barriers that are unique to individuals, or sub-groups of individuals.

The non-use or inconsistent use of needle and syringe programs has previously been associated with insufficient coverage (17, 22), suggesting the acquisition of syringes, reliably from a low-threshold service is superior to inconsistent sources (such as friends or dealers) or paid sources, such as pharmacies (15). Our results suggest the need to pay for syringes at pharmacies is indeed a barrier to coverage. The association between

insufficient coverage and syringe re-use has now been demonstrated in five studies exploring individual-level coverage (21, 23, 24, 26). Whilst the cross-sectional nature of this research means the temporal sequence of events cannot be inferred, it is logical that PWID with insufficient coverage would resort to re-using their own unsterile syringes. This practice may be less risky than receptive syringe sharing, a key driver of BBV transmission amongst PWID (31, 32), but syringe re-use increases the risk of bacterial infection and vein damage (33). Services should aim to reduce this practice as much as possible. Previous research has shown that PWID with >100% coverage have the lowest levels of injecting risk (21). Clients should be encouraged and facilitated to take additional syringes to cover unexpected injecting episodes or times when DICs may be closed and sterile syringes are difficult to access via other channels.

The presence of shooting galleries in Mandalay had definite influence over injecting practices and risk, reflected in the significantly reduced odds of insufficient coverage amongst the Mandalay participants. Perhaps less risky than commonly described shooting galleries (34, 35), the Myanmar shooting galleries operate in collaboration with harm reduction services and are serviced daily, ensuring a consistent and adequate supply of sterile injecting equipment and disposal of used equipment. Consequently, participants recruited from the two Mandalay sites reported much lower rates of insufficient coverage and injecting risk behaviours. Many Mandalay participants also reported exactly 100% coverage, meaning that they acquired only one sterile syringe at the time of each drug injection (nearly always within the shooting gallery). Whilst shooting galleries are illegal, the results suggest there may be public health advantages to PWID injecting drugs at the same place they acquire their sterile syringes. Shooting galleries may be unsterile locations in which to inject drugs (34-36), but afford some level of supervision and potential service delivery (if sterile syringes are provided, as they are at the Mandalay galleries), somewhat akin to supervised injecting facilities (SIFs) (36). Research exploring the dynamics between SIF participation and individual-level coverage has not yet been conducted and is recommended.

This work and its results are consistent with past research. Coverage levels in our sample were comparable with other international PWID samples, and the significant associations between insufficient coverage and syringe re-use and non-use of DICs replicates previous findings, lending support to the value of individual-level coverage

measurement. Though originally devised by Bluthenthal et al. in 2007, the conceptualisation and implementation of individual-level syringe coverage remains a relatively recent development, with measurement conducted in only a handful of countries. Ours and other research (26) show that individual-level coverage can be measured in diverse geographical locations, both high and low-income, to produce meaningful evaluative results. Despite efforts to refine the measure (16, 24), a consistent methodology is yet to be accepted. Further work needs to be done to establish both the optimal coverage formula, and the time frame within which to record coverage. Coverage measurement at the population level plays a vital role in international program evaluation but there remains a definite place for individual-level coverage measurement in international harm reduction reporting and an accepted methodology is required for this.

In describing the sample, other relevant observations were made. Participants recruited in Mandalay city and Pyin Oo Lwin reported substantially lower levels of current drug treatment (ostensibly MMT). MMT reduces injecting frequency (37) and the lower utilisation of drug treatment may partly explain the higher injection frequencies found at those sites. Higher frequency injection has previously been linked to insufficient coverage (21, 22). BI harm reduction staff noted difficulties in accessing drug treatment due to a scarcity of nearby services (personal communication with BI staff). Drug treatment should be available for those PWID seeking it. Differences in BBV testing were also noted. Whilst the majority of participants had been tested for HIV, HCV and/or HBV within the previous 12 months, many participants reported never being tested for HCV or HBV. The self-reported HCV exposure prevalence was 51% (though has previously been reported as high as 79% (7)), and nearly one in five participants reported never receiving a HCV test. HCV testing should be expanded for PWID across sites. Furthermore, approximately half of self-reported HIV positive participants were not receiving ART. Again, BI staff report poor geographical access as a barrier for some HIV positive PWID accessing ART. Tracing and facilitating treatment for HIV positive PWID should be prioritised.

Limitations

Our study was subject to some limitations. First, the vast majority of our participants were male (97% of the sample). This accords with previous Myanmar samples of PWID

(8, 10), but it is possible there are many more female PWID in Myanmar than our sample suggests, though they may be an especially "hidden" sub-population. Our results can only be applied to male PWID.

Second, our survey tool (questionnaire) was constructed in Australia, in collaboration with Myanmar national researchers, then translated into Myanmar language by bilingual researchers. Translations were checked by additional bilingual staff and Myanmar-based field researchers were trained in use of the questionnaire by both Australian and Myanmar national staff. Despite our best efforts, it is possible that some aspects of the questionnaire were lost in translation. We attempted to mitigate this possibility.

Third, our BBV prevalence data was based upon self-report, in some cases from test results over 12 months old. Further, HCV testing in Myanmar is largely restricted to antibody testing, which is only a measure of exposure. Consequently, the prevalence figures should be treated with caution. Moreover, due to the large numbers of participants reporting never receiving a BBV test, this precluded use of BBV positivity as an exposure within our regression model.

Finally, the individual-level coverage measure collects various behavioural data, all reliant upon participant recall. Whilst PWID recall has been shown to be valid and reliable (38) some bias still exists. To reduce this bias and to allow sufficient time to capture pertinent behaviours, we used a two-week time period for measurement.

Conclusion

We measured individual-level syringe coverage among Myanmar PWID. The overall level of insufficient coverage is comparable to other, high-income countries, although coverage was not consistent across recruitment sites. These differences were very likely due to the presence of shooting galleries in some sites and not in others. Whilst harm reduction services in Myanmar work collaboratively with the operators of these illicit shooting galleries, this is not the case in other international locations (35, 36). In the absence of formalised SIFs, the development of similarly collaborative relationships is recommended. PWID acquiring syringes from locations (particularly pharmacies) other than formal harm reduction services had increased odds of insufficient coverage. PWID should be facilitated to have access to consistent and free sources of sterile syringes as

much as possible. Finally, our results highlight areas of expansion in Myanmar harm reduction and BBV transmission reduction programs, in particular, increasing testing and treatment for all BBVs (HCV, HBV and HIV).

References

1. Ministry of Health and Sports. Myanmar national strategic plan on HIV and AIDS (2016-2020). Myanmar: 2016.
2. O'Keefe D, Stoove M, Doyle J, Dietze P, Hellard M. Injecting drug use in low and middle-income countries: Opportunities to improve care and prevent harm. Journal of Viral Hepatitis. 2017;24(9):714-24.
3. Saw. YM, Yasuoka J, Saw. TN, Poudel KC, Tun. S, Jimba M. What are the factors associated with HIV testing among male injecting and non-injecting drug users in Lashio, Myanmar: a cross-sectional study. BMJ open. 2013;3:1-9.
4. Ministry of Health and Sports. Myanmar national strategic plan on HIV and AIDS (2011-2016), revised edition. Myanmar: 2014.
5. UNODC. Myanmar country advocacy brief: Injecting drug use and HIV. Myanmar: 2010.
6. Sports MoHa. Myanmar integrated and behavioural surveillance survey and population size estimates among people who inject drugs: final report. Myanmar: 2014.
7. HRI. Global State of Harm Reduction. London, United Kingdom: Harm Reduction International, 2016.
8. Swe. LA, Nyo KK, Rashid AK. Risk behaviours among HIV positive injecting drug users in Myanmar: a case control study. Harm Reduction Journal. 2010;7(12).
9. Williams CT, Liu W, Levy JA. Crossing over: drug network characteristics and injection risk along the China-Myanmar border. AIDS and Behaviour. 2011 Jul;15(5):1011-6.
10. Zhou Y, Liu F, Yao Z, Duo L, Li H, Sun Y, et al. Comparison of HIV-, HBV-, HCV- and co-infection prevalence between Chinese and Burmese intravenous drug users of the China-Myanmar Border Region. PLoS One. 2011;6(1).
11. Li L, Assanangkornchai S, Duo L, McNeil E, Li J. Cross-border activities and association with current methamphetamine use among Chinese injection drug users (IDUs) in a China-Myanmar border region. Drug and Alcohol Dependence. 2014;138:48-53.
12. WHO. Technical guide for countries to set targets for universal HIV services for injecting drug users. Geneva, Switzerland: World Health Organisation, 2012.

13. WHO. Combating hepatitis B and C to reach elimination by 2030: advocacy brief. Geneva, Switzerland: World Health Organisation, 2016.
14. Kwon JA, Iversen J, Maher L, Law MG, Wilson DP. The impact of needle and syringe programs on HIV and HCV transmissions in injecting drug users in Australia: A model based analysis. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology. 2009;51(4):462-9.
15. O'Keefe D, Scott N, Aitken C, Dietze P. Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis. BMC Health Services Research. 2016;16(1):411.
16. McCormack AR, Aitken CK, Burns LA, Cogger S, Dietze PM. Syringe Stockpiling by Persons Who Inject Drugs: An Evaluation of Current Measures for Needle and Syringe Program Coverage. American Journal of Epidemiology. 2016;183(9):852-60.
17. O'Keefe D, Scott N, Aitken C, Dietze P. Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia. Drug and Alcohol Dependence. 2017;176:7-13.
18. Bluthenthal RN, Ridgeway G, Schell T, Anderson R, Flynn NM, Kral AH. Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. Addiction. 2007;102(4):638-46.
19. Burrows D. Advocacy and coverage of needle exchange programs: results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. Cadernos de Saude Publica. 2006;22(4):871-9.
20. Cooper HLF, Des Jarlais DC, Ross Z, Tempalski B, Bossak B, Friedman SR. Spatial access to syringe exchange programs and pharmacies selling over-the-counter syringes as predictors of drug injectors' use of sterile syringes. Research and Practice. 2011;101(6):1118-25.
21. Bluthenthal RN, Anderson R, Flynn NM, Kral AH. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. Drug and Alcohol Dependence. 2007 Jul 10;89(2-3):214-22.
22. Bryant J, Paquette D, Wilson H. Syringe coverage in an Australian setting: does a high level of syringe coverage moderate syringe sharing behaviour? AIDS and Behaviour. 2012;16(5):1156-63.

23. Iversen J, Topp L, Wand H, Maher L. Individual-level syringe coverage among Needle and Syringe Program attendees in Australia. Drug and Alcohol Dependence. 2012;122(3):195-200.
24. O'Keefe D, McCormack A, Cogger S, Aitken C, Burns L, Bruno R, et al. How does the use of multiple needles/syringes per injecting episode impact on the measurement of individual level needle and syringe program coverage? The International Journal of Drug Policy. 2017;46:99-106.
25. Iversen J, Wand H, Topp L, Kaldor J, Maher L. Reduction in HCV incidence among injection drug users attending needle and syringe programs in Australia: a linkage study. American Journal of Public Health;103(8):1436-44.
26. Noroozi M, Mirzazadeh A, Noroozi A, Mehrabi Y, Hajebi A, Zamani S, et al. Client level coverage of needle and syringe program and high risk injection behaviours: a case study of people who inject drugs in Kermanshah, Iran. Addiction Health. 2015;7(3-4):164-73.
27. Craney TA, Surles JG. Model-dependent variance inflation factor cutoff values. Quality Engineering. 2002;14(3):391-403.
28. Larney S, Peacock A, Leung J, Colledge S, Hickman M, Vickerman P, et al. Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. The Lancet Global Health. 2017.
29. WHO. Guidance on prevention of viral hepatitis B and C among people who inject drugs. Geneva, Switzerland: 2012.
30. UNAIDS. Do no harm: health, human rights and people who use drugs. Geneva, Switzerland: 2016.
31. Wodak A, McLeod L. The role of harm reduction in controlling HIV among injecting drug users. AIDS. 2008;22 (supp 2):S81-S92.
32. Aceijas C, Hickman M, Donoghoe MC, Burrows D, Stuikyte R. Access and coverage of needle and syringe programmes (NSP) in Central and Eastern Europe and Central Asia. Addiction. 2007;102(8):1244-50.
33. Brett MM, Hood J, Brazier JS, Duerden BI, HahnÉ SJM. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. Epidemiology and Infection. 2005;133(4):575-82.

34. Fuller C, Vlahov D, Latkin CA, Ompad D, Celentano D, Strathdee SA. Social circumstances of initiation of injecting drug use and early shooting gallery attendance: implications for HIV intervention among adolescent and young adult injection drug users. Journal of Acquired Immune Deficiency Syndrome. 2003;32:86-93.
35. Philbin M, Pollini RA, Ramos R, Lozada R, Brouwer KC, Romas ME, et al. Shooting gallery attendance among IDUs in Tijuana and Ciudad Juarez, Mexico: correlates, prevention opportunities and the role of the environment. AIDS and Behaviour. 2008;12:552-60.
36. Kimber J, Dolan K. Shooting gallery operation in the context of establishing a medically supervised injecting centre: Sydney, Australia. Journal of Urban Health: Bulletin of the New York Academy of Medicine. 2007;84(2):255-66.
37. Lawrinson P, Ali R, Buavirat A, Chiamwongpaet S, Dvoryak S, Habrat B, et al. Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. Addiction. 2008;103(9):1484-92.
38. Darke S. Self report among injecting drug users: a review. Drug and Alcohol Dependence. 1998;51:253-63.

5.4 Summary of Chapter Five

The narrative review in Paper Five detailed the inadequacy of current harm reduction implementation in LMICs. Many LMICs face BBV epidemics amongst their PWID populations (9), driven by unsterile syringe sharing, which in turn is driven by insufficient individual-level syringe coverage. The review recommends that LMICs increase their harm reduction service provision and advocacy for PWID. Of relevance, the review also recommends that LMIC data systems be strengthened; that the presence or absence of PWID within countries be confirmed and national PWID-specific data be routinely collected and disseminated.

Paper Six presented primary, quantitative individual-level syringe coverage data from Myanmar, itself an LMIC. I measured individual-level syringe coverage (using the McCormack et al. individual-level syringe coverage measure) amongst 512 PWID across three qualitatively different urban recruitment sites. Insufficient individual-level syringe coverage prevalence was 19%, a percentage comparable to those found in Australian studies. Insufficient individual-level syringe coverage was associated with acquiring syringes from a source other than harm reduction "drop-in-centres" (functionally the same as fixed-site NSPs), a finding replicated in Papers One and Two; and syringe re-use, as replicated in Paper Four. There were also substantial differences in individual-level syringe coverage, syringe acquisition and injecting frequencies across recruitment sites. Significantly, participants from the two Mandalay recruitment sites, where shooting galleries (illicit locations PWID can acquire and inject drugs) are common, had considerably lower prevalence of insufficient individual-level syringe coverage than other sites. The Mandalay shooting galleries work collaboratively with harm reduction services to ensure a constant supply of sterile injecting equipment. Because nearly all injections amongst the Mandalay participants occurred in these shooting galleries, this represents a novel form of service delivery and engagement between shooting gallery operators and the harm reduction drop-in-centres for Myanmar. My findings provide essential information regarding the service of shooting gallery attendees, assisting with program planning towards syringe coverage improvement efforts. Moreover, these findings may not have been reported in other

locations, thereby providing original and potentially innovating examples of harm reduction delivery for other services to follow.

Chapter Six: Integrated discussion and conclusions

Harm reduction is effective at reducing BBV transmission (45), unsterile syringe sharing (45, 46, 73, 170) and cost-effective in reducing associated health care burdens (157). However, levels of service delivery vary dramatically both within and between countries and global syringe distribution is drastically inadequate (8). Only nine countries have "high" syringe distribution, according to WHO recommendations of 200 syringes distributed per PWID per annum (6, 8).

Even in countries that do reach these population-level targets, substantial shortfalls at the individual level persist. In 2017, it was estimated that 461 sterile syringes were distributed per PWID per annum in Australia, (8), well in excess of WHO recommendations (6, 141). Even so, 16–37% of Australian PWID samples report insufficient individual-level syringe coverage at the individual level (171). Multiple structural, environmental and individual barriers have been associated with these insufficiencies, both in Australia (37, 123) and internationally (5, 59, 148). Overcoming these barriers requires enhancing harm reduction service delivery and the targeting of at-risk sub-populations.

My research builds upon the foundation created by Bluthenthal et al. in 2007, when they published their method for measuring syringe coverage at the individual level (5), thereby capturing vital information previously hidden beneath aggregated population-level estimates. The Bluthenthal et al. measure (and adaptations thereof) has since been employed in several studies, producing important findings about syringe coverage deficits amongst PWID overall and amongst sub-groups of PWID (37, 146, 147). My work advances this research substantially by examining the variations in individual-level syringe coverage over time, exploring ways of refining individual-level syringe coverage measurement, and conducting syringe coverage research in diverse settings.

In this final chapter I discuss the findings of my research on individual-level syringe coverage amongst PWID, both in Australia and internationally. First, the key findings of

this research are discussed. Second, the implications of these findings are presented in the context of improving service delivery and individual-level syringe coverage measurement. Third, I suggest ways in which future researchers can extend upon my work. Finally, I discuss the strengths and limitations of this research.

6.1 Key findings

6.1.1 Prevalence of insufficient individual-level needle and syringe coverage

Amongst the Australian sample in Papers One and Two, prevalence of insufficient individual-level syringe coverage was estimated at 20-36%, corroborating previous Australian findings (37, 123, 146). In Paper Six, I reported an insufficient individual-level syringe coverage prevalence of 19% amongst Myanmar-based PWID, again despite relatively high levels of syringe distribution compared to other countries in the region, and indeed, global syringe coverage (82). Additionally, in Papers One and Six, I demonstrated the limitations of population-level measurement. Across the Australian and Myanmar samples, 14,525 and 19,352 sterile syringes were reportedly acquired, respectively, within the two weeks prior to interview, at population-level distribution rates of 1118 and 988 sterile syringes per PWID per annum. This extremely high population-level syringe coverage, which greatly exceed WHO recommendations, mask the insufficiencies in individual-level syringe coverage experienced by many PWID. The idiosyncratic life circumstances of PWID may either hinder or facilitate their achievement of optimal syringe coverage, but when syringe coverage is measured at the population level, those who acquire more syringes than they need (or use) may mask insufficient syringe coverage among those who do not. Individual-level measurement reveals these disparities, as discussed throughout this chapter.

6.1.2 Longitudinal analysis of individual-level needle and syringe coverage

The need for longitudinal analysis of individual-level syringe coverage was raised in Bluthenthal et al.'s original paper (5). Data collected at a single time point cannot capture the variations in individuals' syringe coverage over time, or the causative relationship between a given exposure variable and individual-level syringe coverage. Only longitudinal data can provide insights into these kinds of relationships.

The MIX Study provided a unique opportunity to perform longitudinal analysis of individual-level syringe coverage (126). In Paper One, cohort members were categorised as *consistently covered* (always sufficiently covered across interviews) – 50%, *consistently uncovered* (always insufficiently covered) – 5%, or *inconsistently covered* (fluctuating between states of individual-level syringe coverage) – 45%. Those who oscillate between states of individual-level syringe coverage, rather than those who consistently fail to adequately cover their injecting episodes, account for the greatest proportion of insufficient individual-level syringe coverage. I surmised that time-varying factors that hinder of facilitate sufficient individual-level syringe coverage may drive these oscillations.

In Paper Two, I aimed to examine how these time-varying factors relate to changes in longitudinal individual-level syringe coverage, by focusing specifically on the MIX participants whose individual-level syringe coverage fluctuated over time. Those who had serological evidence of a new HCV diagnosis and those who reported past month methamphetamine injecting (and had not previously reported this behaviour in their previous interview) had higher odds of a change from sufficient to insufficient individual-level syringe coverage. Those who reported recent initiation of OST and those who reported using fixed-site NSPs as their main source of syringe acquisition (and had not previously reported doing so) had reduced odds of a change to insufficient individual-level syringe coverage. These longitudinal associations provide robust evidence of how individual-level syringe coverage can be affected temporally by changes in the lives of PWID, reinforcing the importance of analysing syringe coverage both over time and at the individual level. These factors may be temporary, yet still impede or enhance a person's ability to cover their injecting episodes. For example,

moving from a residence with poor needle and syringe program access to one with easy access will facilitate syringe acquisition and lower the barrier to sufficient individual-level syringe coverage.

The final examination of longitudinal individual-level syringe coverage in Paper Three focused on the behaviours constituting the parameters within the individual-level syringe coverage formula. External factors may exert different levels of influence over these parameters. Change in injecting frequency had almost twice the effect upon individual-level syringe coverage of the other three parameters, with an increase in one unit of injecting frequency leading to an estimated reduction in individual-level syringe coverage of 10.03 percentage points. The next largest effect size was for change in syringe acquisition, with a one unit increase equating to a 5.99 percentage point increase in individual-level syringe coverage. The differing extent to which PWID can acquire syringes vs. the frequency at which they can inject is also relevant. Australian needle and syringe program dispensation policy allows for unlimited syringe acquisition, whilst there is a finite frequency at which a person may inject (in practice). Consequently, my findings imply that interventions designed to decrease injecting frequencies (such as OST) would be associated with greater individual-level syringe coverage improvements than increased syringe provision. Harm reduction services are often poorly resourced (82, 172), meaning that interventions that produce the largest syringe coverage gains, most efficiently, should be prioritised.

6.1.3 Associations with individual-level needle and syringe coverage

My research highlighted the existence of multiple structural, environmental and individual barriers to sufficient individual-level syringe coverage, despite wide availability of and access to sterile syringes in Australia. Traditional conceptions of syringe coverage focus on needle and syringe program service delivery, and particularly the number of syringes distributed across PWID populations. Whilst this is a vital function, simply increasing syringe distribution via existing channels may not increase the proportion of those sufficiently covered at the individual level (173). Identifying

sub-groups of PWID at risk of insufficient individual-level syringe coverage, and targeting responses – such as increased syringe distribution for methamphetamine injectors – may prove a more efficient way of improving syringe coverage (though overall increases in syringe distribution remain important). Optimal syringe coverage may therefore, not be the result of a single intervention, but instead be due to multiple interventions working synergistically.

Despite representing only 28% of all Australian syringe distribution outlets (including pharmacies), primary/secondary needle and syringe programs accounted for approximately 87% of the nearly 50 million syringes distributed in 2015/16 (103), suggesting a clear preference for these services amongst Australian PWID. However, 18% of the Australian sample in Paper One reported another syringe source (pharmacies, peers, drug dealers) as their *usual* source of syringe acquisition at their most recent interview. This non-use or inconsistent use of fixed-site NSPs – a reliable and free method of acquiring syringes – was associated with insufficient individual-level syringe coverage. The Myanmar-based study (Paper Six) replicated this finding, with an even greater percentage of the sample (61%) reporting an alternate source as their main source of syringe acquisition, again associated with increased odds of insufficient individual-level syringe coverage.

Being on OST reduced the odds of insufficient individual-level syringe coverage in Paper One, and a change to being on OST (with no OST at the prior interview) reduced the odds of a change to individual-level insufficient syringe coverage in Paper Two. The mechanism here is presumably a reduction in injecting frequency. OST has been shown to reduce injecting frequencies (13, 51), whereas high injecting frequencies have previously been associated with insufficient individual-level syringe coverage (123). Therefore, if OST effects a reduction in injecting, whilst syringe acquisition remains stable, this will increase a person's individual-level syringe coverage. If those receiving OST were to stop injecting altogether, then syringe coverage is no longer a concern.

Methamphetamine injectors had higher odds of insufficient individual-level syringe coverage than heroin injectors in Paper One, and twice the odds of a change from sufficient to insufficient individual-level syringe coverage in Paper Two. Bluthenthal et al. previously demonstrated differences in individual-level syringe coverage as a result of drug use preferences, with those reporting past month crack cocaine smoking having

reduced odds of sufficient individual-level syringe coverage (59). Multiple studies have associated methamphetamine injection with receptive syringe sharing and other forms of injecting risk (34, 174, 175). These risk behaviours are markers for deficiencies in syringe coverage (151). Other research has also reported reduced access of harm reduction services amongst methamphetamine injectors (34, 95). The reasons for this difficulty in access are somewhat ambiguous. Marshall et al. hypothesised that perhaps methamphetamine injectors find fixed-site NSPs unwelcoming, due to the dominance of heroin injecting clientele (34, 130), or that access to fixed-site NSPs becomes more difficult during multi-day drug "binges" or during periods of drug-induced psychological distress (34, 176). Furthermore, methamphetamine injectors are more likely to inject in groups, which Marshall et al. suggested promotes the sharing of injecting equipment (34). These hypotheses, however, remain unproven, with Marshall et al. stating future research is required to better identify barriers to fixed-site NSP access for methamphetamine injectors (34).

HCV infection has a plausible association with insufficient individual-level syringe coverage. PWID without enough syringes to cover their injecting episodes are more likely to receptively share unsterile and potentially BBV-infected syringes (5, 148), thereby risking HCV infection. Alternatively, those already HCV-positive may be less concerned about BBV infection and therefore less concerned with acquiring enough syringes to cover their injecting episodes. Though there was some evidence of an association between receptive syringe sharing and insufficient individual-level syringe coverage in Paper One, this evidence was relatively weak, and not supported in Paper Two's longitudinal analysis. This may have been due to an insufficient time frame (month prior to interview) to capture incidents of receptive syringe sharing, which may be a relatively infrequent behaviour. There was stronger evidence of an association between insufficient individual-level syringe coverage and HCV-positivity in Papers One and Two. Regardless, there appears to be a relationship between insufficient individual-level syringe coverage, injecting risk behaviours (5) and HCV infection (171). The evidence that needle and syringe programs reduce HIV transmission amongst PWID populations is strong (46, 68). But current levels of service delivery may be ineffective at controlling HCV incidence, due to HCV's higher transmission potential compared to HIV (70, 85), hence the higher HCV-specific population-level syringe distribution recommendations from the WHO (7). Many countries with low PWID-specific HIV

prevalence have persistent HCV transmission, Australia being an example (48). The substantial shortfalls in individual-level syringe coverage described in this thesis may be a key driver of this ongoing HCV transmission.

In Paper Four, I described an association between self-reported ATSI-background and insufficient individual-level syringe coverage. Previous work by Martinez et al. (2011) also showed differences in individual-level syringe coverage among American ethnic groups (128), suggesting ethnicity may represent an individual barrier to culturally inappropriate services. However, in re-analysis using the adaptation of Bluthenthal et al.'s measure, and the McCormack et al. measure, this association between ATSI-background and insufficient coverage was not significant, according with other analysis in Paper One, and other Australian research (37, 123), using ATSI-background as a covariate. The only consistent finding between regression models was the increased odds of insufficient individual-level syringe coverage associated with syringe re-use. This association was replicated in Paper Six, and together, has now been reproduced in five separate studies (5, 37, 148).

6.1.4 Refining the individual-level needle and syringe coverage measure

Despite Bluthenthal et al. first proposing their individual-level syringe coverage measure in 2007 (5), research exploring its composition, methodology and utility is still in its infancy. The optimal structure of the individual-level syringe coverage formula has yet to be determined. Calculation of the measure requires data on two central parameters: *total syringes acquired* and *injecting frequency*. Other behaviours that may influence this bipartite relationship are then included, such as peer-to-peer distribution. McCormack et al. showed convincingly that the inclusion of a syringe stockpiling parameter improves the measurement of individual-level syringe coverage (146). In Paper Four, I explored an additional, but heretofore untested, parameter: the use of multiple sterile syringes per injecting episode, via a similar method as employed by McCormack et al. I showed that a minority of participants (16%) reported this behaviour, but including the parameter within the individual-level syringe coverage

formula did not improve discrimination of cases and non-cases of injecting risk behaviours. Consequently, I did not recommend the parameter's inclusion in the individual-level syringe coverage formula.

In Paper Three, I used a data-driven technique – factor analysis - to assess the underlying structure to a dataset that included the variables used in the calculation of individual-level syringe coverage, whereby a factor or factors could summarise their inherent variability. These factors are assessed in relation to the variance they each explain, as well as the variance explained in the dataset by the overall model. Factor loadings of individual variables are assessed, with the strength of these loadings suggesting the extent to which each variable can be summarised by the common factor/s (177). I tested three parameters used in my research (*total syringes acquired, peer-to-peer syringe distribution* and *injecting frequency)* and one from other research *(instances of syringe acquisition)* (5, 37, 123, 147). In analysis, all parameters loaded most strongly on a single factor, presumed to be individual-level syringe coverage. However, of the four, the *instances of syringe acquisition* parameter loaded upon the single factor with the lowest weight (factor loading: 0.2797). Due to this weakness in factor loading, and the parameters previous omission from McCormack et al.'s improved individual-level syringe coverage measure (146), I concluded its exclusion from future individual-level syringe coverage measurement is warranted.

6.1.5 Needle and syringe coverage in low and middle-income countries

Nearly all studies employing the individual-level syringe coverage measure have been conducted in high-income countries. LMICs have many barriers to adequate service provision (and therefore syringe coverage) that are exacerbated by their relative lack of resources. I reviewed these issues in Paper Five, concluding that harm reduction implementation in LMICs was critically inadequate (8, 64). At the time of writing, of 139 countries classified as LMICs by the World Bank (178), only 52 (37%) had needle and syringe programs, and only 40 (29%) prescribed OST. The countries with reported IDU that fail to intervene are therefore at risk of PWID-specific BBV epidemics (84). Also,

many countries yet to report IDU probably have populations of PWID, but public health surveillance systems are either absent or ill-equipped to detect them (143). This final observation was supported in a recent review by Degenhardt et al., in which an additional 21 countries with reported IDU were added to existing global estimates (9). The authors suggesting that this was partly a result of improved data collection (9), rather than IDU necessarily emerging within the country. In Paper Five, I made five recommendations: an increase in global funding for harm reduction, particularly in LMICs; the expansion of harm reduction in countries with verified populations of PWID; the confirmation of the existence of populations of PWID using rapid assessment and response methods (179); the strengthening of LMICs' public health data systems; and greater advocacy for PWID in LMICs. The paucity of IDU research in LMICs is also a longstanding problem, meaning there is a reliance upon research findings from high income countries of unknown generalisability to these settings (143).

In Paper Six I described my findings about individual-level syringe coverage amongst PWID in Myanmar. I estimated that individual-level syringe coverage was insufficient in 19% of the sample, a level comparable to that reported amongst Australian samples in Papers One to Four. In statistical analysis, those reporting non-use or inconsistent use of harm reduction "drop-in centres" (equivalent in function to Australian primary fixed-site NSPs) and/or outreach, had increased odds of insufficient individual-level syringe coverage, an association that replicated those found in the research described in Papers One and Two, as did those reporting syringe re-use, an association replicated in Paper Four. Significantly, individual-level syringe coverage levels differed substantially across diverse recruitment sites, as did the behaviours related to individual-level syringe coverage. In particular, the presence of shooting galleries (illicit locations, managed by drug dealers, in which PWID can purchase and inject illicit drugs) in the two Mandalay recruitment sites (Mandalay city and Sagaing city) affected syringe coverage dramatically. In Mandalay city 73% and in Sagaing city 99% of participants reported shooting galleries as the main location of injecting, and 99% and 100% respectively, as their main source of syringe acquisition. Shooting galleries are often characterised in international research literature as highly unsterile places with high levels of syringe sharing (180, 181). The Mandalay shooting galleries, in contrast, work in collaboration with harm reduction services, ensuring consistent provision of sterile syringes and

minimising the potential for syringe sharing amongst clientele. Consequently, only 3–6% of Mandalay participants reported insufficient individual-level syringe coverage, compared to 14–40% in the other three recruitment sites. Crucially, these findings could only have been revealed by measuring syringe coverage at the individual level. Population-level syringe coverage data in Myanmar has neither the detail nor sophistication to capture the syringe coverage nuances reported in Paper Six.

6.2 Implications

6.2.1 Methods to increase needle and syringe coverage

My work, both in Australia and internationally, demonstrates the different levels of engagement PWID have with harm reduction services due to their demographics, drug use preferences and other variable characteristics. In order to cater to these differing levels of need and improve syringe coverage (173), harm reduction services need to be adaptive, offering multiple avenues for syringe acquisition, in complement to one another.

Australia's National Drug Strategy 2017-2026 (as briefly described in section 1.1.12) has adopted harm reduction as a key pillar, extending a similar approach since 1985 (153). However, the strategy does not specify national NSP access or syringe distribution targets. Similarly, Australia's National HIV Strategy 2014-2017 makes no specific recommendations in terms of syringe distribution objectives, instead opting for general action areas, such as "ensure the provision of sterile injecting equipment and safe-injecting education among people who inject drugs" and "reduce the risk behaviours associated with transmission of HIV" (182) (p.17, p.5). The absence of clearly defined indicators in the HIV strategy may be a product of the comparatively low prevalence of HIV amongst PWID in Australia, what the HIV strategy classifies as "virtual elimination"(182), or a prevalence so low that HIV is essentially eliminated amongst the target population. Perhaps due to the much higher prevalence of HCV amongst Australian PWID, the National HCV Strategy 2014-2017 provides greater guidance in terms of syringe distribution, prioritising an "increase (in) availability, access to and use of sterile injecting equipment among people who inject drugs" (183)

(p.15). Reference to WHO population-level coverage measurement is made, but no specific target is provided, implying that the WHO target of 200 sterile syringes distributed per PWID, applies.

Australia has rightly positioned PWID as a priority population in its BBV prevention efforts, particularly in its national HIV and HCV strategies (PWID are strangely not mentioned as a priority population in the National Drug Strategy). However, more consistent recommendations are needed across the three strategies in relation to needle and syringe coverage, including specific syringe coverage targets as indicators of performance. In this regard, syringe coverage would be measured according to WHO population-level methodology, in keeping with international standards. However, there is no reason for Australia to rely on the WHO recommended population-level syringe coverage target. Instead, targets could be set within the Australian national strategies that are particular to the Australian context (albeit, above the WHO recommendations). Simply relying on a generalised international target, being the WHO target, wouldn't encourage improvements in syringe coverage in Australia, especially because Australian population-level coverage already exceeds WHO recommendations. Importantly, the strategies could make specific recommendations to harmonise effective syringe distribution and NSP policy across the states and territories. For example, New South Wales has over 200 SVMs (103) compared to only six in Victoria (184), but the effects of variations such as this on coverage are poorly understood. Australia's national strategies could make explicit references to these differences and encourage a more consistent practice and optimal collection of policies between jurisdictions.

From 2006 to 2016, sterile syringe distribution in Australia increased by 48%, yet the estimated PWID population only slightly increased (89,000 – 93,000) (10, 156). In 2009 Kwon et al. called for a doubling of nationwide syringe distribution (130, 152), but how to effect improvements in syringe coverage at the individual level via these distribution increases requires special consideration, in view of the substantial prevalence of insufficient individual-level syringe coverage between individuals and over time. There is evidence that oversupply of syringes to PWID – effectively providing them with more syringes than they request – reduces syringe sharing (58), and Bluthenthal et al. showed that those PWID with excessive individual-level syringe coverage (≥150%) had the lowest reports of injecting risk (5). Future research should explore what exactly

happens to excessively acquired syringes. However, such a blanket provision policy may be impractical, with some PWID refusing to carry more syringes than is adequate for their immediate needs. Targeted oversupply, to methamphetamine injectors for example, may be an alternative.

Some aspects of needle and syringe programs make them unattractive to particular PWID (47, 60, 94). Identification as PWID, the presence of other PWID, and fear of police attention can mean many PWID are reticent to use fixed-site NSPs (60, 94, 106, 107). These issues do not affect all needle and syringe programs or PWID equally, but exemplify how the characteristics of particular services and their location can deter access. Australian fixed-site NSP clientele populations have previously been described as relatively homogenous, servicing mainly older, long-term injecting, white males (94, 130). Additional research amongst samples using pharmacies or SVMs describe demographically different samples (60, 61, 185), demonstrating the need for alternate methods of syringe dispensation, beyond fixed-site NSP. Additionally, fixed-site NSPs may be unacceptable to some members of ethic or sexual minorities (129, 186-188). Pharmacies provide an alternative means of syringe access, as does secondary syringe exchange (peer-to-peer distribution) (130). Nonetheless, these methods of syringe acquisition have their own barriers, such as the financial burden of pharmacy purchase (65, 189) and the potentially inconsistent nature of secondary exchange (190), hence the associations between non-use of fixed-site NSPs and insufficient individual-level syringe coverage in Papers One, Two and Six. Enhancing access to sterile syringes (both at fixed-site NSPs and other modalities of syringe distribution) to all PWID is therefore an important step in maximising syringe coverage, particularly for those reticent to use fixed-site NSPs or who may think of needle and syringe programs as inappropriate to their specific needs. In this regard, syringe distribution within other targeted, non-needle and syringe program, services may be effective. Health services targeting cultural minorities (such as Australian Aboriginal health services) or sexual minorities (such as sexual health clinics) should consider providing syringe distribution as part of their suite of services.

For existing needle and syringe programs, expanding existing methods of syringe delivery is recommended. Fixed-site needle and syringe program opening hours (generally Monday–Friday 9am–5pm) have repeatedly been reported as a barrier to

access (34, 60, 94, 104). Though most drug use in Australia occurs during daylight hours, drug use continues to occur outside of the hours when syringes are available (either via fixed-site NSPs or pharmacies) (93), and access on weekends is particularly poor. Expanding 24-hour access to syringes may extend syringe coverage to more groups of PWID (129). However, due to high staff costs, this may not be feasible for many fixed-site NSPs.

SVMs are a cost-effective (60) means of dispensing syringes outside of fixed-site NSP opening hours or to PWID reluctant to access fixed-site NSPs, such as the minority groups discussed above. Whilst evaluative work has supported the efficacy of SVMs in increasing geographical and temporal syringe availability (60), SVMs were only introduced to the Australian state of Victoria (where the research reported in Papers One to Three was conducted) in 2014. Increasing Victoria's network of SVMs as an adjunct to current fixed-site NSP operations should be prioritised, and SVMs should be considered in other settings. SVMs present their own challenges, such as running out of stock, so strategies need to be in place to ensure their constant supply (191). Additionally, outreach methods of syringe distribution, whereby harm reduction workers (often peers) deliver sterile injecting equipment to PWID, should be expanded. These services operate throughout Australia and in the settings I studied in Myanmar, and are a common component of harm reduction service delivery, which like SVMs, can reach groups of PWID reluctant to use fixed-site NSPs (129, 192).

Syringe coverage measured at the individual level captures variations between PWID. If PWID have unique levels of need and engagement, this suggests they require tailored forms of service provision. In Paper Two I recommended the targeting of known methamphetamine injectors with increased syringe distribution. Methamphetamine injectors could be identified by including questions about the last or primary drug of injection within routine data collection when PWID present to fixed-site NSPs. In Queensland, Australia, PWID nominate the drug to be injected when acquiring syringes, during instances of service contact (193). Similar models could be adopted in other Australian jurisdictions to identify methamphetamine injectors and subsequently dispense an oversupply of syringes to them. Other PWID may be appropriate for similarly targeted distribution efforts, such as those with high or recently increased injecting frequencies. For PWID who inject opioids, OST has been shown to reduce

injecting frequencies (13), thereby reducing the number of injecting episodes that require a sterile syringe and facilitating higher syringe coverage. This effect could explain the demonstrated influence of injecting frequency on individual-level syringe coverage evident in Paper Three. PWID receiving OST and utilising needle and syringe programs regularly ("full harm reduction"), have shown the highest odds of sufficient individual-level syringe coverage (compared to "partial coverage") (37) and the lowest levels of injecting risk behaviours (72, 77). However, retention in OST is vital. Longer OST retention is associated with better health outcomes (161), and Australian clinical guidelines recommend at least 12-month retention (161). In reality, most PWID do not meet this target (161) and methods to improve OST retention need to be developed. Reaching PWID appropriate for OST, but with difficulties in access is an additional issue. Whilst Australian OST coverage is high (8) (contrasting low provision globally (8)), there are inefficiencies in Australia's OST network, such as too few prescribers and coordination issues between services (129). These problems need to be overcome to increase OST provision and retention and improve syringe coverage.

In Paper Six, I noted substantial geographic differences in individual-level syringe coverage and the behaviours that underpin individual-level syringe coverage in Myanmar. Across the five recruitment sites, there were large variations in injecting frequencies and syringe acquisition. Importantly, 3 to 40% of participants reported insufficient individual-level syringe coverage across sites and the reporting of injecting risk behaviours was similarly disparate (for example, prevalence of syringe re-use ranged from 2% to 62%). These differences speak to the contextual barriers on syringe coverage. Whilst injecting frequency was highest at the Pyin Oo Lwin site (reported median of 42 injections in the two weeks before interview), insufficient individual-level syringe coverage prevalence was only 14%. In comparison, at the two Yangon sites, insufficient individual-level syringe coverage prevalence ranged from 31% to 40%, despite much lower injecting frequencies. Significantly, I reported that shooting galleries in Mandalay, which provided harm reduction services, had a protective effect. Mandalay participants reported most of their injecting episodes and syringe acquisition occurring within the shooting galleries, and the extremely low insufficient individual-level syringe coverage prevalence of these participants suggests other international harm reduction programs should adopt similarly collaborative relationships with shooting gallery operators. These findings are also supportive of supervised injecting

facility (SIF) implementation. SIFs provide safe, sterile locations for PWID to inject in, under medical supervision (194). They control the environment in which injections take place, simultaneously providing sterile injecting equipment and thereby reducing injecting risk. The shooting galleries in Myanmar fulfil a similar function and emphasise the importance of providing harm reduction services to PWID in the settings in which drug use occurs. Although, servicing shooting galleries should not be seen as equivalent to SIFs for reducing injecting risks.

No public health program can expect to reach its entire target population all of the time. Accordingly, 100% individual-level syringe coverage across the entire PWID population is an aspirational rather than a practical goal. Previous modelling work has indicated that modest improvements in harm reduction interventions and coordination can lead to substantial and beneficial public health outcomes. Vickerman et al. estimated that if implemented in combination, a coverage target of 14% for needle and syringe programs, OST and ART can reduce HIV incidence by 30%, despite high endemicity (195). This supports the rationale behind the provision of a "spectrum of services" for PWID, which, alongside needle and syringe programs, includes OST and ART (3). UN agencies have developed indicators for these interventions in isolation (6), but syringe coverage will be maximised for individual PWID via a combination of services, tailored to their unique needs and risk-levels. Incremental improvements, via targeted and broad-reaching interventions, can optimise syringe coverage. My research identifies the targets for these interventions.

6.2.2 Reliability of the individual-level needle and syringe coverage measure

Formal work to validate the individual-level syringe coverage measure (in any form) is yet to be performed. However, the few studies that have explored syringe coverage at the individual level have reported several consistent results. The regression analyses in Papers One, Two and Six showed a relationship between the utilisation of fixed-site NSPs as the *usual* source of syringe acquisition and individual-level sufficient syringe coverage, replicating findings by Iversen et al. and Bryant et al. (37, 123).

Papers Four and Six describe an association between insufficient individual-level syringe coverage and syringe re-use. The re-use of one's own unsterile syringes, though not a risk factor for BBV transmission, carries other hazards (35, 36), such as increased risk of bacterial infection (14). The association between insufficient individual-level syringe coverage and syringe re-use has now been reported in five separate studies (including my work) (5, 37, 148). The strong effect on syringe coverage by increased injecting frequency supports a similar independent association, reported by Bryant et al., between insufficient individual-level syringe coverage and high-frequency injecting (123). Similarly repeated relationships between individual-level syringe coverage and OST have been demonstrated (37, 72).

The consistency of these results indicates the reliability of individual-level syringe coverage measurement. The replicated findings described above are logical extensions of both sufficient individual-level syringe coverage (e.g. the common use of fixed-site NSPs) and insufficient individual-level syringe coverage (e.g. syringe re-use), and have now been reproduced in multiple samples in various countries.

6.2.3 Refining and improving individual-level needle and syringe coverage measurement

The Bluthenthal et al. individual-level syringe coverage measure has been adapted, altered, and implemented in multiple ways since first proposed. Bluthenthal et al. used an extrapolation method to calculate individual-level syringe coverage (5), with the outcome – percentage of injecting episodes covered by sterile syringes – derived by multiplying the number of sterile syringes *retained* at the most recent instance of acquisition via a fixed-site NSP, by the total fixed-site NSP visits within the previous month. The method assumes the number of syringes acquired at each instance is stable. Several subsequent researchers adopted the Bluthenthal et al. method (37, 123, 148). McCormack et al. refined it by explicitly by enumerating each syringe coverage behaviour for the time frame considered, and importantly, syringe acquisition was not limited to fixed-site NSPs, as Bluthenthal et al. had done (146). By specifying the "total syringes acquired" as a parameter in their formula, the McCormack et al. measure can

account for the variety of sources PWID may acquire syringes from. My work has shown that PWID may acquire syringes from sources other than typical needle and syringe program outlets, such as fixed-site NSPs, sometimes as their main source of syringe acquisition. Limiting syringe acquisition to only those instances occurring via a fixed-site NSP, as Bluthenthal et al. did, the number of syringes acquired may result in an underestimate (123). Researchers using the Bluthenthal et al. method have responded to this limitation by specifying other possible sources of acquisition (37), whilst still relying on an extrapolated estimate of the total syringes acquired. Even so, a more explicit method of recording syringe acquisition (as McCormack et al. used), that accounts for the variety of potential acquisitive sources, should be more accurate than an estimate. I therefore recommend the McCormack et al. enumeration method for future syringe coverage work.

The optimal combination of parameters within the individual-level syringe coverage formula is yet to be determined. McCormack et al. tested, and based on their findings, recommended the inclusion of a syringe stockpiling parameter (146). In Paper Three, I provided evidence supporting the omission of the *instances of syringe acquisition* parameter (as used in the Bluthenthal et al. measure). In Paper Four, I tested the inclusion of a parameter for the use of multiple sterile syringes per injecting episode within the individual-level syringe coverage formula. Ultimately, this parameter was rejected on the grounds that it appeared to add little benefit to individual-level syringe coverage measurement, whilst increasing the potential for bias. The identification and testing of these parameters is part of the ongoing refinement of individual-level syringe coverage measurement, establishing the groundwork necessary for the measure's use as an internationally accepted program evaluation tool.

6.2.4 Individual-level needle and syringe coverage measurement as an international planning and monitoring tool

My research demonstrates that shortfalls in individual-level syringe coverage are often overlooked due to the aggregate nature of population-level measures. Without

individual-level measurement, these shortfalls go undetected and at-risk populations are neglected. The argument for implementing individual-level syringe coverage measurement internationally for programmatic planning and monitoring is therefore strong. Individual-level measurement could act as a complement to currently prescribed population-level measurements, broadening the understanding of harm reduction service delivery and performance, identifying areas of inefficiency and strength, and certain groups or contexts that require focus. Population-level measurement is a crucial element of program evaluation, not least because it is an easily-computed standardised methodology enabling the WHO and UNAIDS (7, 137) to set targets that can be accepted and understood by harm reduction practitioners and governments worldwide. However, the limitations of these measures are acknowledged (3, 56, 139). They include the necessity for highly uncertain and poorly-defined PWID population estimates (56). Also, they assume homogenised risk amongst PWID and the environments in which drug use occurs. Population-level measurements are useful for estimating service reach, but individual-level measurements can capture elements of the *quality* of this delivery. This vital knowledge about differences in syringe coverage and their causes can only be captured at the individual level. Used alongside population-level estimates, individual-level syringe coverage information can assist not only the ongoing monitoring of harm reduction programs, but also the planning of prospective services using evidence-based practice (3). Although the goal of 100% of PWID attaining at least 100% individual-level syringe coverage is aspirational, it is most likely not feasible given the barriers to coverage outlined above. Therefore, setting targets for insufficient individual-level syringe coverage (similar to targets for population-level syringe coverage) is probably unnecessary. Instead, using individual-level syringe coverage measurement as a tool for monitoring service delivery can indicate areas in need of focus and service expansion rather than the setting of overall targets.

Population-level measures are readily calculated from routinely collected service-level data applied to PWID population estimates. The main barrier to individual-level measurement is the need for primary data collection amongst samples large enough to generate meaningful results. The Myanmar research described in Paper Six generated a substantial dataset despite few resources and minimal staff burden. The study used a short-form quantitative questionnaire, delivered to participants (including informed

consent) in approximately 20 minutes. Research staff were workers from local harm reduction services, trained in research ethics and methodology in two days. Ultimately, 512 participants were recruited in three months, with results revealing important harm reduction information. The Australian Needle and Syringe Program Survey (ANSPS) follows a similar methodology. Conducted since 1995 by harm reduction staff, the survey recruits over 2,200 NSP-presenting participants nationwide in a two-week period every October (196). Recent iterations of the survey have included questions necessary to calculate individual-level syringe coverage, and the results published (37). This kind of data collection can be easily absorbed into existing service delivery and data recording activities with minimal impact on harm reduction staff or clientele. If primary-data collection is unfeasible, it may be appropriate to include the necessary coverage parameter questions in data collected routinely during point of service contact, similar to the data system in Queensland, Australia, previously described (193).

6.3 Recommendations for future research

6.3.1 Further refinement of individual-level needle and syringe coverage measurement

Unidentified behaviours that mediate individual-level syringe coverage may exist, and if so, their omission from individual-level syringe coverage measurement biases its accuracy. For example, due to free and liberal syringe dispensation in Australia, it is possible that some sterile syringes are discarded, stored and forgotten, or simply never used. Future researchers should attempt to identify these behaviours, possibly using qualitative methods, and explore the appropriateness of their inclusion within the individual-level syringe coverage formula. The methodology developed by McCormack et al. (146) and replicated in Paper Four is appropriate for this work. However, the introduction of bias through the inclusion of additional parameters must be weighed against a parameter's potential influence. For example, whilst 14% of the sample reported the use of multiple sterile syringes, the parameter did not improve the measurement of individual-level syringe coverage enough to warrant its inclusion.

A consistent time frame for individual-level syringe coverage calculation is yet to be determined. In Papers One, Two, Three and Six, data related to the two weeks prior to interview, whilst in Paper Four, data related to the month prior to interview. Again, the need for a long enough time frame to capture important behavioural data (e.g. some Australian PWID report acquiring, and stockpiling, syringes only once a month) needs to be reconciled with potential recall bias. Future researchers should attempt to identify the most appropriate time frame for syringe coverage calculation.

Finally, Bluthenthal et al. recommended formal reliability and validity testing of syringe acquisition and injecting frequency reporting (5). Such work would support the overall confidence in the individual-level syringe coverage measure and its accuracy.

6.3.2 Individual-level needle and syringe coverage measurement in diverse contexts

Just as PWID are a diverse population, so too are the local contexts in which drugs are injected. Across settings, certain drug types dominate (105, 197), harm reduction access may be widely available or heavily restricted (8, 59, 82, 83) and methods of drug administration and PWID population demographics vary markedly (167, 197). This variation leads to unique structural, environmental and individual influences on syringe coverage.

PWID living in regional Australia are an understudied sub-population. The research in this PhD was focused on urban-dwelling PWID. Differences exist in Australia between urban and regional PWID in both service access and availability of certain drug types (198, 199). Understanding the effects these differences have on syringe coverage is important. For example, higher levels of pharmaceutical opioid use has been reported amongst both injecting and non-injecting regional Australian populations compared to metropolitan counterparts (199, 200), though this variation was not associated with greater frequency of injecting amongst the regional PWID (199). More focussed research and monitoring is recommended to improve our understanding of PWID living in regional Australia, particularly in regional cities. Adequate sampling of regional PWID is difficult in consumer surveys such as the Illicit Drug Reporting System (201), though

routine NSP presentational data could include questions to monitor basic trends across regional Australia.

The geographically varying individual-level syringe coverage characteristics described in Paper Six are partly the result of a combination of a local public health issue, being the presence of shooting galleries, and an innovative response, being the collaboration being shooting gallery operators and harm reduction services. This exemplifies not only the utility of the individual-level syringe coverage measure in highlighting important variations in service utilisation, syringe coverage and risk, but the importance of individual-level syringe coverage measurement in diverse contexts. Numerous factors, many unique to particular locations, drive changes in syringe coverage, both within and between countries. For example, the higher individual-level syringe coverage experienced by the PWID frequenting the Myanmar shooting galleries in Paper Six is consistent with evidence about SIFs. SIF-using PWID, who perform all or most of their injecting episodes within the SIF, may have different syringe coverage levels than PWID who don't use SIFs. Individual-level syringe coverage measurement could reveal these differences. Bryant et al. previously measured individual-level syringe coverage amongst pharmacy-recruited PWID (123). Similar research could explore individual-level syringe coverage according to engagement with various services that come under the needle and syringe program umbrella (e.g. fixed-site NSP, outreach, pharmacy, SVM, secondary exchange) (5, 56), that is, those who use certain services exclusively, against those who acquire their syringes from different combinations of sources.

The Myanmar participants reported injecting a median of 27 times within the two weeks prior to interview, which translates to approximately 702 times per annum. Recent estimates of population-level syringe coverage in Myanmar are that 165 sterile syringes are dispensed per PWID per annum, a figure inadequate for the needs of the sample. Despite this, prevalences of insufficient individual-level syringe coverage were similar to those in Australian samples. It may be that Australian PWID with sufficient individual-level syringe coverage acquire syringes in vastly excessive quantities (thereby elevating population-level distribution and masking insufficient individual-level syringe coverage), or that those in the Myanmar sample are not representative of average PWID across the country, being particularly highly engaged with services and with higher than average syringe coverage (despite the insufficient individual-level

syringe coverage prevalence in the Yangon sites). Sampling bias is an issue that must be acknowledged in regards to both the Australian and Myanmar samples in my studies. The PWID in my samples may not be representative of other PWID with low service engagement, and therefore, potentially lower levels of individual-level syringe coverage. Epidemiological evidence suggests that without reaching particularly vulnerable PWID with low engagement, HIV prevention goals may not be achieved (3). Future syringe coverage research needs to broaden our understanding of the contexts of low syringe coverage, particularly with respect to PWID recruited from locations other than fixed-site NSPs.

6.4 Strengths and limitations

The research presented in this thesis had several strengths and limitations. A key strength in Papers One, Two and Three is the longitudinal nature of the analyses. The MIX cohort dataset, with many thousands of observations over nearly 10 years, includes data appropriate for individual-level syringe coverage calculation, providing an excellent opportunity to explore intra-individual variations in individual-level syringe coverage. Additionally, the cohort is based in Melbourne, Australia, a location with comprehensive harm reduction implementation and syringe coverage at the population level. Whilst this may limit the generalisability of findings to other locations, especially LMICs, the extensive reach and overall quantity of needle and syringe provision in Melbourne, with mostly unrestricted syringe dispensation via numerous complementary delivery modalities, reduces disparities in access between PWID, and it was in this service climate that the research presented in Papers One to Three was conducted.

Several limitations of my research must be considered. Calculation of individual-level syringe coverage is reliant on multiple self-reported parameters, which unavoidably admits weaknesses. First, the necessity for complete and valid parameter data to successfully measure individual-level syringe coverage increases the likelihood of missing individual-level syringe coverage outcome data as any missing data on any parameter means the outcome is void. In Papers One to Three, substantial minorities of individual-level syringe coverage observations were classified as missing due to invalid

parameter data. Second, the MIX survey was conceptualised prior to McCormack et al.'s findings about syringe stockpiling (146), meaning this variable was not initially included. On examination of the dataset, I observed many participants reporting no syringe acquisition in the two weeks prior to interview, but with injecting frequencies above what could be accounted for by the use of existing unsterile syringes (11% of Australian PWID report recent receptive syringe sharing) (32). This disparity was assumed to be the result (at least partially) of stockpiling, meaning the omission of stockpiling had very likely introduced bias. This bias was accounted for by limiting individual-level syringe coverage calculation to only those participants reporting injecting frequency *and* syringe acquisition, again reducing the number of individual-level syringe coverage outcome observations. In Papers Four and Six I was able to include the stockpiling parameter; however, the existence of other, unrecognised behaviours that mediate individual-level syringe coverage cannot be discounted. Third, recall bias is a consistent concern in survey research. In my studies participants had to try to recall the numbers of syringes acquired, distributed and stockpiled, and the number of injections performed in a specified time frame. There are bound to be inaccuracies in this recall – especially if the recall period is substantial – an issue compounded as the number of parameters increases. Together, these limitations mean the variations in individual-level syringe coverage between PWID, as determined by the individual-level syringe coverage measure, may be partly the result of measurement inaccuracies. These are unavoidable, and can only be reduced by the continued refining and strengthening of the individual-level syringe coverage measure.

Though the Australian setting of the research was a strength in many respects, it also posed limitations. Because Australia is a high-income country, with relatively progressive harm reduction policies (8, 82, 202), its population-level syringe coverage is amongst the highest in the world (8, 173). Many countries, both high-income and LMICs, cannot match Australia's level of harm reduction provision, due to competing health priorities and funding concerns (172), a point explored in detail in Paper Five. These barriers to adequate syringe coverage may be too great for most PWID to overcome, despite their best efforts. Due to the much lower population-level syringe coverage in Myanmar compared to Australia, I anticipated much lower individual-level syringe coverage amongst the Myanmar sample. Prevalence of insufficient individual-level syringe coverage between the samples, however, was comparable; suggesting

population-level syringe coverage deficiencies in Myanmar had little impact on syringe coverage at the individual-level. When stratified by recruitment site, insufficient individual-level syringe coverage in the sites without shooting galleries was much higher than those without, exemplifying the unusually positive effect of the shooting galleries on syringe coverage. Even so, prevalence of insufficient individual-level syringe coverage in sites without shooting galleries (14-40% across the three recruitment sites without shooting galleries) remained similar to the reported range of the Australian samples (both in my studies and others), and below the prevalence (56%) reported amongst PWID in Iran (another LMIC). It may be that our sample was composed of PWID particularly well-engaged with services, meaning individual-level syringe coverage could be even lower overall if sampling strategies were more representative. Greater effort needs to be made to recruit a greater diversity of PWID.

Finally, all research in this thesis was conducted in urban locations – a common limitation of PWID research worldwide (143). As is the case for many health services (203), harm reduction access is highest in urban centres (103). PWID living in regional or rural areas have relatively limited access to sterile injecting equipment (103). The findings from this research may therefore be inapplicable to many PWID internationally, and especially PWID outside metropolitan settings.

6.5 Conclusion

Syringe coverage is a concept crucial to the evaluation of the effectiveness of any public health intervention. Its calculation is a means of assessing the likely impact of programs upon target populations. However, the ways in which we conceptualise and measure syringe coverage have direct bearing on the resulting estimates. Whilst population-level syringe coverage is vital to ongoing harm reduction work, its limitations are recognised in that it homogenises risk for PWID and the environments in which IDU occurs. Syringe coverage measurement at the individual level can provide essential complementary information, such as identifying PWID sub-groups at risk of insufficient individual-level syringe coverage. However, the development and utilisation of individual-level syringe coverage measurement is a relatively recent advance, meaning numerous knowledge gaps exist. In the research described in this thesis, I aimed to address these gaps. I

demonstrated how individual-level syringe coverage varies over time, exemplifying the person-level barriers to achieving adequate individual-level syringe coverage, and recommend numerous ways of reducing some of these barriers. I explored ways of improving individual-level syringe coverage measurement, making a substantial contribution towards the eventual creation of an accepted and robust measure for use as an international planning, monitoring and evaluation tool. Finally, I measured individual-level syringe coverage in new and diverse contexts, producing new insights regarding innovative service provision, such as the collaborative relationships between shooting galleries and harm reduction services. This work broadens our understanding of syringe coverage and its barriers, and provides recommendations for the improvement of harm reduction service delivery and hence the reduction of injecting risk behaviours and BBV transmission.

References:

1. Jolley E, Rhodes T, Platt L, Hope V, Latypov A, Donoghoe M, et al. HIV among people who inject drugs in Central and Eastern Europe and Central Asia: a systematic review with implications for policy. BMJ Open. 2012;2(5).
2. Davis SM, Daily S, Kristjansson AL, Kelley GA, Zullig K, Baus A, et al. Needle exchange programs for the prevention of hepatitis C virus infection in people who inject drugs: a systematic review with meta-analysis. Harm Reduction Journal. 2017;14(1):25.
3. Sharma M, Burrows D, Bluthenthal R. Coverage of HIV prevention programmes for injection drug users: confusions, aspirations, definitions and ways forward. International Journal of Drug Policy. 2007;18(2):92-8.
4. Scott N, Caulkins JP, Ritter A, Dietze P. How patterns of injecting drug use evolve in a cohort of people who inject drugs. Trends and Issues in Crime and Criminal Justice. 2015;502.
5. Bluthenthal RN, Anderson R, Flynn NM, Kral AH. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. Drug and Alcohol Dependence. 2007;89(2-3):214-22.
6. WHO. Technical guide for countries to set targets for universal HIV services for injecting drug users. Geneva, Switzerland: World Health Organisation, 2012.
7. WHO. Global health sector strategy on viral hepatitis 2016-2021. Geneva, Switzerland: 2016.
8. Larney S, Peacock A, Leung J, Colledge S, Hickman M, Vickerman P, et al. Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. The Lancet Global Health. 2017.
9. Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. The Lancet Global Health. 2017;5(12):e1192-e207.
10. Mathers BM, Degenhardt L, Phillips B, Wiessing L, Hickman M, Strathdee SA, et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet. 2008;372(9651):1733-45.

11. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepaitits C in people who inject drugs: results of systematic reviews. Lancet. 2011;378:571-83.
12. Aspinall EJ, Nambiar D, Goldberg DJ, Hickman M, Weir A, Van Velzen E, et al. Are needle and syringe programmes associated with a reduction in HIV transmission among people who inject drugs: a systematic review and meta-analysis. International Journal of Epidemiology. 2014;43(1):235-48.
13. MacArthur GJ, van Velzen E, Palmateer N, Kimber J, Pharris A, Hope V, et al. Interventions to prevent HIV and Hepatitis C in people who inject drugs: a review of reviews to assess evidence of effectiveness. International Journal of Drug Policy. 2014;25(1):34-52.
14. Brett MM, Hood J, Brazier JS, Duerden BI, HahnÉ SJM. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. Epidemiology and Infection. 2005;133(4):575-82.
15. Koester S. Commentary on Harris & Rhodes (2012): Discouraging syringe re-use by addressing drug injectors' everyday suffering. Addiction. 2012;107:1097-8.
16. Dietze P, Jolley D, Fry C, Bammer G. Transient changes in behaviour lead to heroin overdose: results from a case-crossover study of non-fatal overdose. Addiction. 2005;100(5):636-42.
17. Bohnert AS, Roeder KM, Ilgen MA. Suicide attempts and overdoses among adults entering addictions treatment: comparing correlates in a U.S. National Study. Drug and Alcohol Dependence. 2011;119(1-2):106-12.
18. Mathers BM, Degenhardt L, Bucello C, Lemon J, Wiessing L, Hickman M. Mortality among people who inject drugs: a systematic review and meta-analysis. Bulletin of the World Health Organisation. 2013;91(2):102-23.
19. Pieper B, Kirsner RS, Templin TN. Injection drug use: an understudied cause of venous disease. Archives of Dermatology. 2007;143(10):1305-9.
20. Richardson L, Wood E, Li K, Kerr T. Factors associated with employment among a cohort of injection drug users. Drug and Alcohol Review. 2010;29(3):293-300.
21. Topp L, Iversen J, Baldry E, Maher L. Housing instability among people who inject drugs: results from the Australian needle and syringe program survey. Journal of Urban Health. 2013;90(4):699-716.

22. Mills KL, Lynskey M, Teesson M, Ross J, Darke S. Post-traumatic stress disorder among people with heroin dependence in the Australian treatment outcome study (ATOS): prevalence and correlates. Drug and Alcohol Dependence. 2005;77(3):243-9.
23. Dolan K, Moazen B, Noori A, Rahimzadeh S, Farzadfar F, Hariga F. People who inject drugs in prison: HIV prevalence, transmission and prevention. International Journal of Drug Policy. 2015;26(Supplement 1):S12-S5.
24. Mathers BM, Degenhardt L, Hammad A, Wiessing L, Hickman M, Mattick RP, et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet. 2010;365:1014-28.
25. Dewing S, Pluddemann A, Myers B, Parry C. Review of injection drug use in six African countries: Egypt, Kenya, Mauritius, Nigeria, South Africa and Tanzania. Drugs: Education, Prevention and Policy. 2006;13(2):121-37.
26. Cornberg M, Razavi HA, Alberti A, Bernasconi E, Buti M, Cooper C, et al. A systematic review of hepatitis C virus epidemiology in Europe, Canada and Israel. Liver international : official journal of the International Association for the Study of the Liver. 2011;31 Suppl 2:30-60.
27. Hellard M, Rolls DA, Sacks-Davis R, Robins G, Pattison P, Higgs P, et al. The impact of injecting networks on hepatitis C transmission and treatment in people who inject drugs. Hepatology. 2014;60(6):1861-70.
28. Kerr T, Small W, Buchner C, Zhang R, Li K, Montaner J, et al. Syringe sharing and HIV incidence among injection drug users and increased access to sterile syringes. American Journal of Public Health. 2010 Aug;100(8):1449-53.
29. Shaw SY, Shah L, Jolly AM, Wylie JL. Determinants of injection drug user (IDU) syringe sharing: the relationship between availability of syringes and risk network member characteristics in Winnipeg, Canada. Addiction. 2007;102(10):1626-35.
30. Vickerman P, Hickman M, Judd A. Modelling the impact on Hepatitis C transmission of reducing syringe sharing: London case study. International Journal of Epidemiology. 2007;36(2):396-405.
31. Nguyen TQ, Weir BW, Des Jarlais DC, Pinkerton SD, Holtgrave DR. Syringe exchange in the United States: a national level economic evaluation of hypothetical increases in investment. AIDS and Behaviour. 2014;18(11):2144-55.
32. Stafford J, Burns L. Illicit Drug Reporting System (IDRS) National Report 2015. Sydney, Australia: National Drug and Alcohol Research Centre (NDARC), 2016.

33. Pouget ER, Deren S, Fuller C, Blaney S, McMahon JM, Kang S, et al. Receptive syringe sharing among injection drug suers in Harlem and the Bronx during New York state expanded syringe access demonstration program. Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology. 2005;39(4):471-7.
34. Marshall BD, Shoveller JA, Wood E, Patterson TL, Kerr T. Difficulty accessing syringes mediates the relationship between methamphetamine use and syringe sharing among young injection drug users. AIDS and Behaviour. 2011 Oct;15(7):1546-53.
35. Dahlman D, Hakansson A, Bjorkman P, Blome MA, Kral AH. Correlates of Skin and Soft Tissue Infections in Injection Drug Users in a Syringe-Exchange Program in Malmo, Sweden. Substance Use and Misuse. 2015;50(12):1529-35.
36. Harris M, Rhodes T. Venous access and care: harnessing pragmatics in harm reduction for people who inject drugs. Addiction. 2012 Jun;107(6):1090-6.
37. Iversen J, Topp L, Wand H, Maher L. Individual-level syringe coverage among Needle and Syringe Program attendees in Australia. Drug and Alcohol Dependendence. 2012 ;122(3):195-200.
38. Rhodes T. The 'risk environment': a framework for understanding and reducing drug-related harm. International Journal of Drug Policy. 2002;13(2):85-94.
39. Strathdee SA, Hallett TB, Bobrova N, Rhodes T, Booth RE, Abdool R, et al. HIV and risk environment for injecting drug users: the past, present, and future. Lancet. 2010;376:268-84.
40. Ciccarone D. Heroin in brown, black and white: structural factors and medical consequences in the US heroin market. International Journal of Drug Policy. 2009;20(3):277-82.
41. Binswanger IA, Stern MF, Deyo RA, Heagerty PJ, Cheadle A, Elmore JG, et al. Release from prison - a high risk of death for former inmates. New England Journal Medicine. 2007;356:157-65.
42. Farrell M, Marsden J. Acute risk of drug-related death among newly released prisoners in England and Wales. Addiction. 2008;103(2):251-5.
43. Eckhardt B, Winkelstein ER, Shu MA, Carden MR, McKnight C, Des Jarlais D, et al. Risk factors for hepatitis C seropositivity among young people who inject drugs in New York City: Implications for prevention. PLoS One. 2017;12(5).

44. Stoltz J, Wood E, Small W, Li K, Tyndall M, Montaner J, et al. Changes in injecting practices assoicated with the use of a medically supervised safer injection facility. Journal of Public Health. 2007;29(1):35-9.
45. Wodak A, McLeod L. The role of harm reduction in controlling HIV among injecting drug users. AIDS. 2008;22 (supp 2):S81-S92.
46. Wodak A, Cooney A. Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence. Substance Use and Misuse. 2006;41(6-7):777-813.
47. Aceijas C, Hickman M, Donoghoe MC, Burrows D, Stuikyte R. Access and coverage of needle and syringe programmes (NSP) in Central and Eastern Europe and Central Asia. Addiction. 2007;102(8):1244-50.
48. Jones L, Pickering L, Sumnall H, McVeigh J, Bellis MA. Optimal provision of needle and syringe programmes for injecting drug users: A systematic review. International journal of Drug Policy. 2010;21(5):335-42.
49. Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy. Clinical Infectious Diseases. 2013 Aug;57 Suppl 2:S39-45.
50. Vickerman P, Martin N, Turner K, Hickman M. Can needle and syringe programmes and opiate substitution therapy achieve substantial reductions in hepatitis C virus prevalence? Model projections for different epidemic settings. Addiction. 2012 Nov;107(11):1984-95.
51. Gowing L, Ferrell M, Bornemann R, Sullivan L, Ali R. Substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Systematic Review. 2008;2.
52. Fisher DG, Fenaughty AM, Cagle HH, Wells RS. Needle exchange and injection drug use frequency: a randomized clinical trial. Journal of Acquired Immune Deficiency Syndrome. 2003;33:199-205.
53. Dolan K, MacDonald M, Silins E, Topp L. Needle and syringe programs: A review of the evidence. Canberra, Australia: Australian Government Department of Health and Ageing, 2005.

54. Peak A, Rana S, Maharjan SH, Jolley D, Crofts N. Declining risk for HIV among inject drug users in Kathmandu, Nepal: the impact of a harm reduction programme. AIDS. 1995;9:1067-70.
55. Burrows D. Advocacy and coverage of needle exchange programs: results of a comparative study of harm reduction programs in Brazil, Bangladesh, Belarus, Ukraine, Russian Federation and China. Cadernos Saude Publica. 2006;22(4):871-9.
56. Donoghoe MC, Verster A, Pervilhac C, Williams P. Setting targets for universal access to HIV prevention, treatment and care for injecting drug users (IDUs): towards consensus and improved guidance. International Journal of Drug Policy. 2008;19 Suppl 1:S5-14.
57. Broadhead RS, van Hulst Y, Heckathron DD. The impact of a needle exchange's closure. Public Health Reports. 1999;114(5):439-47.
58. Khan AA, Khan A. Performance and coverage of HIV interventions for injection drug users: Insights from triangulation of programme, field and surveillance data from Pakistan. International Journal of Drug Policy. 2011;22(3):219-25.
59. Bluthenthal RN, Ridgeway G, Schell T, Anderson R, Flynn NM, Kral AH. Examination of the association between syringe exchange program (SEP) dispensation policy and SEP client-level syringe coverage among injection drug users. Addiction. 2007;102(4):638-46.
60. Islam M, Wodak A, Conigrave KM. The effectiveness and safety of syringe vending machines as a component of needle syringe programmes in community settings. International Journal of Drug Policy. 2008;19(6):436-41.
61. McDonald D. The evaluation of a trial of syringe vending machines in Canberra, Australia. International Journal of Drug Policy. 2009;20(4):336-9.
62. Islam MM, Conigrave KM. Assessing the role of syringe dispensing machines and mobile van outlets in reaching hard-to-reach and high-risk groups of injecting drug users (IDUs): a review. Harm Reduction Journal. 2007;4(14).
63. Hayashi K, Wood E, Wiebe L, Qi J, Kerr T. An external evaluation of a peer-run outreach-based syringe exchange in Vancouver, Canada. International Journal of Drug Policy. 2010;21(5):418-21.
64. Sawangjit R, Khan TM, Chaiyakunapruk N. Effectiveness of pharmacy-based needle/syringe exchange programme for people who inject drugs: a systematic review and meta-analysis. Addiction. 2017;112(2):236-47.

65. Sarang A, Rhodes T, Platt L. Access to syringes in three Russian cities: implications for syringe distribution and coverage. International Journal of Drug Policy. 2008;19 Suppl 1:S25-36.
66. Iversen J, Wand H, Topp L, Kaldor J, Maher L. Extremely low and sustained HIV incidence among people who inject drugs in a setting of harm reduction. AIDS. 2014;28:275-83.
67. MacDonald M, Law M, Kaldor J, Hales J, Dore G. Effectiveness of needle and syringe programmes for preventing HIV transmission. International Journal of Drug Policy. 2003;14(5-6):353-7.
68. Kral AH, Bluthenthal RN. What is it about needle and syringe programmes that make them effective for preventing HIV transmission? International Journal of Drug Policy. 2003;14(5-6):361-3.
69. Falster K, Kaldor J, Maher L. HCV acquisition among injecting drug users: A cohort analysis of a national repeated cross sectional survey of needle and syringe program attendees in Australia 1995-2004. Journal of Urban Health. 2009;86(1):106-18.
70. Bruggmann P, Grebely J. Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. International Journal of Drug Policy. 2015;26 Suppl 1:S22-6.
71. Palmateer NE, Taylor A, Goldberg DJ, Munro A, Aitken C, Shepherd SJ, et al. Rapid decline in HCV incidence among people who inject drugs associated with national scale-up in coverage of a combination of harm reduction interventions. PLoS One. 2014;9(8):e104515.
72. Turner KM, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011;106(11):1978-88.
73. Palmateer N, Kimber J, Hickman M, Hutchinson S, Rhodes T, Goldberg D. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews. Addiction. 2010 May;105(5):844-59.

74. Arnaud S, Jeannin A, Dubois-Arber F. Estimating national-level syringe availability to injecting drug users and injection coverage: Switzerland, 1996-2006. International Journal of Drug Policy. 2011 May;22(3):226-32.
75. Brener L, Spooner C, Treloar C. Preventing transitions to injecting amongst young people: what is the role of Needle and Syringe Programmes? International Journal of Drug Policy. 2010;21(3):160-4.
76. Day CA, Topp L. Commentary on Turner et al. (2011): Significant global scale-up of harm reduction interventions and pragmatic research approaches needed to prevent hepatitis C transmission. Addiction. 2011;106:1989-90.
77. Van Den Berg C, Smit C, Van Brussel G, Coutinho R, Prins M, Amsterdam C. Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and hepatitis C virus: evidence from the Amsterdam Cohort Studies among drug users. Addiction. 2007 Sep;102(9):1454-62.
78. Cooper H, Des Jarlais D, Ross Z, Tempalski B, Bossak BH, Friedman SR. Spatial access to sterile syringes and the odds of injecting with an unsterile syringe among injectors: a longitudinal multilevel study. Journal of Urban Health. 2012;89(4):678-96.
79. Heimer R. Community coverage and HIV prevention: assessing metrics for estimating HIV incidence through syringe exchange. International Journal of Drug Policy. 2008 Apr;19 Suppl 1:S65-73.
80. Kaplan EH, Heimer R. A circulation theory of needle exchange. AIDS. 1994;8:567-74.
81. Zamani S, Vazirian M, Nassirimanesh B, Razzaghi EM, Ono-Kihara M, Mortazavi Ravari S, et al. Needle and syringe sharing practices among injecting drug users in Tehran: a comparison of two neighborhoods, one with and one without a needle and syringe program. AIDS and Behaviour. 2010;14(4):885-90.
82. HRI. Global State of Harm Reduction. London, United Kingdom: Harm Reduction International, 2016.
83. Degenhardt L, Mathers BM, Wirtz AL, Wolfe D, Kamarulzaman A, Carrieri MP, et al. What has been achieved in HIV prevention, treatment and care for people who inject drugs, 2010-2012? A review of the six highest burden countries. International Journal of Drug Policy. 2014;25(1):53-60.

84. Sharma M, Oppenheimer E, Saidel T, Loo V, Garg R. A situation update on HIV epidemics among people who inject drugs and national responses in South-East Asia Region. AIDS. 2009;23:1405-13.
85. Hagan H, Des Jarlais D. HIV and HCV infection among injecting drug users. The Mount Sinai Journal of Medicine. 2000;67(5&6):423-8.
86. Sarkar S, Das N, Panda S, Naik TN, Sarkar K, Singh BC, et al. Rapid spread of HIV among injecting drug users in north-eastern states of India. Bulletin on Narcotics. 1993;45(1):91-105.
87. Garten RJ, Lai S, Zhang J, Liu W, Chen J, Vlahov D, et al. Rapid transmission of hepatitis C virus among young injecting heroin users in Southern China. International Journal of Epidemiology. 2004;33:182-8.
88. Neaigus A, Zhao M, Gyarmathy A, Cisek L, Friedman SR, Baxter RC. Greater drug injecting risk for HIV HBV and HCV infection in a city where syringe exchange and pharmacy distribution are illegal. Journal of Urban Health. 2008;85(3):309-22.
89. Carrillo JE, Carrillo VA, Perez HR, Salas-Lopez D, Natale-Pereira A. Defining and targeting health care access barriers. Journal of Health Care for the Poor and Underserved. 2011;22(2):562-75.
90. Small D, Glickman A, Rigter G, Walter T. The Washington Needle Depot: fitting healthcare to injection drug users rather than injection drug users to healthcare: moving from a syringe exchange to syringe distribution model. Harm Reduction Journal. 2010;7:1.
91. Sherman SG, Patel SA, Ramachandran DV, Galai N, Chaulk P, Serio-Chapman C, et al. Consequences of a restrictive syringe exchange policy on utilisation patterns of a syringe exchange program in Baltimore, Maryland: Implications for HIV risk. Drug and Alcohol Review. 2015 Nov;34(6):637-44.
92. UNODC. Implementing comprehensive HIV and HCV programmes with people who inject drugs: practical guidance for collaborative interventions. Vienna, Austria: 2017.
93. Scott N, Caulkins JP, Ritter A, Dietze P. Understanding and describing Australia illicit drug markets: Drug price variations and associated changes in a cohort of people who inject drugs. Canberra, Australia: National Drug Law Enforcement Research Fund, 2015.

94. Treloar C, Cao W. Barriers to use of Needle and Syringe Programmes in a high drug use area of Sydney, New South Wales. International Journal of Drug Policy. 2005;16(5):308-15.
95. Wood E, Tyndall MW, Spittal P, Li K, Hogg RS, O'Shaughnessy MV, et al. Needle exchange and difficulty with needle access during an ongoing HIV epidemic. International Journal of Drug Policy. 2002;13:95-102.
96. Wright NMJ, Tompkins CNE, Jones L. Exporing risk perception and behaviour of homeless injecting drug users diagnosed with hepatitis C. Health and Social Care in the Community. 2004;13(1):75-83.
97. Dolan K, Teutsch S, Scheuer N, Levy M, Rawlinson W, Kaldor J, et al. Incidence and risk for acute hepatitis C infection during imprisonment in Australia. European Journal of Epidemiology. 2010;25(2):143-8.
98. Treloar C, McCredie L, Lloyd AR, investigators HI-p. Acquiring hepatitis C in prison: the social organisation of injecting risk. Harm Reduction Journal. 2015;12:10.
99. Des Jarlais D, Feelemyer JP, Modi SN, Abdul-Quader A, Hagan H. High coverage needle/syringe programs for people who inject drugs in low and middle income countries: a systematic review. BMC Public Health. 2013;13(53).
100. Wilton RD. The constitution of difference: space and psyche in landscapes of exclusion. Geoforum. 1998;29(2):173-85.
101. Shaw S, Singer M. Communities in conflict: the struggle for AIDS prevention. Practicing Anthropology. 2003;25(3):32-6.
102. Tempalski B, Friedman R, Keem M, Cooper H, Friedman SR. NIMBY localism and national inequitable exclusion alliances: the case of syringe exchange programs in the United States. Geoforum. 2007;38(1250-1263).
103. Iversen J, Linsen S, Kwon JA, Maher L. Needle and syringe program national minimum data collection: national data report 2016. Sydney, Australia: Kirby Institute, UNSW, 2017.
104. Klein A. Sticking points: Barriers to access to needle and syringe programs in Canada. Toronto, Canada: Canadian HIV/AIDS Legal Network, 2007.
105. Shannon K, Rusch M, Shoveller J, Alexson D, Gibson K, Tyndall MW, et al. Mapping violence and policing as an environmental-structural barrier to health service and syringe availability among substance-using women in street-level sex work. International Journal of Drug Policy. 2008;19(2):140-7.

106. Aitken C, Moore D, Higgs P, Kelsall J, Kerger M. The impact of a police crackdown on a street drug scene: evidence from the street. International Journal of Drug Policy. 2002;13(3):193-202.
107. Wood E, Kerr T, Small W, Jones J, Schechter MT, Tyndall MW. The impact of police presence on access to needle exchange programs. Journal of Acquired Immune Deficiency Syndrome. 2003;34(1):116-7.
108. Rhodes T, Mikhailova L, Sarang A, Lowndes CM, Rylkov A, Khutorskoy M, et al. Situational factors influencing drug injecting, risk reduction and syringe exchange in Togliatti City, Russian Federation: a qualitative study of micro risk environment. Social Science and Medicine. 2003;57(1):39-54.
109. Cooper HLF, Des Jarlais DC, Ross Z, Tempalski B, Bossak B, Friedman SR. Spatial access to syringe exchange programs and pharmacies selling over-the-counter syringes as predictors of drug injectors' use of sterile syringes. Research and Practice. 2011;101(6):1118-25.
110. Guagliardo MF. Spatial accessibility of primary care: concepts, methods and challenges. International Journal of Health Geographics. 2004;3(3).
111. Arcury TA, Gesler WM, Preisser JS, Sherman J, Spencer J, Perin J. The effects of geography and spatial behavior on health care utilization among the residents of a rural region. Health Servercies Resesearch. 2005;40(1):135-56.
112. Day CA, Conroy E, Lowe J, Page J, Dolan K. Patterns of drug use and associated harm among rural injecting drug users: comparisons with metropolitan injecting drug users. Australian Journal of Rural Health. 2006;14:120-5.
113. McMutcheon JM, Morrison MA. Injecting on the Island a qualitative exploration of the service needs or PWID in Prince Edward Island Canada. Harm Reduction Journal. 2014;11(10).
114. Gossop M, Griffiths P, Powis B, Strang J. Severity of dependence and route of administration of heroin, cocaine and amphetamines. British Journal of Addiction. 1992;87(11):1527-36.
115. Nutt D, King LA, Saulsbury W, Blakemore C. Development of a rational scale to assess the harm of drugs of potential misuse. Lancet. 2007;369(9566):1047-53.
116. Gahr M, Freudenmann RW, Hiemke C, Gunst IM, Connemann BJ, Schonfeldt-Lecuona C. "Krokodil" - Revival of an old drug with new problems. Substance Use and Misuse. 2012;47(7):861-3.

117. Tyndall MW, Currie S, Spittal P, Li K, Wood E, O'Shaughnessy MV, et al. Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic. AIDS. 2003;17(6):887-93.
118. Horyniak D, Stoove M, Degenhardt L, Aitken C, Kerr T, Dietze P. How do drug market changes affect characteristics of injecting initiation and subsequent patterns of drug use? Findings from a cohort of regular heroin and methamphetamine injectors in Melbourne, Australia. International Journal of Drug Policy. 2015 Jan;26(1):43-50.
119. Dietze P, Fitzgerald J. Interpreting changes in heroin supply in Melbourne: droughts, gluts or cycles? Drug and Alcohol Review. 2002;21:295-303.
120. Scott N, Caulkins JP, Ritter A, Quinn C, Dietze P. High-frequency drug purity and price series as tools for explaining drug trends and harms in Victoria, Australia. Addiction. 2014;110:120-8.
121. Tyndall M, Currie S, Spittal P, Li K, Wood E, O'Shaughnessy MV, et al. Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic. AIDS. 2003;17(6):887-93.
122. Chaisson RE, Bacchetti P, Osmond D, Brodie B, Sande MA, Moss AR. Cocaine use and HIV infection in intravenous drug users in San Francisco. Journal of the American Medical Association. 1989;261(4):561-5.
123. Bryant J, Paquette D, Wilson H. Syringe coverage in an Australian setting: does a high level of syringe coverage moderate syringe sharing behaviour? AIDS and Behaviour. 2012;16(5):1156-63.
124. Larney S, Kopinski H, Beckwith CG, Zaller N, Des Jarlais D, Hagan H, et al. The incidence and prevalence of hepatitis C in prisons and other clsoed settings: Results of a systematic review and meta-analysis. Hepatology. 2013;58(4):1215-24.
125. Rhodes T, Singer M, Bourgois P, Friedman SR, Strathdee SA. The social structural production of HIV risk among injecting drug users. Social Science and Medicine. 2005;61(5):1026-44.
126. Horyniak D, Higgs P, Jenkinson R, Degenhardt L, Stoove M, Kerr T, et al. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. Harm Reduction Journal. 2013;10(11).
127. Swe. LA, Nyo KK, Rashid AK. Risk behaviours among HIV positive injecting drug users in Myanmar: a case control study. Harm Reduction Journal. 2010;7(12).

128. Martinez AN, Bluthenthal R, Flynn NM, Anderson RL, Kral AH. HIV risks and seroprevalence among Mexican American injecting drug users in California. AIDS and Behaviour. 2011;15:95-102.
129. Peach E, Cogger S, Byron K, Francis P, O'Keefe D, Higgs P, et al. Blood-borne virus transmission in an urban, culturally diverse neighbourhood: results from a cross-sectional bio-behavioural survey using innovative outreach methods in a hard-to-reach population. Sexual health. 2017; Epub ahead of print
130. Newland J, Newman C, Treloar C. "We get by with a little help from our friends": Small-scale informal and large-scale formal peer distribution networks of sterile injecting equipment in Australia. International Journal of Drug Policy. 2016;34:65-71.
131. Ayon S, Ndimbii J, Jeneby F, Abdulrahman T, Mlewa O, Wang B, et al. Barriers and facilitators of access to HIV, harm reduction and sexual and reproductive health services by women who inject drugs: role of community-based outreach and drop-in centers. AIDS Care. 2017;Epub ahead of print.
132. Krug A, Hildebrand M, Sun N. "We don't need services. We have no problems": exploring the experiences of young people who inject drugs in accessing harm reduction services. Journal of the International AIDS Society. 2015;18(Suppl 1):71-7.
133. Rich JD, Strong L, Towe CW, McKenzie M. Obstacles to needle exchange participation in Rhode Island. Journal of Acquired Immune Deficiency Syndrome. 1999;21(5):396-400.
134. Fuller C, Galea S, Blaney S, Ompad D, Deren S, Des Jarlais D, et al. Explaining the relationship between race/ethnicity and pharmacy purchased syrignes among injection drug users in New York City. Ethnicity and Disease. 2004;14:589-96.
135. Aitken C. New Zealand needle and syringe exchange programme review: final report. Centre for Harm Reduction, 2002.
136. Nambiar D, Agius PA, Stoove M, Hickman M, Dietze P. Cessation of injecting drug use: The effects of health service utilisation, drug use and demographic factors. Drug and Alcohol Dependence. 2015;154:208-13.
137. WHO. Guidance on prevention of viral hepatitis B and C among people who inject drugs. Geneva, Switzerland: 2012.
138. Des Jarlais D, Burrows D, Friedman SR. Experts' estimates of coverage needed for interventions to control HIV transmission among injecting drug users. Open Society Institute, 2007.

139. Burrows D. Rethinking coverage of needle exchange programs. Substance Use and Misuse. 2006;41(6-7):1045-8.
140. Vickerman P, Hickman M, Rhodes T, Watts C. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. Epidemiology and Social Science. 2006;42(3):355-61.
141. WHO. Combating hepatitis B and C to reach elimination by 2030: advocacy brief. Geneva, Switzerland: World Health Organisation, 2016.
142. Tempalski B, Cooper HL, Friedman SR, Des Jarlais DC, Brady J, Gostnell K. Correlates of syringe coverage for heroin injection in 35 large metropolitan areas in the US in which heroin is the dominant injected drug. International Journal of Drug Policy. 2008 Apr;19 Suppl 1:S47-58.
143. Mathers BM, Cook C, Degenhardt L. Improving the data to strengthen the global response to HIV among people who inject drugs. International Journal of Drug Policy. 2010;21:100-2.
144. Dolan K, Dillon P, Silins E. Needle and syringe programs: Your questions answered. Canberra, Australia: Australian Government Department of Health and Ageing, 2005.
145. Lancaster K, Seear K, Treloar C. Laws prohibiting peer distribution of injecting equipment in Australia: A critical analysis of their effects. International Journal of Drug Policy. 2015;26(12):1198-206.
146. McCormack AR, Aitken CK, Burns LA, Cogger S, Dietze PM. Syringe stockpiling by persons who inject drugs: an evaluation of current measures for needle and syringe program coverage. American Journal of Epidemiology. 2016;183(9):852-60.
147. Heller DI, Paone D, Siegler A, Karpati A. The syringe gap: an assessment of sterile syringe need and acquisition among syringe exchange program participants in New York City. Harm Reduction Journal. 2009;6:1.
148. Noroozi M, Mirzazadeh A, Noroozi A, Mehrabi Y, Hajebi A, Zamani S, et al. Client level coverage of needle and syringe program and high risk injection behaviours: a case study of people who inject drugs in Kermanshah, Iran. Addiction Health. 2015;7(3-4):164-73.
149. Noroozi M, Noroozi A, Mirzazadeh A, Hajebi A, Mehrabi Y, Hashemi SS, et al. Impact of Needle and Syringe Program Coverage on HIV Incidence in People Who Inject Drugs. International Journal of High Risk Behaviors and Addiction. 2016;6(1).

150. Lawrinson P, Ali R, Buavirat A, Chiamwongpaet S, Dvoryak S, Habrat B, et al. Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. Addiction. 2008;103(9):1484-92.
151. Heimer R, Khoshnood K, Bigg D, Guydish J, Junge B. Syringe use and reuse: effects of syringe exchange programs in four cities. Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology. 1998;18(Supp 1):S37-S44.
152. Kwon JA, Iversen J, Maher L, Law MG, Wilson DP. The impact of needle and syringe programs on HIV and HCV transmissions in injecting drug users in Australia: A model based analysis. Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology. 2009;51(4):462-9.
153. MacDonald M, Wodak A, Dolan K, Van Beek I, Cunningham PH, Kaldor J. Hepatitis C virus antibody prevalence among injecting drug users at selected needle and syringe programs in Australia, 1995-1997. Medical Journal of Australia. 2000;172:57-61.
154. Department of Health and Ageing. Return on investment 2: Evaluating the cost-effectiveness of needle and syringe programs in Australia. Darlinghurst, Australia: 2009.
155. Department of Health and Ageing. Return on investment in needle and syringe programs in Australia: summary report. 2002.
156. Larney S, Hickman M, Guy R, Grebely J, Dore GJ, Gray RT, et al. Estimating the number of people who inject drugs in Australia. BMC Public Health. 2017;17(1):757.
157. Kwon JA, Anderson J, Kerr CC, Thein HH, Zhang L, Iversen J, et al. Estimating the cost-effectiveness of needle-syringe programs in Australia. AIDS. 2012;26(17):2201-10.
158. Eckhardt B, Winkelstein ER, Shu MA, Carden MR, McKnight C, Des Jarlais DC, et al. Risk factors for hepatitis C seropositivity among young people who inject drugs in New York City: Implications for prevention. PLoS One. 2017;12(5):e0177341.
159. Ward J, Topp L, Iversen J, Wand H, Akre S, Kaldor J, et al. Higher HCV antibody prevalence among Indigenous clients of needle and syringe programs. Australian and New Zealand Journal of Public Health. 2011;35(5):421-6.
160. Nokhodian Z, Meshkati M, Adibi P, Ataei B, Kassaian N, Yaran M, et al. Hepatitis C among intravenous drug users in Isfahan, Iran: a study of seroprevalence and risk factors. International Journal of Preventative Medicine. 2012;3(Suppl1):S131-S8.
161. Burns L, Randall D, Hall W, Law M, Butler T, Bell J, et al. Opioid agonist pharmacotherapy in New South Wales from 1985 to 2006: patient characteristics and patterns and predictors of treatment retention. Addiction. 2009;104(1363-1372).

162. Stoops W, Rush C. Agonist replacement for stimulant dependence: a review of clincial research. Current Pharmceutical Design. 2013;19(40):7026-35.
163. Rose M, Grant J. Pharmacotherapy for methamphetamine dependence: a review of the pathophysiology of methamphetamine addiction and the theoretical basis and efficacy of pharmacotherapeutic interventions. Annals of Clinical Psychiatry. 2011;20(3):145-55.
164. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982;143(1):29-36.
165. Horyniak D, Armstrong S, Higgs P, Wain D, Aitken C. Poor man's smack: a qualitative study of buprenorphine injecting in Melbourne, Australia. Contemporary Drug Problems. 2007;34(3):525-48.
166. Jenkinson RA, Clark NC, Fry CL, Dobbin M. Buprenorphine diversion and injection in Melbourne, Australia: an emerging issue? Addiction. 2005;100(2):197-205.
167. Saw. YM, Yasuoka J, Saw. TN, Poudel KC, Tun. S, Jimba M. What are the factors associated with HIV testing among male injecting and non-injecting drug users in Lashio, Myanmar: a cross-sectional study. BMJ Open. 2013;3:1-9.
168. Ministry of Health and Sports. Myanmar national strategic plan on HIV and AIDS (2016-2020). Myanmar: 2016.
169. UNODC. Myanmar country advocacy brief: Injecting drug use and HIV. Myanmar: 2010.
170. Strathdee SA, Mailman JL. The effectiveness of needle exchange programs: a review of the science and policy. AIDScience. 2001;1(16).
171. O'Keefe D, Scott N, Aitken C, Dietze P. Individual-level needle and syringe coverage in Melbourne, Australia: a longitudinal, descriptive analysis. BMC Health Services Resesearch. 2016;16(1):411.
172. HRI. The funding crisis for harm reduction: Donor retreat, government neglect and the way forward. London, UK: 2014.
173. Treloar C, Mao L, Wilson H. Beyond equipment distribution in Needle and Syringe Programmes: an exploratory analysis of blood-borne virus risk and other measures of client need. Harm Reduction Journal. 2016;13(1):18.
174. Fairbairn N, Kerr T, Buxton JA, Li K, Montaner J, Wood E. Increasing use and associated harms of crystal methamphetamine injection in a Canadian setting. Drug and Alcohol Dependence. 2007;88:313-6.

175. Richard AJ, Mosier V, Atkinson JS. New syringe acquisition and multi-person use of syringes among illegal drug users. Journal of Public Health Policy. 2002;23(3):324-43.
176. Mahoney JJ, Kalechstein AD, De La Garza R, Newton TF. Presence and persistence of psychotic symptoms in cocaine-versus methamphetamine-dependent participants. The American Journal on Addiction. 2008;17:83-98.
177. Bryant FB, Yarnold PR. Principal-components analysis and exploratory and confirmatory factor analysis. In: Grimm LG, Yarnold PR, editors. Reading and understanding multivariate statistics. Washington D.C., USA: American Psychological Association; 1995.
178. World Bank. World Bank Country and Lending Groups 2017 [23/02/2017]. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.
179. Stimson GV, Fitch C, Des Jarlais D, Poznyak V, Perlis T, Oppenheimer E, et al. Rapid assessment and response studies of injection drug use: knowledge gain, capacity building, and intervention development in a multisite study. American Journal of Public Health. 2006;96(2):288-95.
180. Fuller C, Vlahov D, Latkin CA, Ompad D, Celentano D, Strathdee SA. Social circumstances of initiation of injecting drug use and early shooting gallery attendance: implications for HIV intervention among adolescent and young adult injection drug users. Journal of Acquired Immune Deficiency Syndrome. 2003;32:86-93.
181. Philbin M, Pollini RA, Ramos R, Lozada R, Brouwer KC, Romas ME, et al. Shooting gallery attendance among IDUs in Tijuana and Ciudad Juarez, Mexico: correlates, prevention opportunities and the role of the environment. AIDS and Behaviour. 2008;12:552-60.
182. Australian Department of Health. Seventh National HIV Strategy. Canberra, Australia: 2014.
183. Australian Department of Health. Fourth National Hepatitis C Strategy. Canberra, Australia: 2017.
184. Victorian State Government Department of Health. Needle and Syringe Program 2017. Available from: https://www2.health.vic.gov.au/alcohol-and-drugs/aod-treatment-services/aod-prevention-harm-reduction/needle-and-syringe-program.

185. Craine N, Hickman M, Parry JV, Smith J, McDonald T, Lyons M. Characteristics of injecting drug users accessing different types of needle and syringe programme or using secondary distribution. Journal of Public Health. 2010;32(3):328-35.
186. Senreich E. Are specialized LGBT program components helpful for gay and bisexual men in substance abuse treatment? Substance Use and Misuse. 2010;45(7-8):1077-96.
187. Ritter A. New Australian lesbian, gay, bisexual and transgender research--and the need for more. Drug and Alcohol Review. 2015;34(4):347-8.
188. Reid G, Crofts N, Beyer L. Drug treatment services for ethnic communities in Victoria, Australia: an examination of cultural and institutional barriers. Ethnicity and Health. 2010;6(1).
189. Garfein RS, Stopka TJ, Pavlinac PB, Ross A, Haye BK, Riley ED, et al. Three years after legalization of nonprescription pharmacy syringe sales in California: where are we now? Journal of Urban Health. 2010;87(4):576-85.
190. De P, Cox J, Boivin J, Platt RW, Jolly AM. Social network-related risk factors for bloodborne virus infections among injection drug users receiving syringes through secondary exchange. Journal of Urban Health: Bulletin of the New York Academy of Medicine. 2007;85(1):77-89.
191. Duplessy C, Reynaud EG. Long-term survey of a syringe-dispensing machine needle exchange program: answering public concerns. Harm Reduction Journal. 2014;11(16):epub.
192. Miller CL, Tyndall MW, Spittal P, Li K, Palepu A, Schechter MT. Risk taking behaviours among injecting drug users who obtain syringes from pharmacies, fixed sites, and mobile van needle exchanges. Journal of Urban Health. 2002;79(2):257-65.
193. Queensland Government Department of Health. Queensland minimum data set for needle and syringe programs. Brisbane, Queensland: State of Queensland (Queensland Health), 2014.
194. Wood E, Tyndall M, Montaner J, Kerr T. Summary of findings from the evaulation of a pilot medically supervised safer injecting facility. Canadian Medical Association Journal. 2006;175(11):1399-404.

195. Vickerman P, Platt L, Jolley E, Rhodes T, Kazatchkine MD, Latypov A. Controlling HIV among people who inject drugs in Eastern Europe and Central Asia: insights from modeling. International Journal of Drug Policy. 2014;25(6):1163-73.
196. Kirby Institute. Australian NSP survey: prevalence of HIV, HCV and injecting and sexual behaviour among NSP attendees. National Data Report 2012-2016. Sydney, Australia: University of New South Wales, 2017.
197. Rhodes T, Platt L, Judd A, Mikhailova LA, Sarang A, Wallis N, et al. HCV infection HIV coinfection and associated risk among IDU in Togliatti Russia. International Journal of STD and AIDS. 2005;16(11):749-54.
198. Fisher K, Smith T, Nairn K, Anderson D. Rural people who inject drugs: a cross-sectional survey addressing the dimensions of access to secondary needle and syringe program outlets. Australian Journal of Rural Health. 2017;25:94-101.
199. Day C, Conroy E, Lowe J, Page J, Dolan K. Patterns of drug use and associated harms among rural injecting drug users: comparisons with metropolitan injecting drug users. Austranlian Journal of Rural Health. 2006;14:120-5.
200. Degenhardt L, Gisev N, Cama E, Nielsen S, Larance B, Bruno R. The extent and correlates of community-based pharmaceutical opioid utilisation in Australia. Pharmacoepidemiology and Drug Safety. 2016;25:521-38.
201. Karlsson A, Burns L. Illicit Drug Reporting System (IDRS) National Report 2017. Sydney, Australia: National Drug and Alcohol Research Centre (NDARC), 2018.
202. Ball AL. HIV, injecting drug use and harm reduction: a public health response. Addiction. 2007;102(5):684-90.
203. Hiscock R, Pearce J, Blakely T, Witten K. Is neighborhood access to health care provision associated with individual-level utilization and satisfaction. Health Services Research. 2008;43(6):2183-200.

Appendix A: Myanmar study ethics documents and questionnaire

A-1 Ethics approval: Alfred Hospital Human Research Ethics Committee

ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 319/16

Project Title: Needle and syringe coverage among PWID in Myanmar

Principal Researcher: Professor Paul Dietze

Project Proposal Version 1 **dated:** 4-Jul-2016 (within Module One, 1.14b)

Participant Information and Consent Form Version 1 **dated:** 2-Aug-2016

*was considered by the Ethics Committee on **28-Jul-2016**, meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and was **APPROVED** on **2-Aug-2016***

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project *(forms to be provided)*;

The Ethics Committee may conduct an audit at any time.

All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

Ethical approval by the Alfred Hospital Ethics Committee is contingent upon approval by the relevant local review board in Myanmar. Changes requested (if any) need to be submitted to this Ethics Committee.

SIGNED:

Professor John J. McNeil
Chair, Ethics Committee

A-2 Ethics Approval: Myanmar Department of Medical Research

The Government of the Republic of the Union of Myanmar
Ministry of Health and Sports
Department of Medical Research

[redacted]

ERC Number: 015216
Approval Number: Ethics/DMR/2016/148
Date of Approval: 5 December, 2016 (valid up to 4 December, 2017)

Project Title: **Measuring individual-level needle and syringe coverage among people who inject drugs (PWID) in Myanmar: risk predictors and outcomes research project in Myanmar**

Principal Investigator: Prof. Paul Dietze, Burnet Institute - Australia
Dr. Soe Moe Aung, Burnet Institute - Myanmar

Documents Accepted:

1. Ethical Proposal Form Version Dated 30 November, 2016
2. Full Proposal Protocol Version Dated 30 November, 2016
3. Proposal Summary Version Dated 30 November, 2016
4. Agreement to comply with ethical guideline Dated 30 November, 2016
5. Request for waiver of written consent forms Dated 30 November, 2016
6. Participant Information Sheet (English & Myanmar) Version Dated 30 November, 2016
7. Questionnaires (English & Myanmar) Version Dated 15 November, 2016
8. Ethical Approval from The Alfred Dated 2 August, 2016
9. Agreement Letter from National AIDS Programme Dated 21 October, 2016
10. Investigators' CV Dated 30 November, 2016

The Ethics Review Committee on Medical Research Involving Human Subjects, Department of Medical Research, Ministry of Health and Sports approves to conduct the proposed research project as it is in full compliance with the Declaration of Helsinki, Council for International Organizations of Medical Sciences guidelines and International Conference on Harmonisation in Good Clinical Practice guidelines.

[redacted]

Prof. Pe Thet Khin
Chairperson
Ethics Review Committee
Department of Medical Research

A-3 Myanmar individual-level needle and syringe coverage questionnaire

Verbal consent provided?

- Yes/No.

Section 1: Demographics

Q.1) Recruitment location

Recruitment region	Survey location: Outreach/DIC (O/D)
Yangon East	O/D
MDY	O/D
POL	O/D
SGG	O/D
Yangon West	O/D

Q.2) Sex

- Male
- Female
- Other (free text box).
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.3) How old are you? _____years

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.4) Are you currently in a relationship?

- Married
- Separated
- Single

- Widowed
- Regular/de-facto partner (not married)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.5) What type of accommodation do you currently live in?

- Own residence
- Rented residence
- Staying at parent's house
- Staying at friend's house
- Homeless
- Shelter
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.6) Are you employed at the moment?

- Unemployed
- Employed
- Student
- Self-employed
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.7) What was your income in the **past week**? _____MMK

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.8) How much did you spend on illegal drugs in the **past week**? _____MMK

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Section 2: Drug Use

Q.9) What drug did you use most during the **past month**?

- Heroin
- Methamphetamine
- Opium
- Cannabis
- Methadone
- Buprenorphine/Suboxone
- Cocaine
- Prescription opioids (morphine/oxycodone)
- Hallucinogens
- Benzodiazepines
- Alcohol
- Other (free text box)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.10) What drug did you inject most during the **past month**?

- Heroin
- Methamphetamine
- Opium
- Methadone
- Buprenorphine/Suboxone
- Cocaine
- Prescription opioids (morphine/oxycodone)
- Hallucinogens
- Benzodiazepines
- Other (free text box)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.11) What is your main illicit drug of choice (preferred or favourite drug)?

- Heroin
- Methamphetamine
- Opium
- Cannabis
- Methadone
- Buprenorphine/Suboxone

- Cocaine
- Prescription opioids (morphine/oxycodone)
- Hallucinogens
- Benzodiazepines
- Alcohol
- Other (free text box)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.12) How many times have you injected in the past **two weeks**? _____times

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.13) Where do you mainly inject drugs?

- Home
- Other person's house
- Street
- Public toilet
- Other public place
- Shooting gallery
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.14) Where on your body did you inject the **last time**?

- Arm
- Hand/wrist
- Leg
- Foot
- Groin
- Neck
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.15) Do you usually inject completely alone (without anyone else present)?

- Yes/No
- *Don't know*
- *Refuse to answer*

- *Not applicable*

Section 3: Treatment and coverage

Q.16) Have you received any drug treatment in the **past 6 months**? (More than one option) (if haven't received any treatment or "not applicable", skip to Q.18).

- Haven't received any treatment
- Methadone
  - How long were you on this OST program?_____months
- Drug detox
  - What type of detox was this?
    - residential (with medication assistance eg tincture of opium)
    - other (free text box)
- Other (free text box)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.17) Are you **currently** receiving any kind of drug treatment? (More than one option)

- No current treatment
- Methadone
  - How long have you been on this methadone program? _____ months
- Other (free text box)
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.18) In the **past two weeks**, have you used the following injecting equipment? (More than one option)

- Sterile needles/syringes
  - Kenxin 1cc needles/syringes
  - Kenxin 3cc needles/syringes
  - Terumo 1cc needles/syringes
  - Terumo 3cc needles syringes
  - Nubenco 1cc needles/syringes
  - Nubenco 3cc needles/syringes
  - Hannaco 1cc needles/syringes
  - Hannaco 3cc needles/syringes
  - BD 1cc needles/syringes
  - BD 1cc needles/syringes
- Spirit tissues (swabs)

- Sterile water
- Filter
- Sterile spoon/mixing container
- Haven't used any of the listed equipment
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.19) Do you normally use sterile water when injecting heroin/other drugs?

- Yes, I normally use sterile water. _____mls water
- No, I normally use unsterile water (such as tap water)._____mls water
- No, I normally don't use any kind of water when injecting.
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.20a) Where/from whom have you gotten your syringes in the **past month**?

- DIC
- Outreach
- Friends/partners
- Chemist
- Shooting gallery
- Peer
- Acquaintances (other injectors)
- "Professional injector"
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.20b) Where/from whom did you *mainly* get your syringes in the **past month**?

- DIC
- Outreach
- Friends/partners
- Chemist
- Shooting gallery
- Peer
- Acquaintances (other injectors)
- "Professional injector"
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.21) How many times have you gotten syringes from any source in the **past two weeks**? _____times

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.22) How many sterile syringes have you gotten in total in the **past two weeks**? _____syringes

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.23) How many sterile syringes have you given away (to friends/partners/acquaintances) in the **past two weeks**? _____syringes

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.24) How many sterile syringes do you have stored away at the moment (at home, for example)? _____syringes

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.25) Have you had any trouble getting syringes in the **past two weeks**?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Section 4: Injecting risk behaviour

Q.26) Have you re-used someone else's syringe after they've used it in the **past two weeks**?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.27) Has someone used a syringe after you've used it in the **past two weeks**?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.28) Have you re-used one of your own syringes in the **past two weeks**?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.29) How many times, on average, do you use a syringe before discarding it?
_____times

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.30a) Have you been injected by another person in the **past two weeks**?

- Yes/No (if no, skip to Q.31).
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.30b) If yes, what percentage of your total injections were performed by another person in the **past two weeks**? _____

Q.30c) What percentage of the injections, performed by another person, used a sterile syringe in the **past two weeks**? _____

Q.31) Have you injected another person in the **past two weeks**?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32a) Have you ever had a test for HIV? (if "no" or "not applicable", skip to Q.32f)

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32b) If yes, how long ago was your most recent HIV test?

- <3 months ago

- 3 to <6 months ago
- 6 to <12 months ago
- 12 or more months ago
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32c) What was your *main* motivation for getting your most recent HIV test?

- Had unprotected sex
- Had a needle stick injury
- I shared an unsterile needle
- Received money to be tested
- Received transportation support to attend testing
- DIC or other testing centre encouraged me to be tested
- My partner was getting tested
- I thought I may have HIV+ symptoms
- My partner was recently diagnosed HIV+
- I began a new relationship and wanted to know my HIV status
- Needed to be retested after the "window period"
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32d) What was the result of your most recent HIV test?

- Positive
- Negative
- Indeterminate
- Didn't get result *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32e) If the result was positive, are you currently taking ARVs to treat your HIV infection?

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.32f) If you have not had a HIV test, what was the *main* reason for this?

- Afraid of learning HIV status
- Afraid of blood taking

- I already know my HIV status
- I didn't have enough money for the test
- I had no transportation to the DIC or other testing centre
- I don't know where to get tested
- I don't feel unwell
- I've had no potential exposures
- I know/trust myself not to get HIV
- I know/trust my partner not to get HIV
- The Opening hours of the testing centre are inconvenient
- Afraid of stigmatisation
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.33a) Have you ever had a test for HCV? (if "no" or "not applicable", skip to Q.34a)

- Yes/No
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.33b) If yes, how long ago was your most recent HCV test?

- <3 months ago
- 3 to <6 months ago
- 6 to <12 months ago
- 12 or more months ago
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.33c) What was the result of your most recent HCV test?

- Positive
- Negative
- Previous exposure
- Indeterminate
- Didn't get result
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.34a) Have you ever had a test for HBV? (if "no" or "not applicable", skip to Q.35)

- Yes/No

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.34b) If yes, how long ago was your most recent HBV test?

- <3 months ago
- 3 to <6 months ago
- 6 to <12 months ago
- 12 or more months ago
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.34c) What was the result of your most recent HBV test?

- Positive
- Negative
- Indeterminate
- Vaccinated
- Didn't get result
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Section 5: Sexual risk

Q.35) How many sexual partners have you had in the **past 3 months**? _____ (if "0" sexual partners, skip to Q.39a)

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.36a) How many of these partners would you consider causal? _____

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.36b) How often have you used condoms with the casual partners in the **past 3 months**?

- Never
- Sometimes (<50%)

- Often (≥50%)
- Always
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.36c) If you've had any casual partner(s), do any of them have a positive HIV status?

- Not willing to disclose
- Yes, one or more casual partner is HIV positive
- No, I think all my casual partners are HIV negative
- I suspect one/some may be positive
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.37a) How many of these partners would you consider regular? _____

- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.37b) How often have you used condoms with the regular partners in the **past 3 months**?

- Never
- Sometimes (<50% of the time)
- Often (≥50% of the time)
- Always
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.37c) If you've had a regular partner(s), do any of them have a positive HIV status?

- Not willing to disclose
- Yes, one or more regular partner is HIV positive
- No, I think all my regular partners are HIV negative
- I suspect one/some may be positive
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.38) How many same-sex partners have you had in the **past 3 months**?_____

- *Don't know*

- *Refuse to answer*
- *Not applicable*

Q.39a) In the **past 3 months**, have you been paid with money, gifts or favours in exchange for sexual contact (oral/anal/vaginal sex)**?**

- Yes/no
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.39b) In the **past 3 months**, have you paid someone with money, gifts or favours in exchange for sexual contact (oral/anal/vaginal sex)**?**

- Yes/no
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Q.40) If you choose not to use condoms during sex, is it because of any of the following reasons (multiple options allowed)?

- Condoms ruin sex
- Condoms are uncomfortable
- Condoms mean you feel less when having sex
- My partner doesn't like me to use a condom
- My partners don't have any transmissible infections/diseases
- I find condoms difficult to use
- I feel embarrassed getting condoms from services
- I don't know where to get condoms
- I'm not concerned about transmissible infections/diseases
- *Don't know*
- *Refuse to answer*
- *Not applicable*

Appendix B: Additional peer-reviewed publications produced during candidature

B-1 Publication: From initiating injecting drug use to regular injecting: Retrospective survival analysis of injecting progression within a sample of people who inject drugs regularly

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Short communication

From initiating injecting drug use to regular injecting: Retrospective survival analysis of injecting progression within a sample of people who inject drugs regularly

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ABSTRACT

Background: The initiation of injecting drug use and the commencement of a pattern of regular injecting are key milestones in injecting careers. The progression from initiation to regular injecting is a poorly understood period in these careers.
Methods: Cross-sectional baseline data from a sample of people who inject drugs regularly ($N = 691$), recorded the age at which participants initiated injecting drug use and the age they became regular (at least once per month) injectors. Survival analysis compared the rapidity of progression to regular injecting across sub-groups within the sample using bivariate log-rank testing and multivariable Cox regression.
Results: Half of all participants progressed to regular injecting within 1 year of initiation and by the fourth year post-initiation, 91% had progressed. In bivariate analysis, there were significant differences in equality of hazards by sex ($X^2 = 7.75$, $p < 0.01$), from whom participants learnt to inject ($X^2 = 22.32$, $p < 0.01$) and the drug of injection initiation ($X^2 = 18.36$; $p < 0.01$). In the multivariable Cox model, only initiating injecting with heroin (HR = 1.28; 95% CI: 1.09–1.50) compared with other drugs (predominantly methamphetamine) showed a significantly greater hazard, suggesting a faster progression to regular injecting.
Conclusion: This study showed that among our sample of eventual regular injectors, progression from initiation to regular injecting was rapid. By gaining a greater understanding of the dynamics of this progression, the ability to appropriately target interventions and future research is subsequently informed.

1. Introduction

The natural history of the injecting careers of people who inject drugs (PWID) contains periods of heightened risk and harm (Huo et al., 2006). For example, the period following initiation of injecting drug use has been shown to be a period of heightened risk, with a substantial proportion of blood-borne virus (BBV) infections amongst PWID occurring within the first years after initiation (Bulled and Singer, 2011; Hagan et al., 2008; Maher et al., 2006; Miller et al., 2003; Stoove et al., 2008) As careers progress other risks are heightened, such as the risk of overdose, which has been shown to be highest amongst older, more experienced PWID (Dietze et al., 2006; McGregor et al., 2001). There are, however, considerable individual differences in natural histories; for example, although many PWID initiate injecting in late adolescence or early adulthood (Day et al., 2005; Huo et al., 2006), others initiate when substantially older (Carneiro et al., 1999).

The initiation of injecting drug use and the commencement of a pattern of regular injecting are milestones in injecting careers. Extensive literature examines both initiation (Day et al., 2005; Van Ameijden et al., 1994; Werb et al., 2013) and entrenched injecting drug use (Chitwood et al., 2001; Des Jarlais et al., 2007; Horyniak et al., 2013; Miller et al., 2003), but we could find no studies exploring the temporal characteristics of injecting progression. Lai et al. (2000) showed that the time from first use of heroin to first injection of heroin was a median 11 months for males and 22 months for females, whilst Lee et al. (2012) showed that the average time from first methamphetamine use to regular methamphetamine use was 2 years. However, neither of these studies analysed progression from injecting initiation through to regular injecting.

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Unlike other chronic health problems, the progression of injecting drug use is not well understood (Hickman et al., 2012). The gap highlighted here has implications for the targeting of public health interventions for newly initiated PWID. Improved knowledge of progression would allow risk reduction interventions to be tailored towards the transitional phase between initiation and regular injecting, just as interventions have been designed to prevent the transition from non-injecting to injecting drug use (Werb et al., 2013).

This paper presents an examination of cross-sectional data from a sample of people who inject drugs regularly, to retrospectively examine the rapidity of progression from initiation to regular injecting drug use and how this varies across different sub-groups. Evidence suggests that age (Miller et al., 2006), sex (Martin, 2010), ethnicity (Day et al., 2005), social networks (Day et al., 2005) and the influence of initiators (Bryant and Treloar, 2008) affect the dynamics of injecting initiation. We analysed these and other exposures and their influence upon the rapidity of progression from initiation to regular injecting drug use.

2. Methods

2.1. Recruitment

Baseline data were obtained from the Melbourne injecting drug user cohort study (MIX), which was designed to examine trajectories of injecting drug use. MIX began in Melbourne, Australia in 2008 and is described in detail elsewhere (Horyniak et al., 2013). Our analysis includes the original MIX participants ($N = 688$) along with an additional 69 participants enrolled into the study in 2011 via past involvement in the Networks II cohort (commenced in 2005; Sacks-Davis et al., 2012). Eligibility criteria for the original MIX cohort were being aged between 18 and 30 years and reported injecting of heroin and/or methamphetamine regularly (at least once a month in the previous 6 months). Networks II eligibility criteria were largely identical and both cohorts were similar across key characteristics such as sex (66% male in both samples), mean age (baseline age of 27 in both samples), mean age at first injection (18 in N2, 17 in MIX) and median past-week frequency of injecting (6 in N2, 5 in MIX). The Victorian Department of Health Human Research Ethics Committee and the Monash University Human Research Ethics Committee approved the study.

2.2. Measures

At baseline, participants were asked: "How old were you when you first injected a drug?" and "How old were you when you first started injecting drugs regularly (i.e. at least once a month)?" Responses to these questions were measured in years and recorded as discrete numbers. Though arbitrary, the recruitment criterion and the survey question specifying "at least once a month" align with other Australian research (Butler et al., 2015; Whittaker et al., 2015) that seeks to define an ongoing pattern of behaviour. Also, because MIX recruited "regular" injectors, all participants inherently met the criteria for our outcome of interest (regular injecting) by virtue of their involvement within the cohort.

A variable "time to regular injecting" was created by subtracting the age of initiation from the age of regular injecting. This meant that participants who responded with the same age for both questions received a value of zero for the time to regular injecting variable. In analysis, all time to regular injecting responses were increased by the value of one.

Time-invariant factors—that is, those occurring prior to initiation and could influence the progression to regular injecting—were identified and analysed. We examined sex (male female), country of birth (Australia, other), Indigenous status (Aboriginal & Torres-Strait Islander (ATSI), non-ATSI), age at initiation (<15 years, 15–18 years,>18 years), the drug used at initiation (coded as "heroin" (64%) vs. "other" (32% methamphetamine, 4% other drugs including ecstasy, pharmaceutical stimulants, cocaine, LSD or pharmaceutical opioids)) and non-injecting use of the drug of initiation prior to initiating (yes no).

We also analysed how or from whom participants learnt to inject (possible responses: "don't inject self", "self-taught", "close friends", "partner", "dealer", "acquaintances", "siblings", "parents", "Needles and Syringe Program (NSP) staff", "information pamphlet/other resource"). Due to very small response numbers, the categories of "dealer", "NSP staff" and "information pamphlet" were re-coded into a combined "other" variable ($n = 12$). Methods of learning to inject were not mutually exclusive (participants could choose more than one option). In order to achieve exclusive dichotomy in responses, participants who responded in more than one category ($n = 63$) were excluded from analysis. An additional three participants were excluded due to missing data for key variables, resulting in a final sample of 691 participants.

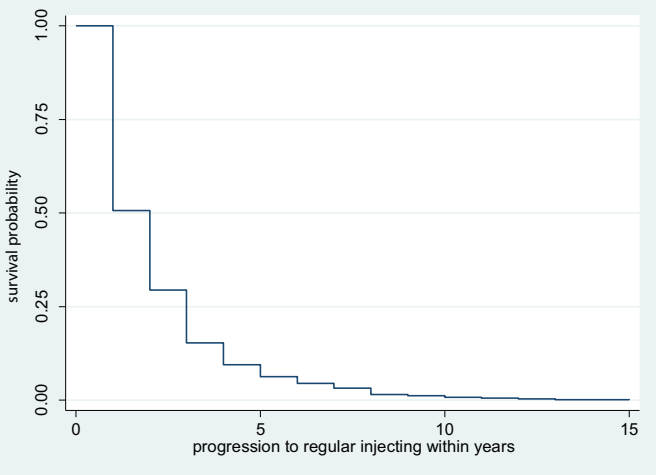

Fig. 1. Kaplan-Meier estimate of survival probability to regular injecting.

2.3. Analysis strategy

Log-rank testing compared bivariate proportional variance in the progression to regular injecting between specified covariates. Multivariable Cox regression was performed to explore the relationships between time to regular injecting and its covariates with sex, age at initiation and Indigenous status (selected due to the significantly younger mean age at initiation of Indigenous participants, t-value(689) = 3.17, $p < 0.01$) retained as potential confounders a priori. Aside from potential confounders, only those variables significant in log-rank testing were included within the multivariable model.

Statistical significance was set at $p < 0.05$. All analyses were carried out using Stata 13.1 for Windows (StataCorp LP, TX, USA).

3. Results

3.1. Demographics

Of the 691 participants included in analysis, 66% were male, 79% Australian-born and 6% identified as Indigenous. Mean age at baseline interview was 27 years.

3.2. Time to regular injecting

The range of reported ages at first injection was 8–30 years (median 17, IQR 15–19). The range of ages at commencement of regular injecting was 10–38 years (median 18, IQR 16–21). The range of time progression to regular injecting was 1–15 years. Half of all participants (49%) progressed to regular injecting within 1 year of initiation. A further 21% had progressed to regular injecting within 2 years of initiation. By the fourth year post-initiation, 91% of the sample reported progressing to regular injecting. Fig. 1 presents the Kaplan-Meier estimate of survival function (the progression to regular injecting) for the sample.

3.3. Survival analysis

In bivariate analysis, there were significant differences in equality of hazards by sex ($X^2 = 7.75$, $p < 0.01$), from whom participants learnt to inject ($X^2 = 22.32$, $p < 0.01$) and the drug of injection initiation ($X^2 = 18.36$; $p < 0.01$). There were no significant differences between age at initiation, country of birth, Indigenous status and the non-injecting use of the drug of initiation prior to initiating.

The variables excluded from the multivariable model due to non-significance in log-rank testing were country of birth and non-injecting drug use. In the final model, only initiating injecting with heroin (HR = 1.28; 95% CI: 1.09–1.50) compared with other drugs (predominantly methamphetamine) showed a significantly greater

Table 1
Multivariable Cox regression results.

	n (%)	AHR (95% CI)
Sex		
Female	232 (34%)	1
Male	459 (66%)	0.88 (0.74–1.04)
Age at initiation		
< 15 years	137 (20%)	1
15–18 years	346 (50%)	1.15 (0.93–1.41)
> 18 years	208 (30%)	1.23 (0.98–1.54)
Indigenous status		
Non-ATSI	650 (94%)	1
ATSI	41 (6%)	0.93 (0.67–1.29)
Drug of initiation		
Other drugs	248 (36%)	1
Heroin	443 (64%)	1.28 (1.09–1.50)
How/from whom learnt to inject		
Self-taught	136 (20%)	1
Don't inject self	14 (2%)	1.03 (0.59–1.79)
Friends	386 (56%)	0.87 (0.71–1.06)
Partner	68 (10%)	1.08 (0.78–1.48)
Siblings	30 (4%)	0.83 (0.55–1.23)
Parents	15 (2%)	1.58 (0.55–1.23)
Acquaintances	30 (4%)	1.11 (0.75–1.66)
Dealer/NSP staff/info pamphlet	12 (2%)	0.79 (0.44–1.45)

hazard, suggesting a faster progression to regular injecting. Full results are presented in Table 1.

4. Discussion

4.1. Findings

Our study suggests that progression to regular injecting within our sample of eventual regular injectors occurred relatively quickly, with nearly half of the sample progressing to regular injecting within a year of initiation, and over 90% progressing within 4 years.

After controlling for other variables, we found the only significant result was the initiation of injecting drug use with heroin over other drug types (primarily methamphetamine), with a resulting greater level of hazard. Previous research has shown heroin to have a greater severity of dependence than amphetamines (Gossop et al., 1992) particularly when the heroin is injected, which may account for its association with a faster progression to regular injecting.

The practice of regular injecting is an inherently established or entrenched behaviour requiring substantial effort to modify (Brener et al., 2010). Consequently, the transition period prior to regular injecting is important with respect to intervention. In a recent systematic review of interventions to prevent the initiation of injecting drug use by non-injectors, Werb et al. (2013) identified four studies that observed significant effects, with peer-based behaviour modification and addiction treatment found to be the most effective. No similar inventions have been developed to forestall the progression to regular injecting amongst newly initiated PWID, though if these PWID can be identified and targeted by services (possibly through unknown clients presenting to services or via client disclosure), the potential of similar peer-based interventions and treatment could be trialled. Given the social influences on injecting, the use of peers may also be an effective targeting strategy. Other risk-reduction strategies, such as counselling and testing for BBV infection (a particularly heightened risk amongst new initiates, Maher et al., 2006) may also be helpful in highlighting the risks for newly initiated PWID in order to facilitate behaviour change.

Because this research focussed on a particular sub-set of initiates (those who would definitely become regular injectors), recommendations are limited in their generalisability. Also, in seeking to target new initiates, there is inherent difficulty in identifying those most at risk of progressing to regular injecting. Future research may facilitate targeting, but until then, any possible intervention would require indiscriminate application, with our findings suggesting that the time-frame within which to intervene is potentially narrow.

4.2. Limitations

Our study is limited by the selection bias inherent in the study. Involvement in the MIX cohort (which recruited regular injectors) meant all participants had experienced the event of interest (becoming a regular injector). Consequently, we lacked a comparison group of participants who initiated injecting but did not progress to regular injecting. Our results cannot be extended beyond people similar to those in our sample.

The definition "at least once a month" is somewhat arbitrary but is consistent with other established national research. Furthermore, the survey asked participants how often they were injecting per week at the point of "regular" injecting. The median number of reported injections per week was 7 (IQR: 3–14), that is, approximately daily.

Our analysis was constrained by recording progression time in 1-year blocks, precluding a more fine-grained analysis. Future research with smaller units of time would provide a more nuanced picture of the progression to regular injecting.

Participants were asked to recall events that, in some cases, occurred many years in the past. However, the events in question are both significant in the careers of PWID, suggesting a greater potential for reliable recall, as shown in previous research (Best et al., 2007).

Finally, as with much PWID research, our sample was recruited from a population with unknown parameters, thereby reducing the generalisability of our results (Hope et al., 2010, Horyniak et al., 2013).

5. Conclusion

This study showed that progression from initiation to regular injecting was relatively rapid in our sample of long-term, regular injectors. Although the sole significant association with progression in multivariable analysis was initiation with heroin (over other drugs), the finding of rapid progression to regular injecting is important. By gaining a better understanding of the dynamics of injecting progression amongst regular injectors our ability to appropriately target interventions and future research is improved.

Contributors

DO'K led the analysis and writing of the article. DH and PD assisted with conceptualisation and provided essential input and support during analysis and writing. All authors have read the article and approve of its submission to Drug and Alcohol Dependence.

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Conflict of interest

PD has received funding from Gilead Sciences Inc and Reckitt Benckiser for work unrelated to this study.

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References

Best, D., Manning, V., Strang, J., 2007. Retrospective recall of heroin initiation and the impact on peer networks. Addict. Res. Theory 15, 397–410.
Brener, L., Spooner, C., Treloar, C., 2010. Preventing transitions to injecting amongst young people: what is the role of Needle and Syringe Programmes? Int. J. Drug Policy 21, 160–164.
Bryant, J., Treloar, C., 2008. Initiators: an examination of young injecting drug users who initiate others to injecting. AIDS Behav. 12, 885–890.
Bulled, N., Singer, M., 2011. Syringe-mediated syndemics. AIDS Behav. 15, 1539–1545.
Butler, K., Day, C., Dietze, P., Bruno, R., Alati, R., Burns, L., 2015. The potential reach of opioid substitution settings to deliver HCV care to people who inject drugs in Australia. J. Subst. Abuse 58, 90–94.
Carneiro, M., Fuller, C., Doherty, M.C., Vlahov, D., 1999. HIV prevalence and risk behaviours among new initiates into injection drug use over the age of 40 years old. Drug Alcohol Depen. 54, 83–86.
Chitwood, D.D., Comerford, M., Kitner, K.R., Palacios, W., Sanchez, J., 2001. A comparison of HIV risk behaviours between new and long-term injection drug users. Subst. Use Misuse 36, 91–111.
Day, C.A., Ross, J., Dietze, P., Dolan, K., 2005. Initiation to heroin injecting among heroin users in Sydney Australia: cross sectional survey. Harm Reduct. J. 2, 2.
Des Jarlais, D.C., Arasteh, K., Perlis, T., Hagan, H., Heckathorn, D.D., Mcknight, C., Bramson, H., Friedman, S.R., 2007. The transition from injection to non-injection drug use: long-term outcomes among heroin and cocaine users in New York City. Addiction 102, 778–785.
Dietze, P., Jolley, D., Fry, C.L., Bammer, G., Moore, D., 2006. When is a little knowledge dangerous? Circumstances of recent heroin overdose and links to knowledge of overdose risk factors. Drug Alcohol Depen. 84, 223–230.
Gossop, M., Griffiths, P., Powis, B., Strang, J., 1992. Severity of dependence and route of administration of heroin, cocaine and amphetamines. Brit. J. Addict. 87, 1527–1536.
Hagan, H., Rouget, E.R., Des Jarlais, D., Lelutiu-Weinberger, C., 2008. Meta-regression of hepatitis C virus infection in relation to time since onset of illicit drug injection: the influence of time and place. Am. J. Epidemiol. 168, 1099–1109.
Hickman, M., Vickerman, P., Degenhardt, L., 2012. Commentary on Mehta et. al (2012): natural History of Injecting Drug Use. Addiction 107.
Hope, V., Parry, J., Marongui, A., Ncube, F., 2010. Hepatitis C infection among recent initiates to injecting in England 2000–2008: is a national hepatitis C action plan making a difference? J. Viral Hepatitis 19, 55–64.
Horyniak, D., Higgs, P., Jenkinson, R., Degenhardt, L., Stoove, M., Kerr, T., Hickman, M., Aitken, C., Dietze, P., 2013. Establishing the Melbourne injecting drug user cohort study (MIX): rationale, methods, and baseline and twelve-month follow-up results. Harm Reduct. J., 10.
Huo, D., Bailey, S.L., Ouellet, L.J., 2006. Cessation of injection drug use and change in injection frequency: the Chicago needle exchange evaluation study. Addiction 101, 1606–1613.
Lai, S., Chen, J., Celentano, D., Page, J.B., Lai, H., Yang, J., Liu, W., Mccoy, C.B., Yu, X., 2000. Adoption of injection practices in heroin users in Guangxi Province China. J. Psychoactive Drugs 32, 285–292.
Lee, N.K., Harney, A.M., Pennay, A.E., 2012. Examining the temporal relationship between methamphetamine use and mental health comorbidity. Adv. Dual Diagn. 5, 23–31.
Maher, L., Jalaludin, B., Chant, K.G., Jayasuriya, R., Sladden, T., Kaldor, J.M., Sargent, P.L., 2006. Incidence and risk factors for HCV seroconversion in injecting drug users in Australia. Addiction 101, 1499–1508.
Martin, F.S., 2010. Becoming vulnerable: young women's accounts of initiation to injecting drug use. Addict. Res. Theory 18, 511–527.
Mcgregor, C., Ali, R., Christie, P., Darke, S., 2001. Overdose among heroin users: evaluation of an intervention in South Australia. Addict. Res. Theory 9, 481–501.
Miller, C.L., Strathdee, S.A., Kerr, T., Li, K., Wood, E., 2006. Factors associated with early adolescent initiation into injection drug use: implications for intervention programs. J. Adolescent Health 38, 462–464.
Miller, M., Mella, I., Moi, H., Eskild, A., 2003. HIV and hepatitis C virus risk in new and longer-term injecting drug users in Oslo Noway. J. Acq. Immune Def. Synd. 33, 373–379.
Sacks-Davis, R., Daraganova, G., Aitken, C., Higgs, P., Tracy, L., Bowden, S., Jenkinson, R., Rolls, D., Pattison, P., Robins, G., Grebely, J., Barry, A., Hellard, M., 2012. Hepatitis C virus phylogenetic clustering is associated with the social-injecting network in a cohort of people who inject drugs. PLoS One 7, e47335.
Stoove, M.A., Fry, C.L., Lintzeris, N., 2008. Quantifying hepatitis C transmission risk using a new weighted scoring system for the Blood-Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ): applications for community-based HCV surveillance, education and prevention. Harm Reduct. J. 5, 12.
Van Ameijden, E., Van Den Hoek, J., Hartgers, C., Coutinho, R., 1994. Risk factors for the transition from noninjection to injection drug use and accompanying AIDS risk behaviour in a cohort of drug users. Am. J. Epidemiol. 139, 1153–1163.
Werb, D., Buxton, J., Shoveller, J., Richardson, C., Rowell, G., Wood, E., 2013. Interventions to prevent the initiation of injection drug use: a systematic review. Drug Alcohol Depen. 133, 669–676.
Whittaker, E., Swift, W., Roxburgh, A., Dietze, P., Cogger, S., Bruno, R., Sindicich, N., Burns, L., 2015. Multiply disadvantaged: health and service utilisation factors faced by homeless injecting drug consumers in Australia. Drug Alcohol Rev. 34, 379–387.

B-2 Publication: The association between intentional overdose and same-sex sexual intercourse in a cohort of people who inject drugs in Melbourne, Australia

ORIGINAL ARTICLE

The Association between Intentional Overdose and Same-Sex Sexual Intercourse in a Cohort of People who Inject Drugs in Melbourne, Australia

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ABSTRACT

Background: People who inject drugs (PWID) are at disproportionately high risk of suicidal behaviors, as are individuals who report same-sex attraction or experience. However, there is little evidence of compounded risk of suicide for individuals who report same-sex sexual intercourse (SSI) and are PWID. *Objectives*: To explore the associations of lifetime intentional overdose amongst a cohort of PWID, with particular attention to those reporting SSI. *Methods*: The sample included 529 participants, from an ongoing cohort of 757 PWID. An "ever" SSI variable was created for participants who reported sexual intercourse with a same-sex partner at any longitudinal interview. We explored the adjusted associations between SSI and lifetime intentional overdose using logistic regression. *Results*: Ninety-one (17%) participants reported ever experiencing an intentional overdose. Forty-one (8%) participants reported SSI at any interview. Three hundred and sixty (68%) participants reported diagnosis of a mental health condition. Diagnosis of a mental health condition (AOR = 2.02, 95% CIs: 1.14, 3.59) and SSI (AOR = 2.58, 95% CIs: 1.22, 5.48) significantly increased the odds of lifetime intentional overdose. *Conclusions/Importance*: We found a heightened risk of intentional overdose amongst PWID reporting SSI, after controlling for diagnosis of a mental health condition. Services need to be aware of this heightened risk and target interventions appropriately.

KEYWORDS

People who inject drugs; lesbian/gay/bisexual; sexual orientation; intentional overdose; suicide

Background

People who inject drugs (PWID) experience poorer physical and mental health than the general population (Ross, Wodak, Gold, & Miller, 1992). Similarly, individuals reporting homosexual or bisexual experience/orientation experience high rates of mental illness (King et al., 2008; Mills, Lynskey, Teesson, Ross, & Darke, 2005; Pearson and Wilkinson, 2013), blood-borne virus infection (Lea et al., 2013; O'Keefe, Aitken, Higgs, & Dietze, 2013) and violence (Brown, 2014; Eisenberg & Resnick, 2006; McElrath, Chitwood, & Comerford, 1997). Drug use, and particularly injecting drug use, is also more prevalent among lesbian, gay, and bisexual (LGB) individuals than in the general population (Deacon, Mooney-Somers, Treloar, & Maher, 2013; Lea et al., 2013; Marshal et al., 2008).

These populations are also at disproportionately high risk of self-harm and suicidal behaviors. Individuals reporting homosexual or bisexual experience/orientation have high rates of suicidal ideation and attempts (Brown, 2014; Eisenberg & Resnick, 2006; Silenzio, Pena, Duberstein, Cerel, & Knox, 2007; Skerrett, Kolves, & De Leo, 2012). King et al.'s meta-analysis of 25 studies showed that non-heterosexual people had twice heterosexual people's lifetime risk of suicide attempt (King et al., 2008; Skerrett, Kolves, & De Leo, 2012). Similarly, numerous studies have shown an elevated suicide risk among PWID (Bohnert Roeder, & Ilgen, 2010; Heale, Dietze, & Fry, 2003; Neale, 2000). It is estimated that 3–10% of deaths among people who use heroin are due to suicide (Darke, Ross, Lynskey, & Teesson, 2004; Neale, 2000), whilst studies have reported lifetime history of attempted suicide in 17–47% of PWID (Darke et al., 2007).

Many PWID have histories and life circumstances that predispose them to suicidal ideation and attempts (Darke & Ross, 2002). Indeed, injecting drug use itself is often a response to difficult life circumstances (Wasserman Weinstein, Havassy, & Hall 1998). Neale (2000) interviewed 38 PWID in hospital emergency departments after overdose with suicidal intent and categorized the precipitative factors as mental health issues, histories of physical/sexual abuse, homelessness, unemployment and poor coping strategies. Whilst few participants were motivated by an unambiguous desire to die, overdose was seen as a method of release or escape from these stressful problems (Neale, 2000).

Sexual orientation encompasses facets of identity, attraction and sexual behavior (Sell, 1997). The increased risk of suicide and self-harm experienced by those reporting LGB identity or same-sex attraction, regardless of whether the two align, is explained by multiple pathways. Homophobic prejudice or discrimination at home and in the community can exacerbate poor mental health amongst LGB (Meyer, 2003) and same-sex attracted individuals (Brown, 2014), as do developmental stressors related to concealed sexuality or "coming out" (Brown, 2014; Skerrett, Kolves, & De Leo, 2012). Trauma and exposure to violence amongst LGB (mainly as a result of their sexual orientation) is pervasive, whilst similarly high levels of victimization amongst same-sex attracted youth has been reported, resulting in disproportionate rates of mental illness (Brown, 2014; Roberts, Austin, Corliss, Vandermorris, & Koenen, 2010) and youth homelessness (Rosario, Schrimshaw, & Hunter, 2012).

However, despite much evidence of the increased risk for suicidal behavior amongst these populations separately, there is little evidence about risk for individuals who are PWID and report same-sex sexual intercourse (SSI).

Objectives

In this paper, we investigate the predictors of lifetime occurrence of intentional overdose in a cohort of PWID, with a focus on those reporting a particular behavior of interest in this context, SSI. Our hypothesis is that the intentional overdose rate in PWID reporting SSI is significantly higher than in PWID who do not report SSI.

Methods

Our data are drawn from the Melbourne injecting drug user cohort study (MIX), which has been described in detail elsewhere (Horyniak et al., 2013). The cohort includes PWID recruited through the original MIX recruitment phase in 2008–2010 (n = 688), and those rolled into the study in 2011 via past involvement in the Networks II cohort (a demographically similar cohort of regular injectors; n = 69) (Scott et al., 2016). Both studies aimed to recruit current injectors who were younger than most Australian PWID population averages (Aitken et al., 2008).

Eligibility criteria for the original MIX cohort were being aged 18–30 years and reporting injecting of heroin and/or methamphetamine regularly (at least once a month in the six months prior to recruitment). Human Research Ethics Committees at the Victorian Department of Health and Monash University approved the study.

Participant sample

As of February 2015 (data set end), 2862 interviews using a structured questionnaire had been conducted, with a maximum of seven annual interviews per participant. This analysis is based on interviews conducted since August 2011, when relevant sexual behavior questions were introduced into the questionnaire, totalling 1466 interviews with 529 participants.

Key measures

Same-sex sexual intercourse was defined in response to two repeated, longitudinal questions, the first being: *"In the last 12 months how many FEMALES have you had sexual (vaginal or anal) intercourse with?"* Answers were given on an ordinal scale ranging from "none" to "more than 10." The question was repeated in relation to "*MALES*." We classified participants as engaging in SSI if they reported sexual intercourse with a same-sex partner in the previous 12 months at any interview in the study period.

Lifetime experience of intentional overdose was coded as "yes" if participants reported an intentional overdose ever (at baseline) or since any of their previous interviews.

A mental health condition was defined as self-reported formal diagnosis of at least one of the following: depression, anxiety, bipolar disorder, mania, panic, posttraumatic stress disorder, any personality disorder (including borderline), schizophrenia, other psychosis, drug-induced psychosis, phobias, other mental health conditions not listed. These were reported in response to the question "Have you ever been formally diagnosed with any mental health conditions?" at any interview.

Analysis strategy

Bivariable and multivariable logistic regression were used to test associations between exposure subgroups and experience of intentional overdose (outcome). Exposure subgroups were selected primarily as time-invariant factors; that is, factors that either would not change with time (e.g., sex) or were (generally) indications of long-term status (e.g., lifetime mental health diagnosis) among PWID. Exposure subgroups were: "sex" (male/female); "youth [WHO definition]" (≤24 years/>24 years); "Indigenous status" (no/yes); "SSI" (no/yes/no sexual intercourse); "expelled from school" (no/yes); "injecting career" (around median: <14 years/≥14 years); "age of injection initiation" (<15 years/15–19 years/≥20 years); "drug of injection initiation" (heroin/methamphetamine/other); "ever formal mental health diagnosis" (no/yes). Bivariable and multivariable associations were tested for each

subgroup. Proportional differences between subgroups were tested using chi-square statistics. Significance was set at alpha <0.05.

Because the key measures were recorded and coded longitudinally, the time point selected for regression analysis was each participant's most recent interview.

Results

Demographics

At participants' first interview in the amended dataset, the sample was predominately male (64%), Australian-born (82%), non-Indigenous (95%), unemployed (74%), and living in stable accommodation (83%). Mean age at first interview was 31 years. For those reporting injecting within the month prior to interview (n = 423, 80% of participants), heroin was the most commonly injected drug (68%), followed by methamphetamine (16%). Median weekly injecting frequency at first interview (for those reporting injecting) was five times (range 1–70).

The demographics of the analyzed sample and overall cohort were largely comparable, although there was a larger proportion of unemployed participants in the latter (74% vs 85%).

Key measures

Based on responses to sexual behavior questions, 434 (82%) participants reported sex with only opposite-sex partners, 11 (2%) reported sex with only same-sex partners, 30 (6%) reported sex with partners of both sexes, and 54 (10%) reported no sexual intercourse at any interview. Overall, 41 (8%) participants reported SSI at any interview, with 24 (59% of all SSI participants) reporting multiple instances of SSI over time.

Participants reporting SSI, compared to those reporting heterosexual intercourse or no sexual intercourse, were significantly more likely to be female (76% vs 35% vs 13% for variable sub-groups respectively, $p = <0.001$; 16% of all female participants reported SSI, compared with 3% all male participants). Individuals reporting SSI were less likely to have been expelled from school (20% vs 46% vs 35%, respectively, p = 0.001).

Ninety-one participants (17%) reported ever intentionally overdosing. Participants reporting intentional overdose were similar to those who did not, although the proportion of women was higher in the former (49% vs 33%, $p = 0.002$) and mental health diagnosis was also more prevalent in that group (80% vs 65%, $p = 0.005$). The age of initiation subgroups had significant differences, with more participants reporting intentional overdose in the "15–19 years" subgroup than in either the "<15 years" subgroup or the "≥20 years" subgroup (45% vs 25% vs 30%, respectively, $p = 0.007$).

Up to their most recent interview, 37% of participants reporting SSI (n = 15) also reported lifetime intentional overdose, compared with 16% in PWID reporting heterosexual sexual intercourse (n = 68) and 15% in PWID reporting no sexual intercourse across interviews (n = 8) ($p = 0.003$).

Up to their most recent interview, 360 participants (68%) reported ever being diagnosed with a mental health condition – approximately 50% with depression and/or anxiety. Seventy-eight per cent of participants reporting SSI (n = 32) also reported a mental health diagnosis, compared with 68% in PWID reporting heterosexual intercourse (n = 295) and 61% in PWID reporting no sexual intercourse (n = 33) ($p = 0.214$).

Logistic regression results

Differences between significant bivariable and multivariable outcomes were minimal. Drug of injecting initiation showed a significant bivariable association, with those initiating with methamphetamine (compared to heroin) having reduced odds of lifetime intentional overdose (Table 1). This result was not significant after inclusion of potentially confounding exposures.

In the multivariable model, PWID reporting SSI at any interview (compared to those reporting heterosexual intercourse) had significantly increased odds of lifetime intentional overdose (AOR = 2.58). Those reporting no sexual intercourse were not significantly different from those reporting heterosexual intercourse with respect to lifetime intentional overdose prevalence.

Those reporting ever receiving a formal mental health diagnosis had increased odds of lifetime intentional overdose (AOR = 2.02). The relationship between SSI and mental health was tested in further analysis by including an interaction term in a separate regression model, and found to be non-significant ($p = 0.897$). We did not include this interaction term in the final model.

Women had nearly twice the odds of experiencing lifetime intentional overdose (compared with men), as did those initiating injecting <15 years of age or ≥20 years of age compared to those initiating at 15–19 years of age.

Conclusions/Importance

We explored the relationship between SSI and intentional overdose in a cohort of PWID. Overall, 17% of PWID reported ever intentionally overdosing, but 37% of PWID reported SSI. As hypothesized, those participants

Table 1. Bivariable and multivariable logistic regression results for lifetime experience of intentional overdose at most recent interview.

	n (%)	SSI n (%)	Intentional OD (ever) n (%)	OR (95% CIs)	AOR (95% CIs)
Sex					
Male	339 (64)	10 (24)	46 (51)	1	1
Female	190 (36)	31 (76)	45 (49)	1.78 (1.35, 2.34)***	1.84 (1.10, 3.08)*
Age (WHO youth definition)					
≤24 years	39 (6)	2 (5)	6 (7)	1	1
>24 years	499 (94)	39 (95)	85 (93)	1.01 (0.61, 1.70)	0.95 (0.32, 2.81)
Indigenous status					
No	501 (94)	39 (95)	87 (96)	1	1
Yes	26 (5)	2 (5)	4 (4)	0.89 (0.47, 1.67)	0.72 (0.23, 2.25)
Missing	2 (1)	0	0		
Same-sex sexual intercourse					
No	434 (82)		68 (75)	1	1
Yes	41 (8)		15 (16)	3.07 (1.55, 6.10)**	2.58 (1.22, 5.48)*
No sexual intercourse	54 (10)		8 (9)	0.95 (0.43, 2.10)	1.16 (0.51, 2.67)
Expelled from school					
No	300 (56)	33 (80)	53 (58)	1	1
Yes	227 (43)	8 (20)	38 (42)	0.99 (0.76, 1.31)	1.11 (0.67, 1.84)
Missing	2 (1)	0	0		
Injecting career				1	
13 years	196 (37)	20 (49)	37 (41)		1
≥14 years	331 (62)	21 (51)	54 (59)	0.86 (0.66, 1.13)	0.97 (0.55, 1.72)
Missing	2 (1)	0	0		
Age of injection initiation					
<15 years	91 (17)	6 (15)	23 (25)	2.11 (1.49, 2.99)***	2.36 (1.28, 4.35)**
15–19 years	312 (59)	23 (56)	41 (45)	1	1
≥20 years	123 (23)	12 (29)	27 (30)	1.85 (1.35, 2.55)***	1.93 (1.06, 3.54)*
Missing	3 (1)	0	0		
Drug of injection initiation					
Heroin	323 (61)	19 (46)	59 (65)	1	1
Methamphetamine	179 (34)	20 (49)	25 (27)	0.70 (0.52, 0.94)*	0.66 (0.39, 5.84)
Other	25 (4)	2 (5)	7 (8)	1.70 (0.98, 2.93)	1.78 (0.64, 4.91)
Missing	2 (1)	0	0		
Mental health diagnosis (ever)					
No	169 (32)	9 (22)	18 (20)	1	1
Yes	360 (68)	32 (78)	73 (80)	2.54 (1.77, 3.63)***	2.02 (1.14, 3.59)*

*p-value = <0.05.
**p-value = <0.01.
***p-value = <0.001.
Number of observations in multivariable model: 522; Prob(chi^2): <0.001; Pseudo R^2: 0.08.

reporting SSI at any point throughout the study had significantly elevated odds of lifetime intentional overdose, even after controlling for other variables.

The heightened odds of intentional overdose in individuals reporting SSI who are also PWID—a population known to have an increased likelihood of suicide—represents increased risk. Reasons for this were elucidated in previous qualitative work in LGB-transgender (LGBT) populations, in which it was asserted that "being an LGBT PWID is a qualitatively different experience to being a heterosexual PWID" (Deacon, Mooney-Somers, Treloar, & Maher, 2013). Deacon et al. interviewed Australian LGBT PWID who spoke of other PWID stigmatizing them for their LGBT status, and of isolation from the LGBT community due to their injecting drug use (Deacon, Mooney-Somers, Treloar, & Maher, 2013). LGB PWID therefore reside in a "no-man's land" for peer support (Deacon, Mooney-Somers, Treloar, & Maher, 2013); this simultaneous discrimination plausibly exacerbates many health risks, including risk of suicide. The role of family is crucial in both increasing the risk of suicide (Brown, 2014) and in creating preventative environments via strong support units for people who identify as LGB and same-sex attracted individuals more broadly (Brown, 2014; Eisenberg & Resnick, 2006; Skerrett, Kolves, & De Leo, 2012). The same factors may be protective for PWID reporting homosexual or bisexual experience/orientation, and connections between family and peer groups should be facilitated as an intervention strategy.

Although we only considered SSI in this study, in the research literature, individuals with LGB identity have similarly disproportionate rates of poor mental health, alcohol and other drug use and self-harm behaviors (Deacon, Mooney-Somers, Treloar, & Maher, 2013; King et al., 2008; Skerrett, Kolves, & De Leo 2012). SSI and sexual identity are often disparate (Bowring, Vella, Degenhardt, Hellard, & Lim, 2015; Smith, Rissel, Richters, Grulich, & de Visser, 2003), and for individuals reporting SSI who do not ascribe to a related sexual identity, LGB-specific interventions may not be appropriate. Further, individuals with an identity not aligned

to their behavior may experience additional pressures (Goodenow, Netherland, & Szalacha, 2002). Based on the literature on minority stress, these individuals may have higher rates of substance use and mental health problems, including suicide (Goodenow et al., 2002; Marshal et al., 2008; Meyer, 2003). Further research should explore the intersect between sexual identity, SSI and suicide among PWID (Young Friedman, Case, & Asencio, 2000).

Besides SSI, factors associated with intentional overdose were sex, history of a mental health diagnosis, and age of injecting initiation. Increased risk of intentional overdose amongst PWID reporting a mental health condition was expected; numerous mental health disorders, including major depression (Dumais et al., 2005), schizophrenia (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005), personality disorders (Darke & Ross, 2002) and disorders characterized by anxiety or poor impulse control (Nock et al., 2009) have been associated with increased risk of suicide. In our sample, PWID reporting SSI and intentional overdose had higher prevalence of mental health diagnosis than the overall sample. However, mental health diagnosis did not alter the association of SSI with intentional overdose in the multivariable model.

Both younger and older age of initiation, compared to the reference group (15–19 years), were significantly associated with a greater risk of intentional overdose. It may be that these initiation subgroups are reflective of differing risk potentials. For example, traumatic childhoods increase the likelihood of early injecting initiation (Dube et al., 2003; Ompad et al., 2005).

Whilst the association between female status and intentional overdose was independent of the SSI variable, it should be noted that women within our sample reported SSI at a higher rate than men, highlighting the important differences in the risk profiles of men and women. Just as different sexual identities carry unique risk profiles, so too do different genders. Women have been shown to have different patterns of and different experiences of initiation into injecting drug use (Iversen, Dolan, Ezard, & Maher, 2015). Importantly, our finding of significantly increased odds of intentional overdose amongst women corresponds with past research among PWID populations (Bohnert, Roeder, & Ilgen, 2011; Darke, Ross, Lynskey, & Teesson, 2004). Darke et al. previously showed that female PWID, from a sample of participants in heroin dependence treatment, were significantly more likely than male PWID to report a history of suicide attempt and attempt within the past 12 months, and were more likely to report suicidal ideation (Darke, Ross, Lynskey, & Teesson, 2004). Female PWID are an established risk population for suicide and need to be prioritized in suicide prevention efforts, and the higher proportion of women reporting SSI, a known predictor of suicidal behavior, exacerbates this risk.

Our findings have implications for the targeting of interventions. For example, services tailored to LGB populations differ from services that, whilst potentially sensitive to LGB needs, are not specifically adapted (Ritter, 2015). Previous researchers have suggested that traditional alcohol and other drug treatments do not meet the needs of LGB individuals (Senreich, 2010). LGB individuals may experience heterosexist reactions from treatment peers or inappropriate care from staff untrained in LGB issues (Senreich, 2010) such as the particular contexts of drug use amongst gay and bisexual men (Lea et al., 2016). Similarly, standalone services designed for LGB and same-sex attracted individuals may be ill-equipped to address the particular needs of PWID. Services that can adequately cater for the diverse characteristics and experiences of their clients are needed. Currently targeted services may be inappropriate to meet the combined needs of highly specific populations. Collaborative relationships between services would be beneficial in this regard. Importantly, such targeted services, like those individually targeting LGB or PWID, should not presume similarity of service need across genders. Males, females and transgender people face separate and unique service barriers as a result of their gender and interventional efforts need to be aware of these gendered disparities (Johnson, Mimiaga, & Bradford, 2008; Pinkham and Malinowska-Sempruch, 2008). Finally, little research on alcohol and other drug treatment amongst Australian LGB individuals currently exists; specifically, rates of substance dependence amongst LGB populations are unknown (Ritter, 2015). A much broader understanding of drug use amongst individuals reporting a range of sexual orientations and practices is needed, and future research should address this gap to improve our ability to target services.

Limitations

This study is subject to limitations regarding the classification of the three key variables: SSI, mental health diagnosis and lifetime occurrence of intentional overdose. Our analysis was based on particular sexual behaviors rather than specifically on sexual identity, orientation or attraction. As discussed earlier, there are elements of sexual orientation that we did not measure which may also be associated with intentional overdose. Thus, our findings cannot be generalized to other sexual groups. Additionally, sexual orientation can change over time; we may have classified SSI based upon incidents with little bearing on current or usual behavior (Young Friedman, Case, & Asencio, 2000). However, most participants who reported

SSI did so at multiple interviews, suggesting prolonged behavior. Our definition of sex as penetrative anal or vaginal intercourse may also have underestimated the proportion of SSI participants, particularly among women, although the higher proportion of women reported SSI than men, suggests broad interpretation of "intercourse." However, recent Australian surveillance data for PWID showed that 8% reported a non-heterosexual orientation (Stafford & Burns, 2016), matching the percentage of participants in our sample reporting SSI. Our sample size was insufficient to explore differences across bisexual and exclusively homosexual experience. Other studies have demonstrated heightened mental and physical health risks for bisexual people (Kerr, Santurri, & Peters, 2013, Fredriksen-Goldsen, Kim, Barkan, Muraco, & Hoy-Ellis, 2013; Skerrett, Kolves, & De Leo, 2012).

Considering mental health diagnosis as an aggregate variable may conceal a disproportionate risk of suicide associated with particular conditions (Nock et al., 2009). However, the most prevalent diagnoses under the aggregate variable were depression and anxiety, which are known risk factors for suicide (Dumais et al., 2005; Sareen et al., 2005), hence we believe that our variable is appropriate.

Our coding of intentional overdose was based upon a combination of "ever" responses at baseline and "since previous interview" at follow-up, whilst our coding of SSI was based upon a combination of "in the last 12 months" responses at follow-up. This means that within our analysis, the association between SSI and intentional overdose may be based upon SSI that occurred within the previous 12 months, and an intentional overdose that occurred many years in the past. We make no claim as to any particular sequence of temporal events. Instead, our analysis simply shows the association between experiencing SSI and experiencing intentional overdose.

Finally, the coding of cumulative variables as a lifetime occurrence or across interviews relies on consistent follow-up. Due to attrition and interview timing, some participants have more interviews than others and therefore greater opportunity to experience the outcomes/exposures of interest. Whilst this undoubtedly introduces some bias, most participants (n = 358, 68%) had three or more interviews, suggesting minimal influence, particularly as all participants reported their lifetime experience of intentional overdose at recruitment. However, by selecting (largely) time-invariant factors within our regression model, our analysis precluded the inclusion of transient factors (e.g., injecting drug use relapse, recent assault) that may have contributed to the incidence of intentional overdose (Dietze et al., 2005). Longitudinal research exploring such temporal factors is needed.

Conclusion

Both individuals reporting homosexual or bisexual experience/orientation and PWID have increased risk of suicidal ideation and attempt. We found an increased risk for lifetime intentional overdose amongst PWID reporting SSI. Services should be aware of these individuals' heightened risk, of the multifaceted prejudice they face, and target appropriate support for them.

Nomenclature

LGB	lesbian, gay and bisexual
LGBT	LGB-transgender
MIX	Melbourne injecting drug user cohort study
PWID	people who inject drugs
SSI	same-sex sexual intercourse

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Declarations

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References

Aitken, C. K., Lewis, J., Tracy, S. L., Spelman, T., Bowden, D. S., Bharadwaj, M., Drummer, H., & Hellard, M. (2008). High incidence of hepatitis C virus reinfection in a cohort of injecting drug users. *Hepatology*, *48*, 1746–1752.

Bohnert, A. S., Roeder, K., & Ilgen, M. A. (2010). Unintentional overdose and suicide among substance users: A review of overlap and risk factors. *Drug and Alcohol Dependence*, *110*(3), 183–192.

Bohnert, A. S., Roeder, K. M., & Ilgen, M. A. (2011). Suicide attempts and overdoses among adults entering addictions

treatment: Comparing correlates in a U.S. National Study. *Drug and Alcohol Dependence*, *119*(1–2), 106–112.

Bowring, A. L., Vella, A. M., Degenhardt, L., Hellard, M., & Lim, M. S. (2015). Sexual identity, same-sex partners and risk behaviour among a community-based sample of young people in Australia. *International Journal of Drug Policy*, *26*(2), 153–161.

Brown, R. (2014). Self Harm and Suicide Risk for Same-Sex Attracted Young People: A Family Perspective. *Australian e-Journal for the Advancement of Mental Health*, *1*, 9–19.

Darke, S., & Ross, J. (2002). Suicide among heroin users: Rates, risk factors and methods. *Addiction*, *97*(11), 1383–1394.

Darke, S., Ross, J., Williamson, A., Mills, K. L., Havard, A., & Teesson, M. (2007). Patterns and correlates of attempted suicide by heroin users over a 3-source period: Findings from the Australian treatment outcome study. *Drug and Alcohol Dependence*, *87*(2–3), 146–152.

Darke, Shane, Ross, Joanne, Lynskey, Michael, & Teesson, Maree. (2004). Attempted suicide among entrants to three treatment modalities for heroin dependence in the Australian Treatment Outcome Study (ATOS): Prevalence and risk factors. *Drug and Alcohol Dependence*, *73*(1), 1–10.

Deacon, R. M., Mooney-Somers, J., Treloar, C., & Maher, L. (2013). At the intersection of marginalised identities: Lesbian, gay, bisexual and transgender people's experiences of injecting drug use and hepatitis C seroconversion. *Health & Social Care in the Community*, *21*(4), 402–410.

Dietze, P., Jolley, D., Fry, C., & Bammer, G. (2005). Transient changes in behaviour lead to heroin overdose: Results from a case-crossover study of non-fatal overdose. *Addiction*, *100*(5), 636–642.

Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003). Childhood abuse neglect and household dysfunction and the risk of illicit drug use: The adverse childhood experiences study. *Pediatrics*, *111*(3), 564–572.

Dumais, A., Lesage, A. D., Alda, M., Rouleau, G., Dumont, M., Chawky, N., … Turecki, G. (2005). Risk factors for suicide completion in major depression: A case control study of impulsive and aggressive behaviours in men. *American Journal of Psychiatry*, *162*, 2116–2124.

Eisenberg, M. E., & Resnick, M. D. (2006). Suicidality among gay, lesbian and bisexual youth: The role of protective factors. *Journal of Adolescent Health*, *39*(5), 662–668.

Fredriksen-Goldsen, K. I., Kim, H. J., Barkan, S. E., Muraco, A. & Hoy-Ellis, C. P. (2013). Health disparities among lesbian, gay, and bisexual older adults: Results from a population-based study. *American Journal of Public Health*, *103*, 1802–1809.

Goodenow, C., Netherland, J. & Szalacha, L. (2002). AIDS-related risk among adolescent males who have sex with males, females or both: Evidence from a statewide survey. *American Journal of Public Health*, *92*, 203–210.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Deeks, J. J. (2005). Schizophrenia and suicide: Systematic review of risk factors. *British Journal of Psychiatry*, *187*, 9–20.

Heale, P., Dietze, P., & Fry, C. L. (2003). Intentional overdose among heroin overdose survivors. *Journal of Urban Health*, *80*(2), 230–237.

Horyniak, D., Higgs, P., Jenkinson, R., Degenhardt, L., Stoove, M., Kerr, T., … Dietze, P. (2013). Establishing the Melbourne injecting drug user cohort study (MIX): Rationale, methods, and baseline and twelve-month follow-up results. *Harm Reduction Journal*, *10*(11).

Iversen, J., Dolan, K., Ezard, N., & Maher, L. (2015). HIV and Hepatitis C Virus Infection and Risk Behaviors Among Heterosexual, Bisexual, and Lesbian Women Who Inject Drugs in Australia. *LGBT Health*, *2*, 127–134.

Johnson, C. V., Mimiaga, M. J., & Bradford, J. (2008). Health care issues among lesbian, gay, bisexual, transgender and intersex (LGBTI) populations in the United States: Introduction. *Journal of Homosexuality*, *54*, 213–224.

Kerr, D. L., Santurri, L. & Peters, P. (2013). A comparison of lesbian, bisexual, and heterosexual college undergraduate women on selected mental health issues. *Journal of American College Health*, *61*, 185–194.

King, M., Semlyen, J., Tai, S. S., Killaspy, H., Osborn, D., Popelyuk, D., & Nazareth, I. (2008). A systematic review of mental disorder, suicide, and deliberate self harm in lesbian, gay and bisexual people. *BMC Psychiatry*, *8*, 70.

Lea, T., Mao, L., Bath, N., Prestage, G., Zablotska, I., de Wit, J., & Holt, M. (2013). Injecting drug use among gay and bisexual men in Sydney: Prevalence and associations with sexual risk practices and HIV and hepatitis C infection. *AIDS & Behaviour*, *17*(4), 1344–1351.

Lea, T., Mao, L., Hopwood, M., Prestage, G., Zablotska, I., de Wit, J., & Holt, M. (2016). Methamphetamine use among gay and bisexual men in Australia: Trends in recent and regular use from the Gay Community Periodic Surveys. *International Journal of Drug Policy*, *29*, 66–72.

Marshal, M. P., Friedman, M. S., Stall, R., King, K. M., Miles, J., Gold, M. A., … Morse, J. Q. (2008). Sexual orientation and adolescent substance use: A meta-analysis and methodological review. *Addiction*, *103*(4), 546–556.

McElrath, K., Chitwood, D. D., & Comerford, M. (1997). Crime victimization among injection drug users. *Journal of Drug Issues*, *27*(4), 771–783.

Meyer, I. H. (2003). Prejudice, social stress and mental health in lesbian, gay and bisexual populations: Conceptual issues and research evidence. *Psychological Bulletin*, *129*(5), 674–697.

Mills, K. L., Lynskey, M., Teesson, M., Ross, J., & Darke, S. (2005). Post-traumatic stress disorder among people with heroin dependence in the Australian treatment outcome study (ATOS): Prevalence and correlates. *Drug and Alcohol Dependence*, *77*(3), 243–249.

Neale, J. (2000). Suicidal intent in non-fatal illicit drug overdose. *Addiction*, *95*(1), 85–93.

Nock, M. K., Hwang, I., Sampson, N., Kessler, R. C., Angermeyer, M., Beautrais, A., … Williams, D. R. (2009). Cross-national analysis of the associations among mental disorders and suicidal behavior: Findings from the WHO World Mental Health Surveys. *PLoS Medicine*, *6*(8).

O'Keefe, D., Aitken, C., Higgs, P., & Dietze, P. (2013). Concordance between self-reported and actual hepatitis C virus infection status in a cohort of people who inject drugs. *Drug and Alcohol Review*, *32*(2), 208–210.

Ompad, D. C., Ikeda, R. M., Shah, N., Fuller, C. M., Bailey, S., Morse, E., … Strathdee, S. A. (2005). Childhood sexual abuse and age at initiation of injection drug use. *American Journal of Public Health*, *95*(4), 703–709.

Pearson, J., & Wilkinson, L. (2013). Family relationships and adolescent well-being: Are families equally protective for

same-sex attracted youth? *Journal of Youth and Adolescence*, *42*, 376–393.

Pinkham, S., & Malinowska-Sempruch, K. (2008). Women, harm reduction and HIV. *Reproductive Health Matters*, *16*, 168–181.

Ritter, A. (2015). New Australian lesbian, gay, bisexual and transgender research-and the need for more. *Drug and Alcohol Review*, *34*(4), 347–348.

Roberts, A. L., Austin, S. B., Corliss, H. L., Vandermorris, A. K., & Koenen, K. C. (2010). Pervasive trauma exposure among US sexual orientation minority adults and risk of posttraumatic stress disorder. *American Journal of Public Health*, *100*(12), 2433–2441.

Rosario, M., Schrimshaw, E. W., & Hunter, J. (2012). Homelessness among lesbian, gay, and bisexual youth: Implications for subsequent internalizing and externalizing symptoms. *Journal of Youth and Adolescence*, *41*(5), 544–560.

Ross, M. W., Wodak, A., Gold, J., & Miller, M. E. (1992). Differences across sexual orientation on HIV risk behaviours in injecting drug users. *AIDS Care*, *4*(2), 139–148.

Sareen, J., Cox, B. J., Afifi, T. O., De Graaf, R., Asmundson, G. J., ten Have, M., & Stein, M. B. (2005). Anxiety disorders and risk for suicidal ideation and suicide attempts. *Archives of General Psychiatry*, *62*, 1249–1257.

Scott, N., Carrotte, E. R., Higgs, P., Cogger, S., Stoove, M. A., Aitken, C. K., & Dietze, P. M. (2016). Longitudinal changes in psychological distress in a cohort of people who inject drugs in Melbourne, Australia. *Drug and Alcohol Dependence*, *168*, 140–146.

Sell, R. (1997). Defining and measuring sexual orientation: A review. *Archives of Sexual Behavior*, *26*(6), 643–658.

Senreich, E. (2010). Are specialized LGBT program components helpful for gay and bisexual men in substance abuse treatment? *Substance Use & Misuse*, *45*(7–8), 1077–1096.

Silenzio, V. M. B., Pena, J. B., Duberstein, P. R., Cerel, J., & Knox, K. L. (2007). Sexual orientation and risk factors for suicidal ideation and suicide attempts among adolescents and young adults. *American Journal of Public Health*, *97*(11), 2017–2019.

Skerrett, D. M., Kolves, K., & De Leo, D. (2012). *Suicidal behaviours in LGB populations: A literature review of research trends*. Brisbane, Australia: Australian Institute for Suicide Research and Prevention.

Smith, A. M. A., Rissel, C. E., Richters, J., Grulich, A. E., & de Visser, R. O. (2003). Sex in Australia: Sexual identity, sexual attraction and sexual experience among a representative sample of adults. *Australian and New Zealand Journal of Public Health*, *27*(2), 138–145.

Stafford, J., & Burns, L. (2016). *Illicit Drug Reporting System (IDRS) National Report 2015*. Sydney, Australia: National Drug and Alcohol Research Centre (NDARC).

Wasserman, D. A., Weinstein, M. G., Havassy, B. E., & Hall, S. M. (1998). Factors associated with lapses to heroin use during methadone maintenance. *Drug and Alcohol Dependence*, *52*, 183–192.

Young, R. M., Friedman, S. R., Case, P., & Asencio, M. W. (2000). Women injection drug users who have sex with women exhibit increased HIV infection and risk behaviours. *Journal of Drug Issues*, *30*(3), 499–524.

B-3 Publication: Blood-borne virus transmission in an urban, culturally diverse neighbourhood: results from a cross-sectional bio-behavioural survey using innovative outreach methods in a hard-to-reach population

Sexual Health

Blood-borne virus transmission in an urban, culturally diverse neighbourhood: results from a cross-sectional bio-behavioural survey using innovative outreach methods in a hard-to-reach population

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Abstract. ***Background*:** Following a HIV outbreak among Aboriginal people in a culturally diverse inner-city suburb of Melbourne, a blood-borne virus (BBV) screening program was conducted to inform public health interventions to prevent transmission and facilitate timely diagnosis and linkage to care. ***Methods*:** In August–September 2014, community health workers recruited people who inject drugs (PWID) from a local needle and syringe program. Participants were tested for hepatitis C virus (HCV), hepatitis B virus (HBV), HIV and syphilis and completed a bio-behavioural questionnaire. ***Results*:** In total, 128 PWID participated in the study. Serological evidence of exposure to HCV and HBV was detected among 118 (93%) and 57 participants (45%) respectively. Five participants were HIV positive. Independent risk factors for needle sharing were Aboriginality (AOR = 6.21, $P < 0.001$), attending health care for mental health problems (AOR = 2.79, $P = 0.023$) and inability to access drug treatment in the previous 6 months (AOR = 4.34, $P = 0.023$). ***Conclusions*:** BBV prevalence in this sample was much higher than reported in other recent Australian studies. This local population is at high risk of further BBV transmission, particularly Aboriginal PWID. Individual and service-related factors associated with risk in the context of a dynamic urban drug culture and HIV outbreak suggest an urgent need for tailored harm-reduction measures.

Additional keywords: Aboriginal health, hepatitis B virus, hepatitis C virus, HIV, injecting drug use, people who inject drugs, risk factors, viral hepatitis.

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Introduction

Early and comprehensive harm-reduction measures, including needle and syringe programs (NSPs), peer education, outreach and opioid substitution therapy (OST) have successfully minimised blood-borne virus (BBV) transmissions among people who inject drugs (PWID) in Australia. However, some PWID populations, including ethnic and cultural minorities, remain disproportionately vulnerable to BBV infections.[1–3]

Australians of Aboriginal and Torres Strait Islander origin (henceforth, Aboriginal Australians) suffer a disproportionate and increasing burden of BBV disease. In 2014, HIV and hepatitis C virus (HCV) notification rates were 5.9 and 164 per 100 000 in Aboriginal persons versus 3.7 and 35 per 100 000 in non-Aboriginal persons respectively.[1] Rates of HCV diagnosis among Aboriginal people have also risen disproportionately; population rates were triple those for non-Aboriginal Australians in 2013 and quintuple in 2014.[1] In Victoria, the second most populous Australian state, 48 HIV notifications occurred in Aboriginal Australians in 1984–2014; in 2013–14 alone, 10 (21%) occurred, all with injecting drug use (IDU) as a risk factor. Before 2013–14, most Aboriginal cases solely reported male–male sex as a risk factor, with few reporting injecting drug use (communication from the Health Protection Branch, Department of Health and Human Services, Victoria: based on data from the Victorian HIV Register).

Between 2010 and 2014, the proportion of HIV attributable to IDU was 16% among Indigenous Australians, but 3% in the Australian-born, non-Indigenous general population.[1] Probable explanations include higher rates of injecting risk behaviours among Aboriginal PWID, culturally unacceptable service models, poor access to health care and harm-reduction services, discrimination, and unemployment and low education,[3–6] resulting from socioeconomic, political and historical drivers of ill health.

In May 2014, HIV notifications increased among PWID of Aboriginal origin in an inner-urban suburb of Melbourne, Victoria. Concurrently, high-risk injecting behaviours among Aboriginal PWID were reported to and observed by local community health centre (CHC) staff. The CHC is located on a large public housing estate, near an active street drug market, and provides health care and harm-reduction services to an ethnically and culturally diverse population.

We undertook a BBV screening program for these PWID to inform a public health response to the outbreak, to increase viral testing and diagnosis, and to facilitate linkage to care for those who were newly diagnosed. This paper reports the results of that program.

Methods

Participants who were known to CHC workers as regular service users were recruited on four separate days in August and September 2014 in the NSP or during active outreach in the community.

Eligibility criteria were injecting at least monthly, Victorian residence in the past 6 months, and being aged 18 years or older. All participants gave informed consent.

Study questionnaires were administered and venepuncture was performed by Burnet Institute fieldworkers from an unmarked mobile van parked in a discrete location close to the CHC. Study questionnaires consisting of a range of bio-behavioural questions relevant to injecting risk and sexual health took ~20 min to administer using handheld and laptop computers. Blood samples were transported to St Vincent's Pathology, a National Association of Testing Authorities (NATA)-accredited service, which performed standard laboratory diagnostic testing for HCV, HBV, HIV and syphilis.

Participants were reimbursed AU$40 for completing the questionnaire and a further AU$20 upon receiving their pathology results.

Each participant was given the option of receiving their results from fieldworkers in the mobile van on a specified date in the same location, or assisted to make an appointment with a general practitioner (either at the local CHC or another clinical service of choice). Fieldworkers encouraged participants to attend an appointment with a general practitioner in order to facilitate linkage to further care and treatment.

Approval for the study protocol was granted by the Alfred Hospital Ethics Committee (project 361/14).

Measures

Hepatitis C virus exposure was defined as HCV antibody positivity (positive anti-HCV), and current HCV infection as HCV–RNA positivity. Evidence of HBV exposure was defined as either having current HBV infection (positive HBV surface antigen (HBsAg)) or evidence of previous HBV infection (positive core antibody; anti-HBc). Participants who were HBV surface antibody (anti-HBs) positive but HBsAg and anti-HBc negative were considered vaccinated. HIV infection was defined by a positive HIV antibody test and a confirmatory western blot. Active syphilis infection was defined as a positive antibody test followed by a reactive rapid plasma reagin test.

The questionnaire asked about sociodemographic characteristics, recent BBV risk behaviours (injecting/sexual) and recent healthcare and harm-reduction service access. Additional qualitative information on reasons for needle sharing and inability to access drug treatment was collected if reported.

Statistical analysis

Descriptive analysis was performed on key sociodemographics, BBV prevalence, reported BBV risk behaviours and indicators of service access. Bivariate and multivariate logistic regression tested predictors of BBV infection and needle sharing (receptive: using a needle after someone else had already used it, or distributive: sharing a used needle with someone else) within the past 3 months.

As few participants were born elsewhere than Australia or New Zealand, ethnicity was defined as Aboriginal origin or not.

Participants with serologic evidence of HBV vaccination were excluded from HBV analyses. Due to the small proportion of participants unexposed to HCV, regression models testing predictors of HCV and predictors of HBV exposure were limited to variables with known associations: age, sex and ethnicity.[7,8] Additional covariates in the final multivariable model of predictors of needle sharing (receptive or distributive;) in the previous 3 months was reached through backwards stepwise elimination, removing variables insignificant at $P < 0.1$.

All analyses were performed using STATA version 13.1 (StataCorp, TX, USA).

Results

Participant characteristics

The sample of 128 PWID had a median age of 37 years (IQR 31–44 years) and 86 (67%) were male. Despite the diversity in the underlying population, only a minority were born outside of Australia; 108 (84%) were born in Australia or New Zealand, with Vietnam reported as the next most common country of birth ($n = 7$, 5%). Of those who were Australian-born, 42 (40%) identified as Aboriginal. Only 12 participants (9%) were employed (full-time, part-time or casual) and 24 (19%) had completed secondary education.

Table 1 summarises sociodemographic, behavioural and service access characteristics of the study sample.

BBV/STI seroprevalence

Approximately one-third of participants reported not having been tested for HIV ($n = 40$, 31%), HCV ($n = 46$, 36%) or either BBV ($n = 36$, 28%) in the year before the study.

The HCV and HBV serology results were available for 127 participants (99%), and HIV serology results were available for

Table 1. Participant sociodemographic, risk behaviour and service access characteristics
Some covariates may add to less than the column total due to missing data

Participant characteristics	*n*	%
Sociodemographics		
Age group		
≤37 years	67	52
>37 years	61	48
Sex		
Male	86	67
Female	42	33
Aboriginal Australian		
Yes	42	33
No	86	67
Educational level		
Less than Year 10	52	41
Completed Year 10–12	76	59
Currently employed		9
Yes	12	9
No	116	91
Injecting risk behaviours		
Drug type injected most in past month		
Opioids	114	89
Amphetamines	14	11
Injecting frequency past month		
Less than once per day	65	51
Once per day or more	63	49
Receptive or distributive sharing of needles in the past 3 months		
Yes	52	41
No	76	59
Sexual risk behaviours		
Unprotected sex with casual sex partners in the previous year		
Yes	27	22
No	96	78
Two or more casual sex partners within the previous 12 months		
Yes	36	28
No	91	72
Sexual identity		
Heterosexual	118	92
Gay or bisexual male	4	3
Lesbian or bisexual female	6	5
Healthcare and harm-reduction service access		
Had a HIV test within the previous year		
Yes	40	31
No	88	69
Accessed a healthcare professional for a mental health problem within the previous 6 months		
Yes	62	48
No	66	52
Receiving treatment for drug use during the previous 6 months		
Yes	75	59
No	53	41
Seeking but unable to obtain drug treatment during the previous 3 months		
Yes	19	15
No	108	85
Total	128	100

all participants (Table 2). Almost all ($n = 118$, 93%) participants had evidence of HCV exposure, with 80 (63%) having current HCV infection. Participants born in Vietnam had the highest HCV prevalence (100%), followed by Aboriginal participants ($n = 40$, 98%). Fifty-two (41%) participants reported having not received the full course of three HBV vaccinations in their lifetime. Fifty-seven (45%) participants had serological evidence of exposure to HBV. Similar proportions of Aboriginal and non-Aboriginal participants had serological evidence of exposure to HBV.

Table 2. Detailed HCV, HBV and HIV serology in the study sample
HCV, hepatitis C virus; HBV, hepatitis B virus

	n	%
HCV serology		
Negative (anti-HCV-, HCV RNA-)	9	7
Current infection (anti-HCV+, HCV RNA$^+$)	80	63
Past exposure (anti-HCV+, HCV RNA-)	38	30
HBV serology		
Negative (anti-HBs-, anti-HBc-, HBsAg-)	29	23
Immunised (anti-HBs+ only)	41	32
Past infection (anti-HBs+, anti-HBc+, HBsAg-)	44	35
Past or current infection (anti-HBc + only)	6	5
Current infection (HBsAg+)	4	3
Likely past infection (anti-HBs+, anti-HBc equivocal)	3	2
HIV serology		
Negative	123	96
Positive	5	4
Total	128*	100

*One participant was unable to be tested for HCV or HBV.

Five participants were HIV positive, with an overall HIV prevalence of less than 4%. The proportion of Aboriginal PWID who were HIV positive was eight-fold higher than in non-Aboriginal PWID (further characteristics of these cases are not reported due to concerns around identifiability). All participants who tested positive for HIV reported their sexual orientation as heterosexual, and each reported only having had sexual partners of the opposite sex in the year preceding the study. Four were either first diagnosed as a result of study participation or within the 24 months before the study.

All HIV-positive participants had evidence of exposure to HCV, and 56 (44%) participants had evidence of exposure to both HCV and HBV. One participant had evidence of active syphilis infection.

After adjusting for sex and Aboriginal status, older age (above median) significantly predicted HCV and HBV seropositivity (AOR 11.84, $P = 0.027$ and AOR 7.06, $P = 0.001$ respectively). Although the odds of HCV exposure were higher among older participants, serological evidence of HCV exposure was at near saturation across both age groups; 60 participants (98%) in the older age group had serological markers of HCV exposure, compared with 59 (88%) in the younger age group.

Due to low numbers, it was not possible to model predictors of HIV or syphilis.

BBV/STI risk behaviours

Being of Aboriginal origin was significantly associated with self-reported needle sharing (AOR 6.21, $P < 0.001$). Among Aboriginal participants, 19 (45%) reported receptive sharing versus 12 non-Aboriginal participants (14%). Among Aboriginal participants, 21 (50%) reported distributive sharing versus 18 (21%) non-Aboriginal participants. Eleven Aboriginal participants (26%) reported both receptive and distributive sharing versus seven non-Aboriginal participants (8%). Twenty-nine Aboriginal (69%) and 23 non-Aboriginal participants (27%) reported any needle sharing (receptive or distributive) in the preceding 3 months. Among participants reporting any needle sharing in the previous 3 months, the most commonly given reason was difficulty accessing sterile injecting equipment outside NSP hours ($n = 32$, 62%). Additional reasons included incarceration preventing access to new needles and syringes ($n = 3$, 6%), inability to contact the after-hours NSP ($n = 2$, 4%) and inability to buy new needles and syringes from pharmacies ($n = 2$, 4%).

Reports of having consulted a health professional for a mental health problem in the previous 6 months and unsuccessfully attempting to access drug treatment in the previous 3 months were both associated with reported needle sharing (receptive or distributive). The most common reasons reported by participants for not being able to access drug treatment when they needed it were long waiting lists ($n = 9$, 60%) and being rejected by their program of choice ($n = 5$, 33%). Multivariate logistic regression models of predictors of needle sharing are presented in Table 3.

Linkage to care

Most ($n = 71$, 55%) participants saw a general practitioner at the local CHC to receive their results. Approximately one-quarter ($n = 29$, 23%) opted to receive results from fieldworkers and 19 (15%) elected to see another clinician of choice. Nine (7%) participants were unable to be located and did not receive their results. The five participants with HIV were either already linked into care and treatment services or linked into care as a result of study participation.

Discussion

We found very high prevalence of BBVs in this local PWID population. HCV prevalence was particularly high among Aboriginal and ethnic Vietnamese PWID. We know of no other study to report such high HCV exposure prevalence among Australian Aboriginal PWID, or in an Australian sample of PWID generally. We found a higher prevalence of HCV and HIV than state and national averages[1] and those reported in other recent Australian studies, including populations with well-documented, high-risk behaviours.[2,9] Similar prevalence rates have been found in other high-risk PWID populations, such as in India and Pakistan, where availability of harm reduction and healthcare services is much lower.[10,11] Our findings occur in the context of surveillance data that show recent increases in numbers of new HIV notifications among Aboriginal PWID. International experience with the rapidity of BBV transmission in settings with a similar history of colonisation and disadvantage among Aboriginal people, such as in Canada, highlights the importance of strengthening the Australian public health response to avert even more widespread transmission among vulnerable Aboriginal PWID.[3,12]

An important finding in our study is the high prevalence of HCV infection across age groups. Being older (>37 years) was associated with increased odds of both HCV and HBV seropositivity, while younger participants were more likely to report recent needle sharing. These findings are consistent with the epidemiology of HCV in Australia where higher prevalence of HCV infection is observed in older age groups and in those with a longer injecting history, whereas higher rates of HCV

Table 3. Factors associated with reported needle sharing (receptive or distributive) among study participants

OR, odds ratio; CI, confidence interval. Results in bold are statistically significant at the 5% level

Predictor	Crude OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Age group				
≤37 years	1.00		1.00	
>37 years	**0.31 (0.15–0.65)**	**0.002**	**0.31 (0.13–0.77)**	**0.011**
Sex				
Men	1.00		1.00	
Women	**2.76 (0.31–0.76)**	**0.009**	1.95 (0.79–4.84)	0.148
Aboriginal Australian				
No	1.00		1.00	
Yes	**6.11 (2.72–13.73)**	**<0.001**	**6.21 (2.45–15.78)**	**<0.001**
Consulted health professional for mental health problem in the previous 6 months				
No	1.00		1.00	
Yes	1.88 (0.92–3.83)	0.084	**2.79 (1.15–6.76)**	**0.023**
Unable to access treatment for drug dependence in the previous 3 months				
No	1.00		1.00	
Yes	**5.16 (1.73–15.42)**	**0.003**	**4.34 (1.22–15.43)**	**0.023**

incidence and risky injecting behaviours are observed in younger PWID.[1,9,13] This study found a near saturation of HCV infection in both older and younger age groups, possibly indicating a particularly high incidence of HCV infection and/or early initiation to injecting among young people in this population. Aboriginal Community Controlled Health Organisations (ACCHOs) have identified targeted funding for harm reduction information and services as a critical unmet need for Aboriginal young people at risk of injecting-related harm.[14]

Overall prevalence of risky injecting practices was high in this population. Of particular concern was Aboriginal participants' relatively high reporting of needle sharing. Other studies have described high rates of injecting risk behaviours – including receptive needle sharing, more frequent injecting, younger age of initiation and injecting in public – among Aboriginal PWID.[3,5,15] Most participants in our study reported that inability to access sterile injecting equipment when needed was the main reason for sharing needles. These data suggest that 24-h access to sterile injecting equipment is needed. Service delivery models should expand to incorporate a broad range of options, including peer-led interventions, pharmacy NSPs, mobile outreach services, NSP workers in ACCHOs and Aboriginal health workers in mainstream organisations. Syringe vending machines have already been implemented in Australian jurisdictions, and are particularly effective for hard-to-reach, marginalised PWID populations.[16] In Australia, some Aboriginal people have reported a preference for syringe vending machines as a service delivery model, due to concerns around anonymity.[14] Since this study was conducted, a syringe vending machine has been installed at the CHC site. The Victorian Department of Health also issued a statement to health professionals, including those providing sexual health and alcohol and other drug (AOD) services, to encourage HIV testing for PWID, link PWID testing positive for HIV into care and treatment services, and promote primary prevention through safe sex and harm-reduction information and education.[17] The local CHC was also provided with some funding to increase engagement with the at-risk community and trial rapid testing for HIV.

Some participants were unable to access treatment for drug use when they wanted it, and this was significantly associated with reporting recent needle and syringe sharing. Deficiencies in the Victorian OST system must be addressed, especially inadequate numbers of prescribers and problems with coordination between specialist, community and other AOD services.[18] OST and other essential harm-reduction initiatives have much larger impact on BBV transmission than single interventions.[19,20] Integrated, multidisciplinary, community-based models of care increase access to a comprehensive set of proven interventions including primary prevention, BBV screening, drug treatment, BBV treatment, social support services and psychiatric and medical care.[21] Importantly, this study found that innovative community-based outreach methods can successfully reach and deliver services to high-risk, hard-to-reach PWID populations, and link them into clinical services. Similarly, studies from other settings have demonstrated that the offer of voluntary testing and counselling from community settings like mobile outreach units can increase BBV testing rates and early diagnosis among marginalised populations who do not access traditional clinical services.[22–25] This highlights the importance of employing integrated and more innovative methods of service delivery that are combined with culturally meaningful prevention and education interventions, in addition to traditional services.

Indicators of socioeconomic status, educational and employment levels reveal that study participants were almost universally disadvantaged, a common finding among PWID across many settings. Social and economic inequalities and a multitude of adverse health and social outcomes, including drug dependence and mental health problems, are strongly correlated.[26–28] Social and health disparities between Aboriginal and non-Aboriginal PWID are also evident, as vulnerability arising from social determinants of health are

compounded by current and past injustices, including intergenerational effects of colonisation and child removal, experiences of racism and services that are culturally insensitive.[6,29] Aboriginal people are often particularly vulnerable to high-risk injecting practices due to marginalisation, shame and disempowerment.[30] Aboriginal people may not feel comfortable accessing available services due to fear of stigma or identifiability concerns, or lack of culturally sensitive services.[4,14,30] Aboriginal people in some communities may also be more likely to pool resources to acquire drugs and use them in a group setting (where individualistic behaviour can be seen as selfish), which can pressure Aboriginal injectors to share needles and equipment.[30] For initiatives to be effective, they must acknowledge an Aboriginal definition of health,[5,31] be responsive to community-identified needs, and overcome the specific barriers faced by Aboriginal PWID including shame accessing harm reduction, BBV treatment and AOD services,[14] and geographical inaccessibility of services.[4] Models of care must be affordable, culturally safe and actively address the dual stigma Aboriginal PWID often face.[30] Individual and service-related factors associated with risk in the context of a dynamic local urban drug culture and a clustered HIV outbreak suggest a pressing need for funding for targeted harm-reduction initiatives, tailored to the needs of specific high-risk groups, in combination with efforts to address the upstream social and structural drivers of risk that perpetuate these inequities.

Limitations

Sample size and near saturation of HCV exposure probably precluded detection of some important differences in the analysis. Although the sampling frame was not entirely random, with participants recruited during NSP visits on study days and via active outreach, we believe the study sample is representative of local NSP users. Data collection tools used may not have explored the full extent of possible contributing factors to BBV transmission observed by CHC staff, such as motivation levels to obtain clean injecting equipment, effect of withdrawal on risk-taking behaviours, and other complexities of drug use such as paying back outstanding debts with heroin. Finally, none of the data collectors were Aboriginal; this and the effect of participants' experiences of stigma and discrimination may have limited disclosure of personal information. Although we detected several epidemiologically linked cases of injecting-related HIV in this community, we cannot comment on the overall extent of the cluster.

Conflicts of interest

PD has received funding from Gilead Sciences Inc. for work unrelated to this study. PD has received funding from Reckitt Benckiser for work unrelated to this study.

References

1 The Kirby Institute. HIV, viral hepatitis and sexually transmitted infections in Australia. Annual Surveillance Report 2015 [Internet]. Sydney: Kirby Institute, University of New South Wales; 2015. Available online at: https://kirby.unsw.edu.au/report-type/annual-surveillance-reports [verified 7 September 2017].

2 Hellard ME, Nguyen OK, Guy RJ, Jardine D, Mijch A, Higgs PG. The prevalence and risk behaviours associated with the transmission of blood-borne viruses among ethnic-Vietnamese injecting drug users. *Aust N Z J Public Health* 2006; 30: 519–25. doi:10.1111/j.1467-842X.2006.tb00779.x

3 Ward J, Topp L, Iversen J, Wand H, Akre S, Kaldor J, Maher L. Higher HCV antibody prevalence among Indigenous clients of needle and syringe programs. *Aust N Z J Public Health* 2011; 35: 421–6. doi:10.1111/j.1753-6405.2011.00743.x

4 Kratzmann M, Mitchell E, Ware J, Banach L, Ward J, Ryan J, Sutton L, Griffiths P, Saunders M. Injecting drug use and associated harms among Aboriginal Australians [Internet]. Canberra: Australian National Council On Drugs; 2011. Available online at: http://www.healthinfonet.ecu.edu.au/uploads/resources/20713_20713.pdf [verified 7 September 2017].

5 Bryant J, Ward J, Wand H, Byron K, Bamblett A, Waples-Crowe P, Betts S, Coburn T, Delaney-Thiele D, Worth H, Kaldor J, Pitts M. Illicit and injecting drug use among Indigenous young people in urban, regional and remote Australia. *Drug Alcohol Rev* 2015; 35: 447–55. doi:10.1111/dar.12320

6 Australian Injecting and Illicit Drug Users League. 'Why wouldn't I discriminate against all of them?', A report on stigma and discrimination towards the injecting drug user community [Internet]. Canberra: AIVL; 2011. Available online at: http://www.aivl.org.au/resource/why-wouldnt-i-discriminate-against-all-of-them-a-report-on-stigma-discrimination-towards-the-injecting-drug-user-community/ [verified 7 September 2017].

7 Wand H, Spiegelman D, Law M, Jalaludin B, Kaldor J, Maher L. Estimating population attributable risk for hepatitis C seroconversion in injecting drug users in Australia: implications for prevention policy and planning. *Addiction* 2009; 104: 2049–56. doi:10.1111/j.1360-0443.2009.02704.x

8 Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013; 57: 1333–42. doi:10.1002/hep.26141

9 Falster K, Kaldor JM, Maher L, Hepatitis C. Virus acquisition among injecting drug users: a cohort analysis of a national repeated cross-sectional survey of needle and syringe program attendees in Australia, 1995–2004. *J Urban Health* 2009; 86: 106–18. doi:10.1007/s11524-008-9330-7

10 Eicher AD, Crofts N, Benjamin S, Deutschmann P, Rodger AJ. A certain fate: spread of HIV among young injecting drug users in Manipur, North-East India. *AIDS Care* 2000; 12: 497–504. doi:10.1080/09540120050123891

11 Kuo I, Ul-Hasan S, Galai N, Thomas DL, Zafar T, Ahmed MA, Strathdee SA. High HCV seroprevalence and HIV drug use risk behaviors among injection drug users in Pakistan. *Harm Reduct J* 2006; 3: 26. doi:10.1186/1477-7517-3-26

12 Wood E, Montaner JSG, Li K, Zhang R, Barney L, Strathdee SA, Tyndall MW, Kerr T. Burden of HIV infection among Aboriginal injection drug users in Vancouver, British Columbia. *Am J Public Health* 2008; 98: 515–9. doi:10.2105/AJPH.2007.114595

13 Maher L, Jalaludin B, Chant KG, Jayasuriya R, Sladden T, Kaldor JM, Sargent PL. Incidence and risk factors for hepatitis C seroconversion in injecting drug users in Australia. *Addiction* 2006; 101: 1499–508. doi:10.1111/j.1360-0443.2006.01543.x

14 Mapfumo L, Waples-Crowe P, Ware J. "Action Research - Addressing HIV risks related to injecting drug use in Victorian Aboriginal Communities", A report for the Victorian Department of Health [Internet]. Melbourne: ANEX; 2010. Available online at: http://www.healthinfonet.ecu.edu.au/key-resources/programs-projects?pid=1110 [verified 7 September 2017].

15 Paquette D, McEwan M, Bryant J. Risk practices among Aboriginal people who inject drugs in New South Wales, Australia. *AIDS Behav* 2013; 17: 2467–73. doi:10.1007/s10461-012-0226-x
16 White B, Haber PS, Day CA. Community attitudes towards harm reduction services and a newly established needle and syringe automatic dispensing machine in an inner-city area of Sydney, Australia. *Int J Drug Policy* 2016; 27: 121–6. doi:10.1016/j.drugpo.2015.05.010
17 Victorian Department of Health. Chief Health Officer Advisory: risk of HIV infection in people who inject drugs – 6 October 2014 [Internet]. Melbourne: Victorian Department of Health; 2014. Available online at: https://www2.health.vic.gov.au/searchresults?q=risk%20of%20hiv [verified 7 September 2017].
18 King T, Ritter A, Berends L. Victorian pharmacotherapy review. Sydney: National Drug and Alcohol Research Centre, University of New South Wales; 2011.
19 Nolan S, Dias Lima V, Fairbairn N, Kerr T, Montaner J, Grebely J, Wood E. The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users. *Addiction* 2014; 109: 2053–9. doi:10.1111/add.12682
20 Degenhardt L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed. *Lancet* 2010; 376: 285–301. doi:10.1016/S0140-6736(10)60742-8
21 Bruggmann P, Litwin AH. Models of care for the management of hepatitis C virus among people who inject drugs: one size does not fit all. *Clin Infect Dis* 2013; 57(Suppl 2): S56–61. doi:10.1093/cid/cit271
22 Alvarez-del Arco D, Monge S, Azcoaga A, Rio I, Hernando V, Gonzalez C, Alejos B, Caro AM, Perez-Cachafeiro S, Ramirez-Rubio O, Bolumar F, Noori T, Del Amo J. HIV testing and counselling for migrant populations living in high-income countries: a systematic review. *Eur J Public Health* 2013; 23(6): 1039–45. doi:10.1093/eurpub/cks130
23 de la Fuente L, Delgado J, Hoyos J, Belza MJ, Alvarez J, Gutiérrez J, Neira-León M, Suárez M. Madrid Rapid HIV Testing Group Increasing early diagnosis of HIV through rapid testing in a street outreach program in Spain. *AIDS Patient Care STDS* 2009; 23(8): 625–9. doi:10.1089/apc.2009.0019
24 Suthar AB, Ford N, Bachanas PJ, Wong VJ, Rajan JS, Saltzman AK, Ajose O, Fakoya AO, Granich RM, Negussie EK, Baggaley RC. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. *PLoS Med* 2013; 10(8): e1001496. doi:10.1371/journal.pmed.1001496
25 Spielberg F, Kurth A, Reidy W, McKnight T, Dikobe W, Wilson C. Iterative evaluation in a mobile counseling and testing program to reach people of color at risk for HIV-new strategies improve program acceptability, effectiveness, and evaluation capabilities. *AIDS Educ Prev* 2011; 23: 110–6. doi:10.1521/aeap.2011.23.3_supp.110
26 Douglas BF, Freil S, Denniss R, Morawetz D. Advance Australia Fair? What to do about growing inequality in Australia [Internet]. Weston: Australia21 and The Australia Institute; 2014. Available online at: https://australia21.org.au/product/advance-australia-fair-what-to-do-about-inequality-in-australia/ [verified 7 September 2017].
27 Wilkinson RG. The impact of inequality: how to make sick societies healthier. Revised edition. Oxfordshire: Routledge; 2005.
28 Dube SR, Felitti VJ, Dong M, Chapman DP, Giles WH, Anda RF. Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics* 2003; 111: 564–72. doi:10.1542/peds.111.3.564
29 Wilkie M. Bringing them home: report of the National Inquiry into the separation of Aboriginal and Torres Strait Islander children from their families [Internet]. Sydney: Human Rights and Equal Opportunity Commission; 1997. Available online at: https://www.humanrights.gov.au/publications/bringing-them-home-report-1997 [verified 7 September 2017].
30 Urbis. A review of enablers and barriers of Indigenous drug users accessing needle and syringe programs – a report for the COAG Multilateral Group on Needle and Syringe Programs [Internet]. Canberra: Department of Health and Ageing; 2008. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/content/needle-indig [verified 7 September 2017].
31 National Aboriginal Community Controlled Health Organisation. Definitions [Internet]. Canberra: NACCHO; 2014. Available online at: http://www.naccho.org.au/aboriginal-health/definitions/ [verified 7 September 2017].