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Sex, drugs and intersecting risks – HIV among people who belong to more than one key population in the United States

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SEX, DRUGS AND INTERSECTING RISKS – HIV
AMONG PEOPLE WHO BELONG TO MORE THAN ONE
KEY POPULATION IN THE UNITED STATES
THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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**The thesis will be defended in public at Inghesalen, Widerströmska huset, Karolinska
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This thesis is dedicated to Dr. Piers Nye.

I am sure that wherever you are now,
you are supervising and encouraging others with a great deal of humour and outrageousness.

You are missed.

PREFACE

I did the studies included in this thesis while I was working for the Centers for Disease Control and Prevention (CDC) in Atlanta, GA, in the United States. My work there was with the Behavioural Surveillance Team in the Division of HIV/AIDS Prevention. As my work constituted data collection and analysis, I was able to register as a PhD student at Karolinska Institutet simultaneously which was fantastic. I enjoyed my work at CDC very much and I learned so much about the populations we worked with – people who inject drugs, men who have sex with men and people who lived in low-income areas. My colleagues were wonderful and smart but we also had a great deal of fun together. I appreciated being able to work with staff in Detroit, Newark, Houston and New York and it was a privilege to be able to attend focus groups with our target populations and hear first-hand from them about their challenges. I was thrilled when my team lead asked me to lead a pilot data collection targeted at women who exchange sex and enjoyed every part of it from project planning to data analysis and publication.

I left the CDC in 2017 and started work at the ECDC, the European Centre for Disease Prevention and Control in Stockholm in my native Sweden as an expert on hepatitis B and C. I worked to finish the PhD outside my regular job which was challenging at the best of times and many holiday days were spent in my parents' house on the island of Ven on my laptop. I was about to defend my thesis in May 2020, but it became clear that the COVID-19 pandemic required everyone in public health to set aside their professional and personal lives for the subsequent two years. I postponed the defence and spent a rewarding but exhausting time being part of ECDC's COVID-19 response where I led the work on contact tracing including contact tracing with mobile apps. It is a field I knew very little about – it did not exist earlier – but like everyone else in public health at that time I had no choice but to dig in. The process of bringing research to practice shrank from several years to weeks or even days as pre-publication research or preliminary data from public health agencies was all that was available on which to base policy recommendations. The skills I learned during that response were different from what I learned during the PhD process but the two complemented each other very well and I am grateful to have had both.

I finally scheduled the defence for June 2022 but in late April we realise that another outbreak was emerging of severe acute hepatitis of unknown aetiology among young children and things became very intense at work again. I am grateful for my manager and colleagues for allowing me time to still prepare for the defence and I hope that by the time the defence happens, the aetiology is no longer unknown.

POPULAR SCIENCE SUMMARY

HIV is the virus that causes AIDS. HIV can be transmitted through blood, for example when people who inject drugs share the same needle, or through sexual activity without a condom through exchange of semen and vaginal fluids. Anal sex in particular carries a high risk because compared with vaginal sex it is more likely that the sex results in tears in the mucosa which means infected blood or semen from one person can more easily get into the blood of the other person. There is no vaccine against HIV infection but there is a very effective treatment with what is called ‘antiretroviral therapy’. This medicine cannot cure HIV – the virus will always be in the body. However, if a person takes such medication regularly it is likely that the virus in the body can be suppressed or pushed down to a level where it can no longer be found in the blood and the person cannot infect others. It is also possible for people who do not have HIV to take a small dose of such medication to prevent them from getting infected.

There are some groups of people that are more likely to be infected with HIV. These include people who inject drugs – mainly because they might share the same needle to inject drugs and pass infection between each other. Men who have sex with other men is another group where a larger proportion of people are infected compared with the general population. This is because of the higher risk of HIV transmission associated with anal sex. People who have sex in exchange for money or drugs – often called ‘sex workers’ – is another group that in many parts of the world is more likely to be HIV-infected than others. This applies to both men and women. The reasons that they might be at higher risk are complex and include the fact that people in this group have many partners and might not always use condoms when they are offered more money to not use one. Many people who exchange sex also inject drugs, which puts them at additional risk and is one example of how the groups just described might in some cases overlap – in this example just given, sex work overlaps with injection drug use.

This thesis studies these intersections between groups at high risk for HIV and looks at whether HIV infection is even more common in the subgroups where the main groups overlap. One study examines whether HIV is more common among women who inject drugs and exchange sex compared with women who inject drugs and do not exchange sex. Another study looks at whether HIV is more common among men who have sex with men and exchange sex compared with men who have sex with men and do not exchange sex. The third study looks at women who exchange sex and compares the proportion infected with HIV with women who are poor and have little education but who do not exchange sex. This is because in the United States, people who live in poverty and people belonging to some racial and ethnic minorities are more likely to be infected with HIV than others. Often, women who

exchange sex come from such populations and that is why we wanted to compare women who exchange sex with other women who did not, but who do live in poverty.

The final study included in this thesis looks at men who have sex with men and also inject drugs. This is a group with very high risk for HIV. Within this group I wanted to look at whether the likelihood that someone was infected with HIV was higher if their preferred drug of injection was methamphetamine (or 'meth') compared with heroin or other drugs. The reason this was interesting to look at is that meth is a drug often used by men who have sex with men during sex to increase desire and stamina. This could mean that in this subgroup many men might have HIV.

I worked at the Centers for Disease Control and Prevention (CDC) in Atlanta in the United States with a data collection system where we collected data from three main groups: people who inject drugs, men who have sex with men and people at high risk for HIV because they live in poverty and have a low level of education. Data collection happened each year from one of the groups which means that each group is studied every three years. In 2016 I led a special round of data collection focusing only on women who exchange sex for money or drugs. We collected data in around 20 large cities around the United States.

The populations surveyed are not always easy to find, which is why particular methods have been developed to recruit them into the study. For some of the populations studied, we recruited participants by starting off with a few people from the population and giving them a number of coupons that they can use to recruit other people into the survey. This is called 'respondent-driven sampling'. This means that people who for example inject drugs are asked to recruit other people who also inject drugs, and so on using the coupons. People who have many contacts are more likely to end up in the sample and to adjust for that we ask people who the survey how many other people they know who inject drugs, and that is taken into account during the analysis. To recruit men who have sex with men, we used a different strategy and mapped different types of venue where men who have sex with men would gather, such as gay bars or clubs. Study staff would then attend the venue and recruit men into the study randomly from there.

People who participated in the study were given a survey administered by an interviewer. The survey asked about their background in terms of, for example, education, homelessness, poverty and whether they have been in prison. People are then asked about their sexual behaviour, such as the number of partners in the previous year and if they used condoms or not. They are also asked about whether they had sex with other people in exchange for money or drugs. The survey also asks about whether they inject drugs and share needles with others

and whether they have been tested for HIV before. The survey is completely anonymous, and people are paid around 25 USD for taking it. Everyone who takes the survey is also offered an HIV test for which they are also paid. This means that when looking at the data collected, we can see whether people who report certain behaviour are more or less likely to be infected with HIV.

We found that among women who injected drugs, those who had sex in exchange for money or drugs with one or more male partners in the past 12 months were more likely to have HIV and not know about it than women who did not exchange sex (5.0% compared to 2.6%). We found something similar among men who have sex with men: those who had sex in exchange for money or drugs with one or more male partners in the past 12 months were more likely to have HIV and not know about it than the men who did not exchange sex (13.2% compared to 5.6%). We also found that women who exchange sex were almost three times as likely to be infected with HIV as women living in poverty and with a low level of education, and almost nine times as likely as women in the general population. This indicated that while women who exchange sex are more likely to have HIV than those in the general population, some of this could be explained by the fact that they themselves belong to populations living in poverty which are known to have higher risk for HIV due to several other factors.

Another important finding was that people who exchanged sex were more likely to have many sexual partners with whom they did not use condoms. People who exchanged sex were also more likely to engage in risky behaviours such as sharing needles with others. This means that they are at risk of getting infected with HIV, and also – if they already have HIV – of passing it on to other people.

The final study found that among men who have sex with men and inject drugs, those who primarily injected meth were almost 50% more likely to have HIV than those who primarily injected other drugs. The analysis also showed that this was probably due to the men who injected meth having more sexual partners with whom they did not use a condom.

These findings suggest that it is important to ensure that services that prevent HIV transmission reach the populations studied here such as people who exchange sex and men who have sex with men and inject methamphetamine. This includes reducing sexual risk behaviours and promoting the use of condoms. It also includes ensuring that people who inject drugs can get clean needles for free so that they do not use needles that have already been used by someone else. Also important for people who inject drugs is to help them stop using drugs – this could be through methadone treatment, for example. This means that

people who inject drugs are given a substitute by mouth for the drugs that they normally inject so that they do not inject drugs and share needles with each other.

It is also very important to ensure that people are tested for HIV frequently – every year at least but ideally more often. Once they are diagnosed, it is important to make sure that they are followed up with health care services and get treatment. This can sometimes be challenging for people who live in unstable situations such as those who inject drugs or are homeless. It is important to make sure that those infected are treated, both for their own sake to make sure that they stay healthy, and to prevent transmission of HIV infection to others.

One particular challenge is targeting services to the populations studied is that because they often have more than one set of risk factors – for example they are MSM who also inject drugs, they may not get all the help they need from one type of service that is dedicate mainly to MSM or mainly to people who inject drugs.

Finally, it is important to understand that some of the reasons that people are at risk of getting HIV are related to factors of poverty such as homelessness, a lack of education and unemployment. These factors can mean that people start exchanging sex to get money, or that they are more likely to start using drugs. Addressing these bigger societal factors is part of making sure that people stay safe and free from HIV.

ABSTRACT

Background

The HIV epidemic in the United States (US) is mainly concentrated in so-called ‘key populations’ including men who have sex with men (MSM) and people who inject drugs (PWID). In addition, other groups such as people of low socioeconomic status and people belonging to some ethnic minorities have a higher prevalence of HIV. Globally, people who exchange sex for money or drugs are recognised as another key population with high HIV prevalence, but there is limited recent data from rigorous studies in the United States on HIV prevalence among people who exchange sex.

High prevalence among certain groups may be a combination of individual risk behaviours such as condomless sex, drug use and unsafe injection practices, and structural factors such as poverty, violence and residential segregation that can impact HIV risk indirectly. This thesis examines whether, among populations known to be at high risk for HIV, prevalence is higher among those who belong to more than one key population or vulnerable group and for whom several risk factors intersect. Furthermore, it examines sociodemographic factors and sexual and drug-use risk behaviours in these populations and how they may be relevant to HIV acquisition and transmission.

Methods

Data

I worked with the US National HIV Behavioral Surveillance System (NHBS), which is a surveillance system that collects data from three populations at high risk for HIV in annual rotating cycles: men who have sex with men (MSM), people who inject drugs and heterosexuals at increased risk of HIV (referred to as ‘IDU’ and ‘HET’, respectively). We recruited participants for all three cycles in around 20 large US cities on an annual rotating schedule. For the IDU and HET cycles, we use respondent-driven sampling (RDS), which is a sampling method specifically designed to reach hidden populations and approximate a random sample and where participants recruit each other using coupons. In 2016 I led a pilot data collection focused specifically on women in five cities who exchange sex, also using RDS. During the MSM cycle we recruited participants through venue-based sampling which allows random sampling of venues in a city, time-slots within venues and individual men attending the venue. In all cycles participants take an interviewer-administered survey asking about demographic characteristics, sexual and drug-use risk behaviours and access to services such as frequency of HIV testing and use of health care and preventive services. Participants are also offered a rapid HIV test and receive an incentive for taking the survey and the HIV test.

Analysis

For Papers 1 and 2, I looked at women who inject drugs and MSM to examine whether people who exchange sex are more likely to be HIV-infected, including being HIV-positive but unaware of one's positive status (HIV-positive–unaware), compared with those who do not exchange sex belonging to the same populations. Paper 3 estimates the HIV prevalence among women who exchange sex and compares it with the prevalence among women of low socioeconomic status who do not exchange sex from the same cities three years earlier. In these papers, exchange sex is defined as having had oral, vaginal or anal sex with a male partner in the past 12 months. In Paper 4 I used a subset of the IDU survey data to examine whether MSM who inject drugs (MSM–IDU) are more likely to be HIV infected if they report methamphetamine as their primary drug compared with other drugs.

For bivariable and multivariable analyses in Papers 1, 2 and 4 I used generalised estimating equations (GEE), in PROC GENMOD in SAS v. 9.2 or 9.3. The GEE method enables analyses of clustered data where observations in a cluster are thought to be more similar to each other than to other observations. For Paper 3 we used RDSAT to estimate the prevalence of HIV and risk behaviours among women who exchange sex.

Results

In Paper 1, 10% of women who injected drugs and exchange sex were HIV infected. There was no statistically significant difference in HIV prevalence between those who exchanged sex and those who did not (10.0% vs 7.4%, $P = 0.33$). However, those who exchanged sex were more likely to be HIV-positive but unaware of their positive status (HIV-positive–unaware) compared with those who did not exchange sex: 5.0% vs 2.6% ($P = 0.01$). This difference remained significant in multivariable analysis with an adjusted prevalence ratio (aPR) of 1.97 (95% CI 1.31–2.97).

In Paper 2, HIV prevalence among MSM who exchanged sex was higher than among MSM who did not (29.1% vs 17.7%, $P < 0.001$). However, this difference became non-significant in multivariable analysis. MSM who exchanged sex were also more likely to be HIV-positive–unaware than those who did not exchange sex (13.2% vs 5.6%, $P \leq 0.001$) and this difference remained in multivariable analysis (aPR 1.34, 95% CI 1.05–1.69).

In Paper 3, the prevalence of HIV among women who exchanged sex was 4.9%, approximately three times as high as the prevalence of HIV among women of low socioeconomic status who did not exchange sex (1.6%), and almost nine times as high compared to women in the general population (0.55%).

In Paper 4, MSM who primarily injected methamphetamine were significantly more likely to be HIV-positive (29.3%) than MSM who primarily injected other drugs (15.5%, aPR 1.48, 95% CI 1.08–2.03). This association was mediated by sexual risk behaviours, but not drug-use risk behaviours.

Among people who exchange sex, and among MSM who inject methamphetamine, sexual and drug-use risk behaviours were common, putting people at risk for HIV acquisition as well as onward transmission. Exchange sex was furthermore common among people living in poverty, homelessness or with other markers of low socioeconomic status.

Conclusions

The populations studied in this thesis are already known to be at high risk for HIV. This thesis demonstrates that HIV prevalence – in particular the prevalence of being HIV positive but unaware of one's status – is high among people who belong to more than one key population or vulnerable group. Sexual and drug-use risk behaviours are common. To address the risk for HIV acquisition and onward transmission it is essential to consider a variety of services around prevention, including harm reduction, and testing and linkage to care and treatment. However, narrowly targeted services focusing on a single key population such as people who inject drugs or MSM may not adequately address the needs of those who belong to more than one key population. Additionally, the higher-order structural factors that put individuals and communities at risk for HIV must be addressed.

LIST OF SCIENTIFIC PAPERS

1. **Nerlander LM**, Hess KL, Rose CE, Sionean C, Thorson A, Broz D, et al. Exchange sex and HIV infection among women who inject drugs—20 US cities, 2009. *Journal of acquired immune deficiency syndromes (1999)*. 2017;75(Suppl 3):S333.(1)
2. **Nerlander LM**, Hess KL, Sionean C, Rose CE, Thorson A, Broz D, et al. Exchange sex and HIV infection among men who have sex with men: 20 US cities, 2011. *AIDS and Behavior*. 2017;21(8):2283.(2)
3. **Nerlander LM**, Handanagic S, Hess KL, Lutnick A, Agnew-Brune CB, Hoots BE, et al. HIV Prevalence Among Women Who Exchange Sex for Money or Drugs—4 US Cities. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2020;84(4):345-54. (3)
4. **Nerlander LM**, Hoots BE, Bradley H, Broz D, Thorson A, Paz-Bailey G, et al. HIV infection among MSM who inject methamphetamine in 8 US cities. *Drug and alcohol dependence*. 2018;190:216-23. (4)

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LIST OF ABBREVIATIONS

aPR	adjusted prevalence ratio
ART	antiretroviral therapy
ARV	antiretroviral
CDC	[US] Centers for Disease Control and Prevention
CI	confidence interval
DAG	directed acyclic graph
ECDC	European Centre for Disease Prevention and Control
DBS	dry blood spot
DHAP	Division of HIV/AIDS prevention GA Georgia (US state)
GEE	generalised estimating equations
HET	heterosexuals of low SES, sampling population in NHBS
HET-HRW	heterosexual women of low SES who exchange sex ('high-risk women')
HHS	Health and Human Services
HIV	human immunodeficiency syndrome
HPV	human papillomavirus
IDU	injection drug use; also the name of the NHBS cycle among PWID
MAT	medication-assisted treatment
Meth	methamphetamine
MSM	men who have sex with men; also the name of the NHBS cycle among MSM
NHBS	National HIV Behavioral Surveillance
NHSS	National HIV Surveillance System
PWID	people who inject drugs
PR	prevalence ratio
PrEP	pre-exposure prophylaxis
RDS	respondent-driven sampling
SD	standard deviation
SES	socioeconomic status
SSP	syringe service programmes
STI	sexually transmitted infection
US	United States
USD	United States dollar
VBS	Venue-based sampling

1 INTRODUCTION

Several key population groups in the United States (US) have a high prevalence of HIV, including men who have sex with men (MSM) (5) and people who inject drugs (PWID) (6). Globally, it is known that there is a high prevalence among people who exchange sex for money or drugs and although some data is available from the United States there is a lack of recent, rigorous studies (7, 8).

Some people may belong to more than one such key population – for example MSM who also exchange sex – and several factors may intersect to put them at particularly high risk for HIV acquisition as well as for transmission to others. Similarly, subpopulations within key populations may have a higher prevalence of HIV due to certain factors such as the type of drug used. In order to deliver appropriate services for HIV prevention, diagnosis and treatment it is important to understand which groups are at particularly high risk for HIV acquisition and transmission.

This thesis examines whether, among populations known to be at high risk for HIV, groups of people for whom several risk factors intersect have a higher prevalence compared to other members of that population. Furthermore, it examines sociodemographic factors and sexual and drug-use risk behaviours in these populations and how they may be relevant to HIV acquisition and transmission.

This is done in four papers using data collected from populations at high risk for HIV in the US. The first paper looks at HIV prevalence in relation to sex in exchange for money or drugs among women who inject drugs; the second examines exchange of sex among MSM; the third compares women who exchange sex with others of low socioeconomic status; and the final paper focuses on HIV prevalence among MSM who inject methamphetamine compared with MSM who inject other drugs. The focus is to understand differences in HIV prevalence and possible factors related to risk for both acquisition of infection as well as the risk for onward transmission in order to appropriately target services.

Much of the prior work examining HIV prevalence in these populations is limited to single cities and use convenience sampling. The data used for the papers here come from multiple US cities, sample sizes are large and data collected rigorous methods.

2 LITERATURE REVIEW

2.1 KEY POPULATIONS

Worldwide, so-called ‘key populations’ are important in the understanding of local epidemics. Key populations are defined as populations that ‘due to specific higher-risk behaviours are at increased risk of HIV irrespective of the epidemic type or local context’ (9). These include people who inject drugs (PWID), men who have sex with men (MSM), sex workers, people in prisons and other closed settings, and transgender people. It is recognised that to achieve a sustained response to HIV, the needs of key populations must be addressed. Key populations are not only at disproportionate risk because of individual behaviours but may also face legal and social barriers such as stigma that increase their vulnerability to HIV. Additionally, they face barriers in accessing care. Many people engage in more than one type of risk behaviour – for example, MSM who also inject drugs, or PWID who sell sex – and such groups may have a particularly high prevalence of HIV. Related to key populations, ‘vulnerable populations’ are groups that may be more vulnerable to HIV in certain settings but which are not equally affected across all settings. These groups are also important to identify in order to address their HIV risk (9).

An effective response to HIV is dependent on good data on the affected populations. The very nature of many key populations and some vulnerable groups means that they are not easily reached, and it is challenging to get an accurate picture of the disease burden and behaviours. While national case surveillance data may collect information on transmission category from newly diagnosed cases (10), population prevalence or rates are hard to calculate as underlying population sizes of different key populations are often unknown due to their hidden nature. Additionally, members of key populations may face barriers in accessing HIV testing which results in delayed diagnoses and an underestimation of the true burden of disease. Prevalence surveys together with estimates of population sizes are needed (11).

People belonging to key populations are more likely to be HIV-infected, but some people may belong to more than one key population, such as PWID who are also sex workers. Additionally, there may be subgroups within key populations with behaviours or vulnerabilities that further increase their risk for HIV acquisition. This thesis uses the US context to explore HIV prevalence at these intersections where people may be at additional risk for HIV due to specific combinations of sexual activity, drug use or contextual factors.

2.1.1 The HIV epidemic among key populations in the United States

The numbers of new HIV diagnoses are reported annually in the US to the National HIV Surveillance System by transmission category, age and other demographic characteristics. In 2019 there were an estimated 38 801 new HIV diagnoses in the US. Male-to-male sexual contact accounted for 65% of these, heterosexual transmission for 23%, and injection drug-use for 7% (12). The number of newly diagnosed HIV infections attributed to injection drug use has remained stable in recent years (12), although HIV prevalence remains high among PWID, in particular among subgroups such as racial/ethnic minorities (13-16). There is also evidence of high rates of transmission associated with injection in rural areas (17).

Men who have sex with men and who inject drugs are at particularly high risk for HIV, both from sexual and injection-related risk behaviours. Male-to-male sexual contact *and* injection drug use accounted for 4% of new diagnoses in 2019 (12). Data gathered from injection drug users in 23 US cities in 2018 found an HIV prevalence of 24% among male PWID who reported male-to-male anal sex in the previous 12 months, compared with 6.4% among all PWID (18). HIV prevalence among MSM in the same 23 US cities in 2017 was 23% (19).

There are disparities within the US with regards to which populations have the highest prevalence of HIV or where the rate of new diagnoses is increasing. Overall, the rate of new diagnoses among African Americans is 45.0 per 100 000 population, compared with 21.5 among Hispanics and 5.3 among whites (12). While MSM as a group are highly affected by HIV there is disparity by race/ethnicity even within this population. Among MSM, 38.8% of African-American MSM sampled by the National HIV Behavioral Surveillance (NHBS) in 2017 tested positive for HIV compared with 14.8% of white and 19.3% of Hispanic MSM (19). From 2008 to 2014, HIV infections declined by 18% among white MSM, stabilised among black MSM but increased by 20% among Latino MSM (10).

Sex in exchange for money or drugs is not a specific transmission category reported by US case surveillance data and hence less is known about the burden of disease among people who engage in exchange sex. A meta-analysis of published studies in the US found a pooled estimate of 17.3% (95 % CI: 13.5–21.9%) but many studies are old and only look at single cities (8).

To address the HIV epidemic in the US it is essential to understand not only prevalence and incidence among key populations but also the behavioural and contextual drivers of HIV risk. Specific subpopulations within the key populations may have overlapping risk factors such as, for example, MSM who also inject drugs, or PWID who also exchange sex. Understanding the intersection of risk in different subpopulations can help to identify correlates with HIV

prevalence which could help guide interventions and resource allocation. Additionally, people who belong to more than one risk group or key population may have unique sets of needs that are not addressed by standard interventions targeted to one population only.

2.2 DETERMINANTS OF HIV RISK AMONG KEY POPULATIONS

The following section examines two determinants of HIV risk relevant to the populations studied in this thesis: exchange sex and drug use. The focus is on the US but with relevant example from other contexts as appropriate.

2.2.1 Exchange sex

Most people might have a certain image of a ‘sex worker’, perhaps it is a woman walking the streets or a ‘high-end’ escort meeting clients in a bar – likely originating from the way sex workers are portrayed in the media. Even though most sex workers are female and sell sex to male clients, men and transgender people also sell sex and may do so to people of any gender (20). Among people who sell sex, there is great heterogeneity in terms of how much income they derive from sex work, how and where they recruit clients, whether they exchange sex for money, drugs or other items. These factors lead to difficulties in specifying and quantifying the populations who engage in exchange sex.

People who exchange sex often have many different factors in their lives that put them at risk for HIV other than the direct risk associated with condomless sex with clients (21). These include factors such as poverty, access to care, violence and drug use. These factors can either be directly related to HIV risk, such as unsafe injection practices, or be drivers of sexual risk, such as financial need leading to increased sexual risk taking. This section will look more closely at the different kinds of sex work in the US and the associated terminology, the prevalence of sex work in the US population and what is known about the prevalence of HIV among those who sell sex.

Transgender women who sell sex should be thought of as a population distinct from female and male sex workers (or cis-female and cis-male sex workers) as they have unique needs and vulnerabilities (22). Transgender sex work is beyond the scope of this thesis and the focus is on men who are born male and identify as male, and women who are born female and identify as female. The methods section provides more detailed definitions of the specific variables used for each analysis and how gender and sexual orientation was considered in recruitment and data analysis.

2.2.1.1 *Sex work definitions*

No clear definition exists of what constitutes a sex worker. In reporting data on sex workers to the United Nations General Assembly, countries are requested to use the definition of ‘female, male and transgender adults aged over 18 years who sell consensual sexual services in return for cash or payment in kind, and who may sell sex formally or informally, regularly or occasionally’(23). This is a very broad definition and is suggestive of the heterogeneity in this population which will be discussed below, mainly with reference to the US context.

Vanderpitte et al. suggested that only women with large numbers of partners who earn some or all of their living through exchange sex should be considered sex workers for surveillance purposes (24). However, for the purposes of determining HIV risk, this narrow definition leaves out women who may be at risk for HIV because of exchange sex but who do not have high numbers of partners. To complicate matters further, in some settings sex in exchange for money or goods is commonly accepted in sexual relationships by a wide range of women, irrespective of their socioeconomic status. This phenomenon has mainly been described in locations outside the US, such as sub-Saharan Africa (25).

The term ‘transactional sex’ is sometimes used and refers to economically motivated relationships more broadly, recognising that economic motivations are present in a wide range of relationships beyond what is considered more commercial sex work. Dunkle et al. looked at a random sample of single American women and found that 22% of African-American women and 11% of white women reported starting a relationship because of economic considerations and around a third of women reported staying in a relationship longer because of economic considerations. Thirteen per cent of the African-American women surveyed and 3% of white women reported having transactional sex in their lifetime with someone who was not a regular partner due to economic considerations. Having transactional sex in their lifetime with someone who was not a regular partner was associated with several markers of partner risk behaviours such as concurrency and incarceration. Of those who reported transactional sex with a non-regular partner, only 42% reported sex for money or drugs (26). This highlights that even if we focus on the behaviour of sex in exchange for money, drugs or other items, there is a considerable spectrum that includes transactions easily defined as money in return for sex as well as situations and relationships where the financial concerns are part of the motivation for the sexual behaviour but in a less direct way. All of these situations may put people at risk of HIV, depending on the broader context.

The term ‘survival sex’ is occasionally used, but it mainly refers to people who sell sex out of extreme need to cover the basic necessities of life – items needed to survive (27). In North

America the term is sometimes used in the context of homeless and runaway youth, but it is not clear what proportion of adults who exchange sex in the US could be defined as engaging in survival sex (28, 29).

Among men and women who exchange sex there is also tremendous variation in terms of the economic circumstances under which they work. Some may be homeless or dependent on drugs and engage in exchange sex in return for small amounts of money or drugs (30, 31). Some may exchange sex to cover the basics in life whereas others exchange sex to be able to afford a better lifestyle or avoid student debt. The website ‘Seeking Arrangement’ facilitates so-called ‘Sugar Daddy dating’ where usually younger people may find older people who are willing to give money and gifts in exchange for company and, although not stated explicitly, perhaps sexual services. The terms ‘kept boy/sugar daddies’ is also used for male sex workers (32). Highlighting the tremendous variation in terms of circumstance of how sex is exchanged, there are examples of women who provide more high-end escort services where they may charge thousands of dollars for a night and where the service may include travelling with clients on vacation or business trips in addition to sex (33).

With regards to male sex workers, those working outdoors or on the streets have been shown to be more likely to identify as straight and to have higher rates of drug use and socioeconomic challenges and to have less positive attitudes towards sex work. At the other end of the spectrum, men working as escorts or call boys are more likely to identify as gay or bisexual, make more money and have more positive attitudes towards sex work (34).

This heterogeneity makes for a challenging topic to study. This thesis focuses on the behaviour – exchange sex – as that is what was asked about in the surveys used rather than how the people carrying out the activity define themselves. The term ‘men/women who exchange sex’ is used, which refers to the exchange of sexual services for money or drugs. As mentioned above, transgender people who exchange sex are beyond the scope of this thesis due to the fact that they were not eligible for participation in two the data sets used for analyses and present in too small numbers in the third data set.

2.2.1.2 Different ways in which people who exchange sex find clients

Another dimension that introduces heterogeneity into the population of men and women who exchange sex is how and where they find clients. Lever et al. outlined three basic methods by which sex workers make their availability known to clients: (1) being present in a location where clients will either notice them or expect to find them; (2) advertising their availability in a medium; and (3) through referrals (35).

Female sex work in the US and elsewhere has also been described as either ‘direct’ or ‘open’ versus ‘indirect’. Women who earn their living by selling sex are included in the ‘direct’ category and may define themselves as sex workers, although this is not necessarily the case. By contrast, ‘indirect’ sex work can be more hidden and informal and includes women who may have other professions and use sex work to supplement their income (24, 27). Others, studying the New York City context, have used the term ‘indoor’ sex workers to describe women who do not work on the streets but for whom the entire process, starting with solicitation, occurs indoors (36). MSM also use similar ways to recruit clients such as on the street and online and the division between indoor and outdoor sex workers has also been used here, with the indoor sex workers frequenting gay-identified spaces (34, 37).

Some people find clients on the street or ‘stroll’; this is probably the most common popular image of people – in particular women – who exchange sex in the US. People may also solicit in other public areas such as at bus stops, in stores, in parks or outside sex shops. Clients may also be approached at entertainment venues such as clubs and bars, or at more dedicated sex-related venues such as strip clubs (27). In some parts of the US, so-called ‘cantinas’ are a common location for women to recruit clients (35).

Brothels are another iconic sex work venue globally. There, solicitation and exchange take place in the same venue. It is challenging to describe the distribution of brothels as these establishments are illegal in most of the US. The ‘ranch’ style establishments in Nevada, where sex work is legal in some counties, are the exception rather than the norm (38). Male sex workers may also be found in brothels but their numbers are relatively small compared with female brothel-based sex workers (34).

The internet has facilitated the market of exchange sex and online sex work and solicitation of clients online may be increasingly common (36, 39-43). People who sell sex can reach a larger audience more efficiently, and the risks of arrest are lower for sex workers who solicit online compared with those who solicit on the streets. Clients are also able to choose from a wider range of sex workers and avoid the risk of arrest while doing so. Some websites offer the possibility of reviews and referrals, incentivising individual sex workers to build their reputation. Online platforms allow sex workers – male and female – the possibility for some level of interaction with and vetting of clients via email or phone prior to meeting in person and may even allow workers to review client ratings (32, 34, 42, 44, 45). During the COVID-19 pandemic data showed a temporary decrease in the number of online adverts for sex work (46). However, some sex workers were able moved their work online and offered other types of services (47).

It is hard to find reliable data on how common each location or method of recruitment is within the population that exchanges sex. People who recruit clients on the street are the most visible whereas other populations are more hidden. Additionally, with the increase in the use of technology the landscape is shifting and Cunningham et al. argue that online soliciting has not only displaced some sex workers from the streets but has expanded the market of both sex workers and clients because of the relative safety of online soliciting (42).

Regardless of how they find clients, sex workers may work independently or for a pimp (20). In some cases, the lines are blurred between who constitutes a pimp and who is a regular partner or boyfriend. Pimps may start sexual relationships with the women that work for them, whereas in other cases the relationship starts out as a regular partnership and only later on transforms into that of a pimp and sex worker (31).

In summary, there is a great deal of heterogeneity within the populations that exchange sex both in terms of the frequency of exchange sex, what sex is exchanged for, their financial circumstances and how they find clients.

2.2.1.3 Prevalence of exchange sex

It is challenging to quantify the number of people who exchange sex in the US, or indeed anywhere. Not only are there inherent difficulties in sampling this hidden and stigmatised population (24), but as discussed previously there is no clear definition of what a sex worker is. A 2006 systematic review of various data sources aiming to determine the size of the female population who exchange sex worldwide found no data for North America specifically. However, estimates for Western Europe ranged from 0.1% in Sweden to 1% in Austria (24).

While it is near impossible to estimate the number of sex workers in the US population, there exists some data on the prevalence of the *behaviour* of exchanging sex for money or drugs. A 2010 survey of the general population found that 6.2% of all men and 0.8% of all women report that their last partner was a transactional partner (48). Cunningham et al. quote survey evidence from the General Social Survey that shows that 0.79% of people in 2008 reported having paid for, or received pay for, sex during the past year. This is an increase relative to the 0.54% reported in 1998, and Cunningham et al. suggest that they may be due to an augmentation of the market of exchange sex due to the increase in online solicitation (42). The main limitation of this data is that the surveys did not distinguish whether the respondent gave or received something in exchange for sex.

General population surveys such as these cited above have limitations, however. Many people who sell sex are marginalised in different ways, such as being homeless, and may not be reached by a general population survey. Furthermore, both buying and selling sex are highly stigmatised activities and respondents may not report this behaviour. While sex workers in general are hard to reach, those who work outside the locations and venues where sex workers are usually found may be particularly hard to reach (24). However, it is possible that general population surveys through random digit dialling, or mail-out surveys are more likely to reach those engaged in more indirect sex work as those men and women are probably part of regular society in a way that some full-time sex workers may not be, due to homelessness and drug use. There is evidence that sex workers are under-represented in general population surveys on the number of sex partners as is evident from the fact that when this is corrected for, the discrepancy in the number of reported partners between men and women disappears (49).

Other surveys have targeted more specific populations in the US; a cross-sectional survey of young women attending family planning clinics in Northern California found that 8.1% had ever traded sex for money or other resources (50). Data collected anonymously among heterosexuals of low socioeconomic status (SES) using respondent-driven sampling (RDS) would have the potential of reaching more marginalised populations. This survey found that 15% of HIV-negative women reported receiving, and 11% of HIV-negative men reported giving, money or drugs in exchange for sex with a casual partner in the previous 12 months. Among all HIV-positive respondents, 33% reported exchange sex (51). With regards to PWID, studies looking at the prevalence of exchange sex specifically in this population report that between 26 and 39% reported some exchange sex; however both of these studies are old. (52, 53).

With regards to specific studies on the prevalence of exchange sex among men, there is limited data available from the US, whereas more recent data is available from Canada and Australia. A survey of gay and bisexual men in Vancouver, Canada, found that 22% reported ever receiving drugs, money or goods for sex (54). Seven per cent of MSM recruited through venue-based sampling in Ontario reported receiving money and 5% reported receiving drugs and other non-monetary items in exchange for sex in the previous 12 months (55). A prospective cohort study of MSM aged 18–30 in Vancouver found that 16% reported exchange sex (56). In the 2009 Australian Pleasure and Sexual Health survey, 4.3% of gay and bisexual males reported having been paid for sex with another man in the previous 12 months (57).

Data on exchange sex among MSM in the US is largely confined to local studies in high-risk subpopulations of MSM. Such studies have found that among drug-using or homeless MSM

around 50–68% had a lifetime history of exchange sex, with either men or women (58-60), and 22% had had male-to-male exchange sex with one of their three most recent partners (61). Among single and non-monogamous MSM recruited at community events, 37% had a lifetime history of exchange sex (62). A recent study using a cohort study of MSM between 18 and 45 years of age in Los Angeles found that 17% reported recent transactional sex across all study visits. Interestingly, those who reported receiving money, drugs or shelter in exchange for sex were also more likely to provide these items to others in exchange for sex (63).

In summary, data from general population surveys indicates that around less than 1% of women exchange sex whereas studies on specific populations found much higher prevalence of exchange sex among women. With regards to men who sell sex, studies have found that the prevalence of exchange sex ranges from 17 to 68% depending on the time perspective chosen.

2.2.1.4 HIV prevalence among people who exchange sex

In many parts of the world, female sex workers have a high prevalence of HIV. Globally, it is estimated that 10.4% (95% CI 9.5–11.5) of female sex workers are HIV-positive (7). There is limited recent data on HIV prevalence among women who exchange sex in the US. A meta-analysis of studies reporting HIV prevalence published between 1987 and 2013 provided a pooled estimate of 17.3% with estimates from single studies in this review ranging from 0.3 to 30%. Many studies are decades old and only three look at sex workers beyond a single city or state (8). Apart from four studies (64-67), the vast majority use convenience sampling. Participants in most of these studies were a mix of women who were current or former injectors, and some who had never injected drugs. A *Lancet* review of studies globally found 10 studies from the US published between 2006 and 2017, with HIV prevalence estimates ranging from 0.7 to 23.1% (7). Six studies are included in this review that were not included in the meta-analysis by Paz-Bailey et al. These are all limited to single cities, except the study by Braine et al although that study is limited to women attending syringe exchange programmes (68). Three studies used random sampling (68-70). This review estimates a prevalence of 7.4% for Western and Central Europe and North America but no specific estimate is given for the US. In summary, empirical data on the prevalence of HIV among women who exchange sex in the US is largely limited to older studies, single city studies, studies using convenience sampling or studies among women who inject drugs.

There is mixed evidence with regards to the importance of women who exchange sex in HIV transmission. Estimations are made more challenging by the fact that there is not a clear definition of sex work or exchange sex in use (71). Some evidence from modelling and other

analyses indicate that women who exchange sex play an important role in HIV transmission among heterosexual populations globally but limited evidence is available from the US (21, 72-76). Pruss-Ustun et al. have estimated that 15% of HIV cases in the general female adult population globally can be attributable to unsafe female sex work (Pruss-Ustun, Wolf et al. 2013), but the figure for North America is substantially lower at 0.6%. This may be an underestimate as the authors assumed that all HIV in female sex workers who inject drugs is due to unsafe injection practices, which is a very conservative estimate as other studies have shown that sexual risk behaviours contribute substantially to HIV among PWID (77). Notably, this figure refers only to infections that occur in female sex workers and that can be attributed to sex work and not the infections transmitted to female partners of clients.

Male sex workers receive less attention than female sex workers and HIV risk in this population has not been very well researched (7). A 2015 *Lancet* review of international data on male sex workers found three studies from the US with estimates of HIV prevalence ranging from 14 to 31% (22). Two of these were confined to high-risk subpopulations of MSM such as street sex workers (78) and street-recruited MSM-IDU (59), whereas one study recruited more widely using internet and street sampling, although the sample was small at $n = 31$ (37). Another review found only one study from the US (in Houston, Texas) where the prevalence among male sex workers was 26% (32, 79). A 2006 study among male sex workers attending a peer-based clinic in San Francisco found that 16% were HIV-positive (80).

Associations between exchange sex and higher risk of HIV infection among MSM have been reported in several parts of the world. Findings are, however, not always consistent with HIV prevalence in some studies and regions being higher among MSM in general than among male sex workers (22). Exchange sex was associated with an increased prevalence of HIV infection among MSM recruited using venue-based sampling in Ontario (55). In the prospective cohort study of MSM aged 18–30 years Vancouver mentioned earlier, HIV prevalence was significantly higher among those who exchanged sex and HIV incidence at baseline (7.3% vs 1.1%) and the same was true for incidence (4.7 vs 0.9/100 person-years) (56). Data from the US is mainly limited to higher-risk MSM populations: a marginally housed and homeless adults in San Francisco found that MSM who reported exchanging sex had higher HIV prevalence, and a study among young MSM who also injected drugs found that HIV prevalence was associated with a higher number of paying male partners (59, 60). A 2019 study using a cohort study of MSM between 18 and 45 years of age in Los Angeles found that HIV viral load was independently associated with transactional sex (63). Modelling studies on male sex workers are limited as data is scarce on this population (72). A study in Peru estimated that 3.4% of infections over 10 years in the MSM population could be

averted by providing pre-exposure prophylaxis (PrEP) to 20% of male sex workers (81). Some evidence from MSM indicates that those who solicit on the street were found to have higher rates of HIV risk behaviours compared with other MSM who exchange sex (37).

2.2.1.5 Risk of acquisition and transmission

When considering the risk for acquisition and transmission it is important to consider that these differ depending on gender and type of sex. For vaginal sex without a condom, the risk of HIV acquisition of an uninfected woman from a male partner is approximately double that of the risk of transmission from an infected woman to an uninfected man (8 and 4 per 10 000 exposures respectively). In terms of anal sex, the risk of receptive anal sex is very high (138 per 10 000 exposures) but considerably lower for insertive anal sex (11 per 10 000 exposures) (82). These numbers have implications when considering the risks for HIV acquisition and transmission for people who exchange sex. For women who exchange sex the risk of acquisition is larger (if uninfected) than the risk of transmission (if infected). For MSM who exchange sex, risk for acquisition is substantially higher if they are the receptive partner and for transmission if they are the insertive partner.

High HIV prevalence among people who exchange sex is concerning for several reasons. Firstly, if HIV infected people are not diagnosed and linked to care their health is at risk given that the outcomes for HIV-positive people is better the earlier they are started on antiretroviral therapy (ART) (83). Secondly, a high prevalence indicates that others in the same population who are not yet HIV-positive or who enter that population (for example start exchanging sex) may be at risk for HIV acquisition. Thirdly, people with undiagnosed and/or untreated HIV are at risk of transmitting HIV to others, both clients and other partners.

The risk for acquisition can be modified by use of pre-exposure prophylaxis (PrEP), which refers to the use of antiretroviral drugs by people who are not HIV-infected to prevent the acquisition of HIV. PrEP has been shown to be effective across different populations but that adherence is important for it to be effective (84). Use of PrEP has increased in recent years but a meta-analysis found that only 4.2% of US MSM used PrEP before sex. The proportion of PWID who used PrEP was lower at 3.7% (85). Use of PrEP by people who exchange sex would substantially reduce their risk of acquisition, but there is little data on the prevalence of PrEP use among populations who exchange sex.

2.2.1.6 The importance of HIV status awareness and treatment

Ensuring that people with HIV are tested and become aware of their status is key in order to link them to care and treatment. Early ART is essential for the long-term health outcomes of

those infected (83). Treatment is also a key strategy to prevent transmission to others as HIV-positive people with undetectable viral load have been shown to not transmit infection (86, 87). As antiretroviral treatment has become more widespread this would also affect the contribution of sex work to HIV transmission and highlights the importance of ensuring that key populations are tested and linked to care.

Reductions in risk behaviours is still important, however, as not all people aware of their status are on treatment and virally suppressed. In the US only around 60% of those diagnosed with HIV have sustained viral suppression (88). There is evidence that HIV-positive people who are aware of their infection may reduce their sexual risk behaviours which may also be important for reducing HIV transmission (89). A meta-analysis found that the prevalence of vaginal or anal intercourse without a condom was an average of 53% lower in HIV-positive people who were aware of their status compared with those who were not. When adjusting the data to only look at condomless intercourse with partners who were not HIV-positive the reduction was even larger at 68%. A more recent systematic review also found that HIV-infected aware people are less likely to ‘not always use condoms’ compared with those unaware (90). There are several limitations to the studies looking at sexual behaviours such as recall and social desirability bias, as well as confounding differences between groups – people who are more likely to take sexual risks may also be less likely to seek medical care and testing.

Many of the studies looking at the difference in sexual risk behaviours between those aware and those unaware are before the era where HIV-positive persons on ART were considered to be unable to transmit infection. It is possible that if the studies were to be repeated today, there would be less difference between in behaviours between HIV-positive people who are aware and those who are unaware of their infection. However, even if those aware and unaware of their infection are found to have similar numbers of partners, most of those aware of their infection would likely be on treatment and therefore essentially unable to transmit. This highlights yet again the importance of early diagnosis and linkage to care and treatment.

2.2.1.7 Why are people who exchange sex at risk for HIV?

The risk for HIV acquisition and onward transmission is high for both men and women who exchange sex due to behavioural, biological and structural factors. Men and women who exchange sex often have large numbers of partners and have sex without using a condom (20, 21, 56, 91-93). Condom use may be difficult to negotiate if people are offered more money to not use a condom in particular if they are in a position of drug dependency or economic

hardship (22, 37, 92, 93) and risk taking in this context has been shown to correlate with financial need (94).

With regards to biological factors, sexually transmitted infections (STIs) are prevalent among both men (22, 95) and women (96, 97) who exchange sex. Several STIs including gonorrhoea, chlamydia, syphilis, genital ulcers and certain kinds of HPV infection may increase the risk for HIV transmission (98, 99).

In the US context, several socioeconomic factors that are associated with a higher risk for HIV infection (26, 100, 101) are more common among women who sell sex, such as poverty, having less than a high-school education, being homeless or having unstable housing (26, 66, 102-105). Several of these same factors have also been shown to be more common among MSM who sell sex (22, 56, 58, 60, 63, 106, 107). These factors, together with stigma against women and men who exchange sex, create barriers to preventive services, STI diagnosis and treatment, and delayed diagnosis and treatment of HIV (22). In most of the US, selling sex is an illegal activity, creating additional barriers to accessing services. Men who sell sex to other men may face additional stigma for being gay, and men and women who inject drugs face additional stigma and barriers associated with that behaviour (22, 108).

For many people, a lack of viable alternatives may cause them to start exchanging sex and this also makes it challenging to leave sex work (31, 36). As prostitution and drug use are both illegal in most US states, many women who inject drugs and exchange sex face incarceration at some point. An arrest history and a criminal record then make it even more difficult to obtain housing, state benefits and employment (109-111), potentially trapping people in a position where they resort to exchange sex.

People who exchange sex face other challenges at several levels that puts them at risk for HIV acquisition and transmission. These include coercive relationships with their pimps or boyfriends, a lack of safe spaces to work and legal frameworks and policing practices that push women towards unsafe locations for work, and violence from clients (93).

A meta-analysis of 11 studies found that sex workers who had been exposed to repressive policing practices were at higher risk of HIV infection (112). A systematic review on the effects of policing on HIV-related outcomes found that all studies identified showed an association between police measures and either the primary outcome of HIV or STI infection or symptoms, or with secondary outcomes related to HIV risk such as testing and access, number of clients, condom use and syringe use (113).

A modelling study in Canada found that more than a third of HIV infections among female sex workers and their clients could be averted if sex work was decriminalised (20). An analysis of 27 European countries found that after adjusting for several potential confounders, the burden of HIV among female sex workers was lower in countries where sex work was fully or partially legalised (114).

In summary, behavioural, biological and structural factors affect the risk for HIV acquisition and transmission for both men and women who exchange sex.

2.2.2 Drug use

Injection and non-injection drug use and associated behaviours are the other main determinants of risk for HIV acquisition and transmission explored in this thesis.

2.2.2.1 Drug routes and HIV risk

Many drugs can be administered using more than one route, including intravenous injection, skin popping, snorting and smoking. HIV can be transmitted through unsafe injection practices including sharing contaminated needles or syringes as well as equipment used during preparation such as cotton and cookers (115). The HIV risks associated with unsafe injection practices are exacerbated by contextual factors including the fact that access to sterile needles and syringes is restricted or prohibited in many US states (116). Additionally, some drug users use shooting galleries where a single needle and syringe is rented to multiple users (117). Other modes of drug administration still carry some HIV risk related to their effects on libido and risk taking (118). Substance-use disorder can also cause people to adopt behaviours that put them at risk for HIV, such as risky sexual encounters in exchange for drugs or money (93).

2.2.2.2 Injection drug use and HIV

In the early years of the HIV epidemic, incidence was very high among PWID. Analysis of historically collected serum samples in New York City has allowed incidence to be estimated at 13/100 person-years. As people learned more about how HIV was transmitted, and as efforts increased to provide sterile injection equipment, incidence decreased to 1–4/100 person-years in New York City. After the introduction of ART and policies of treating everyone regardless of CD4 count, incidence dropped to 0.1/100 person-years (119). These figures are from New York City, one of the most progressive cities in the United States when it comes to harm-reduction policies for PWID and in many US states, needle-syringe exchange programmes are still illegal (116).

Injection drug use may also intersect with other risk behaviours in the US and elsewhere: MSM who also inject drugs are at particularly high risk for HIV, both from sexual and injection-related risk behaviours. Injection drug use also intersects with exchange sex with women engaging in either or both behaviours (52, 53, 92, 103, 120, 121). While people who inject drugs are at risk for HIV through needle sharing, sexual transmission has been shown to be an important risk factor for HIV transmission among PWID (77), and exchange sex may confer an additional risk compared with non-exchange sexual transmission. Drug dependency could be a barrier to finding and keeping regular employment, and women may choose riskier situations or behaviours out of desperation to avoid withdrawal (93). With regards to MSM, several studies in the US and Australia have shown that both injection and non-injection drug used to be more common among MSM who exchanged sex than those who did not (56, 58, 91, 122).

With regards to the association between exchange sex and HIV prevalence among those who exchange, evidence is mixed and many studies are old. Among women who injected drugs in Baltimore in the late 1980s, 39% of them had exchanged sex at least once in the previous 10 years, and having 50 or more exchange partners in the previous 10 years was associated with higher HIV prevalence (52). Another study from the 1980s found that 33% of women had exchanged sex in the previous year but exchange sex was not associated with HIV prevalence (123). A longitudinal case-control study from 1986–1998 found that women who reported having traded sex for money in the previous year were 5.1 times more likely to become HIV-infected than those who had not (53). A study from the UK found that PWID who exchanged sex, whether male or female, did not have a higher prevalence of HIV (124). One study indicates that trading sex for drugs specifically may be associated with higher risk for HIV compared with other sex work: Dunne et al. found that HIV prevalence was higher and condom use lower among African-American women who traded sex for drugs only, compared with African-American women who traded sex for economic resources or drugs or both (125).

Among MSM a recent study found that the majority of transactional sex (74%) involved sex for drugs and the remainder for other things such as money or shelter. Methamphetamine was the drug most commonly traded for sex. Transactional sex in exchange for drugs, in comparison to other items, was associated with unemployment, unstable housing and HIV-positive status (63).

2.2.2.3 *Heroin*

Heroin is one of the drugs most commonly injected, but it can also be smoked. People who have initiated heroin use in more recent years are more likely to be white, live in rural areas

and to have first engaged in nonmedical use of prescription opioid pain relievers compared with people who initiated heroin use in the 1960s (126). There are concerns that the perception of HIV risk may be different in populations of new PWID compared with those who lived through the HIV epidemic before treatment was available. In many rural areas in the US there is little or no access to needle-syringe exchange programmes or methadone maintenance programmes. The incidence of reported acute hepatitis C virus infection has increased substantially in several states, mainly in rural areas. The majority of these diagnoses are among young PWID. The increases in diagnoses mirror increases seen in the proportion of treatment admissions for opioid dependency (127). Such trends are seen as a possible precursor to HIV outbreaks, such as the 2015 outbreak in Scott County, Indiana (128).

2.2.2.4 *Methamphetamine*

Meth is a highly addictive stimulant that can be snorted, smoked, ingested orally or rectally, or injected. It is relatively inexpensive and the high can last up to 12 hours (118). Figures from the Substance Abuse and Mental Health Services Administration show that the use of methamphetamine has increased from 0.5% in 2016 to 0.6% in 2017 and 0.7% in 2018 and 2019 (129). These figures are not broken down by sexual behaviours of users, nor method of administration and as a result it is difficult to ascertain how these trends relate to injection meth use among MSM. Individual studies show that meth use is common among US MSM, and estimates of previous 12-month use from different studies range from 10 to 27% (130-134). However, less is known about the proportion who *inject* meth, or about trends over time. Previous 12-month use of non-injection methamphetamine was estimated at 5.9% among HIV-negative MSM and 12.3% among HIV-positive MSM in a survey among MSM (5). The most recent data in the US on prevalence of methamphetamine use among MSM comes from 2017–2019 and shows that 2.8% of gay or bisexual men had used methamphetamine in the previous year compared with 0.9% of heterosexual men (135). A limitation is that the survey asked about sexual identity and not about male-to-male sexual behaviour. A clinic in central London that diagnoses around one in six of all HIV cases in the UK found that in 2011, 30% of MSM who used meth or mephedrone – another club drug – reported injecting these drugs. This proportion had increased to 80% in 2012 (136).

A 2015 meta-analysis found a significant association between use of methamphetamine or amphetamine and HIV infection among MSM (137); however, none of the studies included examined the association specifically between injection meth use and HIV. Evidence from a longitudinal cohort study among MSM recruited via social networking apps found that methamphetamine use was significantly associated with HIV seroconversion and persistent

methamphetamine use accounted for a third of all observed seroconversions in this cohort (138). This study did not, however, measure the method of administration of the drug.

Several of the effects of meth put users at risk for HIV. The drug is used to increase sexual desire, to prolong sex, and make sex more pleasurable and less painful (139-141). Meth is also associated with impulsivity, poor judgement, increased libido and a reduction in inhibitions which can lead to men engaging in behaviours that they would not otherwise have considered (118, 130, 142, 143). Men using meth are more likely to have sex with multiple partners and to have condomless anal sex (144-146). They have also been found to be less concerned about their partner's HIV status (143). In addition to these psychological effects there are also several physiological effects of meth use that increase the risk for HIV transmission, such as mucosal dryness and a reduction in sensitivity. Users are more likely to engage in rough sex and have sex for longer, increasing the risk for mucosal tears that in turn may increase the risk for HIV transmission (118, 143). Meth also makes it harder to achieve a full erection as it restricts blood flow which, which may lead to those who use meth being more likely to engage in receptive anal sex (143) which has a higher risk for HIV transmission (147).

It is not clear whether sexual or injection-related risk behaviours are more important determinants for HIV acquisition among MSM who inject meth (148). No studies have compared the prevalence of HIV between MSM who inject meth and MSM who inject other drugs that are not associated with sexual risk behaviours, such as heroin. Understanding the drivers of HIV risk among different subpopulations of MSM may be key to understanding and addressing the high HIV prevalence among MSM who inject drugs.

2.3 THE CHALLENGES OF SAMPLING HIDDEN POPULATIONS

High-risk populations such as people who exchange sex, people who use drugs and MSM are challenging to study as no sampling frames are available and standard probability methods cannot be used. As seen from many of the studies cited here, samples are often convenience samples, including samples from clinics, outreach programmes or homeless shelters (8). Such samples, known as non-probability samples, can yield biased results as the probability of each respondent of being sampled is not known (149, 150).

2.3.1 Respondent-driven sampling

Respondent-driven sampling (RDS) is a method designed specifically to reach 'hidden' populations for which no standard sampling frame exists, such as PWID or people who exchange sex. Not only are such populations difficult to sample through standard methods,

but due to stigma, response rates can be low as people may not be forthcoming in, for example, a standard household survey. Furthermore, the prevalence of, for example, exchange sex in the general population is relatively low and a large sample would have to be obtained to reach an adequate number. Finally, standard household survey methods would probably not reach people who are homeless, as might often be the case for PWID or those who exchange sex (151).

In RDS, a small number of individuals ('seeds') are chosen from the target population. They are instructed to give recruitment coupons to their peers; for example, other PWID. People who get a coupon can then participate in the survey, and they in turn can recruit others. With several 'waves' of such recruitment, the final sample is not dependent on the initial participants chosen. Participants are also asked to report how many people they know in the target population – their network size – which is used during the analysis (149, 152). RDS has been used to sample PWID (153), sex workers (154), unregulated workers (155) and even jazz musicians (156).

A sample obtained through RDS approximates a population-based sample if certain assumptions are met. Firstly, the individuals being recruited must know one another as members of the target population (i.e. PWID must know each other as PWID), in order to identify and recruit each other. Secondly, respondents must select randomly from their network when choosing people to whom they give coupons. Thirdly, the target population must be adequately networked so that recruitment chains can progress and reach all subpopulations. A fourth assumption of RDS is that the sampling fraction is small, which means that the sample that will be recruited using RDS is small compared with the overall target population in the defined geographical area. This is to ensure that the ability of a participant to recruit remains constant over time. Finally, respondents must be able to accurately report their network size. This is because during the survey, respondents are asked how large their peer networks are, and this information will later be used during analysis. Respondents with smaller networks have a lower probability of being recruited, and their responses will be given a higher weighting than someone with a large network (149, 152, 153, 157).

2.3.2 Venue-based sampling

Another option for reaching hidden populations is to use venue-based sampling (VBS) (158). This method involves creating a sampling frame by systematically mapping days and times at which the target population gathers at different venues within a given geographical area. So-called 'venue-day-time' periods constitute the sampling unit and then are randomly selected

from the created sampling frame. Study teams then attend the venues at the selected times and approach the target population systematically. Further refinement of this method includes collecting data on the total number of people in the target population that are in attendance at the venue, which allows weightings to be created for each participant. Participants recruited at smaller venues are given a lower weighting than those from larger venues, as the latter represent a larger number of people. Other modifications include asking members of the target population how often they attend venues such as the one where the sampling has taken place. Participants who attend venues more often have a higher probability of being sampled at any one time and are given a lower weighting than participants who attend such venues less frequently (159). Venue-based sampling has been used to sample populations such as MSM (159) and street youth in Ukraine (160).

2.3.3 Data on HIV from the US National HIV Behavioral Surveillance System (NHBS)

The NHBS system surveys three populations at high risk for HIV: MSM, people who inject drugs (IDU) and heterosexuals at high risk for HIV (HET) in annual rotating cycles in around 20 metropolitan statistical areas with high HIV prevalence around the US. In 2016, as a pilot, data collection during the HET cycle was focused on women in five of the cities who exchange sex. In all cycles, NHBS participants are tested for HIV and asked about sexual and drug-use risk behaviours using a questionnaire. The resulting data sets permit analyses of factors associated with HIV within the populations sampled, including sexual and drug-use risk behaviours as well as socioeconomic factors. NHBS will be further described in the Methods section.

3 RESEARCH AIMS

3.1 MAIN AIM

To examine whether, among populations known to be at high risk for HIV, people for whom several risk factors intersect are more likely to be HIV-infected compared with other members of that population, and what sociodemographic factors and sexual and drug-use risk behaviours in these populations may be relevant to HIV acquisition and transmission.

3.1.1 Specific aims (Papers 1 and 2)

Paper 1: Exchange Sex and HIV Infection Among Women Who Inject Drugs—20 US Cities, 2009

Paper 2: Exchange Sex and HIV Infection Among Men Who Have Sex with Men: 20 US Cities, 2011

- To estimate the prevalence of exchange sex among women who inject drugs and among MSM in the US.
- To analyse the sociodemographic determinants and HIV risk behaviours of those who exchange sex compared with those who do not.
- To determine whether exchange sex is associated with diagnosed or undiagnosed HIV infection.
- To determine whether the number of condomless sexual partners mediates any association between exchange sex and HIV infection.

3.1.2 Specific aims (Paper 3)

Paper 3: HIV Prevalence Among Women Who Exchange Sex for Money or Drugs—4 US Cities

- To characterise the population of women who exchange sex with regards to sociodemographic characteristics, how they find clients, HIV risk behaviours, HIV prevalence and use of health care services.
- To determine the factors associated with HIV infection.

- To compare the prevalence of HIV among women who exchange sex with that among other women of low SES and with women in the general population in the US.

3.1.3 Specific aim (Paper 4)

Paper 4: HIV infection among MSM who inject methamphetamine in 8 US cities

- To determine whether primary use of injected methamphetamine is associated with HIV infection among MSM who inject drugs.
- To analyse the sociodemographic determinants and sexual and drug use risk behaviours of those who primarily inject methamphetamine compared with those who primarily injected other drugs.
- To determine whether sexual or drug-use risk behaviours mediate any association between methamphetamine injection and HIV infection.

4 METHODS

4.1 DATA COLLECTION

This thesis used data collected as part of the NHBS system based at the US Centers for Disease Control and Prevention (CDC). I worked with this surveillance system between 2013 and 2017 and was part of data collection operations as will be described in more detail below.

NHBS regularly surveys three populations at high risk for HIV: MSM, people who inject drugs (referred to as IDU) and heterosexuals of low SES and at high risk for HIV (HET) in around 20 metropolitan statistical areas with high HIV prevalence around the US. In brief, MSM cycles focus on men who are born male and have ever had oral or anal sex with another man. IDU cycles focus on people who currently inject drugs that are not prescribed for them, and HET cycles focus on men and women of low SES at risk for heterosexually acquired HIV. The eligibility criteria for each target population will be discussed in more detail below.

NHBS is conducted annually in three-year rotating cycles such that each of the populations MSM, IDU and HET are surveyed every three years. In 2016, I led a pilot round of data collection focused specifically on women who exchanged sex for money or drugs. This special cycle took place during a year when data was to be collected from heterosexuals (the HET cycle) and we focused sampling in five cities (Detroit, Chicago, Houston, New York City and Seattle) specifically on women who exchanged sex for money or drugs. This special HET round came to be known as the ‘high-risk women cycle’, or HET4-HRW.

NHBS is run by a team which I was part of in the Division of HIV/AIDS Prevention at the CDC in Atlanta, GA, in collaboration with local city or state health departments in around 20 US cities. The precise number of participating cities varied between rounds. I worked as a project officer which meant I collaborated closely with 2–3 local health departments throughout the annual cycle of data collection, including reviewing reports, monitoring data collection, and conducting site visits. I will now outline the methods we used to collect data from the different populations included in this thesis. At the end I will describe my role in more detail.

4.1.1 People who inject drugs – Paper 1 and Paper 4

Data from IDU cycles were used for Paper 1 on women who inject drugs and exchange sex (IDU2 in 2009) and for Paper 4 on MSM who inject drugs (IDU3 and 4 in 2012 and 2015, respectively).

4.1.1.1 Study population

The study population for IDU cycles was people who had injected drugs in the previous 12 months and who resided in one of the cities participating in the NHBS. Although the preferred term is ‘people who inject drugs’, at the time when NHBS was established the term used was ‘injection drug users’ (IDU). I will use IDU to refer to the NHBS data collection operations and PWID when referring to the populations of people who inject drugs.

4.1.1.2 Formative assessment

Prior to collecting data we conducted a formative assessment, the objective of which was to prepare for data collection. I and others in the team in Atlanta worked with local staff in the participating cities to supervise the process. This formative assessment was done in two stages. Firstly, secondary data was reviewed. This refers to data that has already been collected through other sources. After this, primary formative data collection was carried out when local staff collected qualitative data on the target population.

4.1.1.2.1 Secondary data collection

Local staff carried out a review of secondary data sources such as surveillance data and publications from local community-based organisations or peer-reviewed publications to characterise the PWID population in the city. This involved, among other things, gathering an understanding of what subpopulations had particularly high HIV prevalence to ensure that these were reached during data collection. This could be particular age groups or racial/ethnic groups (161). After the review of secondary data was concluded, I and the other project officers at CDC reviewed and approved the reports and the findings were then used by local staff to plan the primary data collection.

4.1.1.2.2 Primary data collection

Primary data collection involved key informant interviews, focus groups, observations and brief street intercept interviews, carried out by local staff. Key informant interviews were done with organisations that served PWID, or with members of the target population of PWID themselves in the city. Staff also carried out focus groups with PWID, made observations and conducted brief street intercepts with PWID to gather more information.

The purpose of this part of the formative assessment was also to garner support from the local community – including local organisations and members of the target population – which is key to the success of data collection. Formative assessment also seeks to identify barriers to

participation and ways to overcome them. Given that RDS was used for data collection from PWID, a key objective of the formative assessment was to identify ways in which the PWID population was networked as this would determine the characteristics of the seeds that would initiate data collection. For example, in cities where different PWID of different races were not networked with each other it became necessary to recruit seeds from a variety of racial groups to ensure representative participation.

I worked closely with the sites during the process of primary formative data collection, including reviewing and approving questions for focus groups and key informant interviews. I made site visits to some cities and observed focus groups and interviews in order to ensure these were done according to protocol and also to learn more about the study populations. I approved the final report from each site prior to the start of the actual survey.

4.1.1.3 Recruitment and data collection

Survey data collection took place during the second half of the calendar year of an IDU cycle. Data collection procedures are described in detail in standard operations manuals that are reviewed and updated prior to each new cycle (162-164). Sampling began with up to five purposefully selected seed participants in each city, chosen to ensure that all subpopulations of the target population were reached. Seeds were then given coupons that they were instructed to give to other ‘people you know who inject drugs’. Participants were usually given 3 coupons but those who belonged to sub-populations that were harder to recruit were in some cases given up to 5 coupons. Such adjustments were made throughout data collection following inspection of recruitment graphs and the sample composition.

People who had a coupon were invited to attend one or more field sites for interview and HIV testing.

4.1.1.3.1 Eligibility criteria

There were some eligibility criteria for participation that were common to all populations whereas others are unique to each cycle.

General eligibility criteria:

Participants must:

- be 18 years of age or older
- live in the metropolitan statistical area where the study is conducted

- be able to complete the survey in English or Spanish
- not have participated previously in the current year of data collection.

Additional eligibility criteria used during recruitment of PWID during IDU cycles:

Participants must:

- have injected drugs in the past 12 months

Current injection drug use is assessed by inspection of physical evidence of injection such as track marks, and knowledge of injection practices.

Note that transgender participants were eligible for participation, however there were only 53 recruited and they were excluded from the analysis.

4.1.1.3.2 Interviewing and HIV testing

The study team in each city carried out interviews and HIV testing at one or more field sites. I worked with staff in the cities to choose the sites based on the findings of the formative research in order to ensure accessibility for all potential participants.

When participants arrived at the field site, they needed to present a valid coupon before being allowed to be screened for eligibility and take the survey. Participants were tested for HIV, usually by rapid testing. Those who tested positive were asked to provide an additional sample for confirmatory laboratory-based testing (western blot) and were offered the opportunity to anonymously obtain their confirmatory HIV test result at a later date. Participants who tested positive at the field site were also linked to care based on the preliminary result, and all participants were offered other referrals as appropriate, such as drug treatment or housing assistance. Participants were given incentives for participation either as cash or as a gift card. A typical incentive would be 25 USD for taking the survey and an additional 25 USD for taking the HIV test.

Participants were offered the possibility to receive coupons and recruit others into the study and were given an additional incentive – typically 10 USD – for each person that they gave a coupon to who completed the survey. I worked with the study sites to determine the levels of the incentives based on the findings of formative research. The level would vary between cities and was set to encourage enough people to participate without being coercive.

To ensure correct payment of the recruitment incentives, some information was collected about the participant at checkout. This included a unique reproducible code, made up of

information that only the participant knew, such as the first letter of their mother's name. Local staff also documented any unique physical marks such as tattoos or birth marks that could help identify the participant. Such information also helped in case staff suspected that someone had already participated in the survey, in which case they were ineligible to take the survey again.

4.1.1.3.3 The questionnaire

The questionnaire was administered by an interviewer who read out each question and the answer options. The questionnaire contained initial questions on demographic characteristics, education, employment and income. A large portion of the questionnaire was devoted to asking about sexual partners and behaviours with these partners, including sex in exchange for money or drugs. Alcohol and drug use, including both use of non-injection and injection drugs were also covered. Furthermore, the questionnaire asked about past testing and diagnoses of HIV, hepatitis and STIs. Other topics included exposure to violence, perceived stigma, health insurance coverage and access to care, exposure to HIV prevention interventions, perceived HIV risk, and mental health. Participants were also asked about the size of their social networks with regards to other members of the target population, i.e. how many people they knew who lived in the same city and who injected drugs. Each site also had the possibility of adding their own local questions.

For Paper 1, the data used was from IDU2 which used the questionnaire for NHBS Round 2¹

For Paper 4, data used was from IDU3 and IDU4 which used the questionnaires for NHBS Round 3² and Round 4³.

4.1.2 Women who exchange sex for money or drugs – Paper 3

4.1.2.1 Study population

The study population were women who had received money or drugs in exchange for sex in the previous 12 months living in Chicago, Detroit, Houston, New York City and Seattle.

4.1.2.2 Formative assessment

Secondary and primary data collection were used to further understand the subpopulations of women who exchanged sex in terms of how and where they found clients, their demographic

¹ Available from: https://www.reginfo.gov/public/do/PRAViewIC?ref_nbr=200710-0920-001&icID=182202

² Available from:

https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/nhbs_round3_ombapprovedquestionnaire.pdf

³ Available from: <https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/cdc-nhbs-crq-idu4-deployed.pdf>

characteristics, such as race and income level, and whether they injected drugs or not. I designed the manuals used for the formative assessment and advised staff to look online for information in advertisements and fora used by clients to share information about sex workers in each city. These online searches to characterise the so-called ‘spectrum of exchange sex’ in each city in terms of the different ways women who exchanged sex found their clients and at which geographical locations they might be found, such as street locations or certain strip clubs. Focus groups and key informant interviews were also very important for this cycle and women who exchanged sex shared important information including which areas were not safe for project staff to attend as these were frequented by women who exchanged sex involved with members of criminal cartels.

For each subpopulation, staff tried to identify if and how they were networked with each other in order to determine the number and characteristics of seeds that would be needed to reach as many subpopulations as possible. Primary data collection also involved mapping different locations where women found clients around the city to determine where field sites – where interviews would be carried out – might best be placed. A key aspect of formative research during the HET4-HRW cycle was also to garner support from the community of sex-worker-led organisations. Staff at project sites were encouraged to reach out to these organisations, such as the local chapter of the Sex Workers Outreach Project as well as organisations that served women who were sex workers.

Garnering the support of organisations that represent women who exchange sex was important for several reasons, including ensuring that this project would be relevant to and respectful of sex workers’ needs. It was also necessary in order to understand how best to ensure that the safety of both participants and project staff would not be compromised when visiting certain locations and venues. Finally, working closely with this community from the start was with the aim of ensuring that the findings would be well received and used. Failure to do so could result in the community of women who exchange sex viewing the survey as a process that was about them without involving them. Project staff were encouraged to reach out to women across the spectrum of exchange sex given that established organisations that represent or serve female sex workers might not represent *all* women who exchange sex.

4.1.2.3 Recruitment and data collection

Women who exchange sex were recruited through RDS. Sampling began with up to five purposefully selected seed participants in each city, chosen to ensure that all subpopulations of women who exchange sex were reached. Similar to the IDU cycle described above, seeds

were given 3–5 coupons that they were instructed to give to other ‘women you know who have sex in exchange for money or drugs’.

4.1.2.3.1 Eligibility criteria

Eligibility criteria included the general eligibility criteria as listed above for the IDU cycle, but also some specific criteria:

Participants must:

- be female (not transgender)
- have had vaginal or anal sex with a male partner in the previous 12 months.

4.1.2.3.2 Interviewing and HIV testing

Interviewing and HIV testing was largely the same as for the IDU cycle as described above. The questionnaire used was that for NHBS Round 4⁴ with the addition of specific questions around exchange sex (Annex 1). However, only women who during the survey reported receiving money or drugs from one or more male partners were given coupons. While exchange sex was an eligibility criterion for receiving coupons, it was not an eligibility criterion for participation even though participants were instructed to only recruit other women who exchange sex into the survey. In the final analysis, women who did not report exchanging sex during the survey were excluded.

The five participating sites also worked together with the CDC to develop several questions specific to women who exchange sex, which included how they found clients, sexual behaviours specifically with clients, exposure to violence from clients and police, and perceived stigma. These questions were then used as local questions at all five sites which still gave sites some space to add further questions specific to their local context. These are included in Annex 1.

4.1.3 Heterosexuals at increased risk for HIV – Paper 3

Data from the 2013 HET cycle was used for parts of the analysis in Paper 3 in order to compare the prevalence of HIV between women recruited as part of the HET4-HRW cycle with the prevalence of HIV among women recruited from the same cities as part of the HET cycle three years earlier. Data was collected from both men and women but only data from women was used.

⁴ Available from: <https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/cdc-nhbs-crq-idu4-deployed.pdf>

4.1.3.1 Study population

The study population for the 2013 HET cycle in general was men and women of low SES living in one of the 20 cities participating in the NHBS. Only data from women residing in Chicago, Detroit, Houston, New York City or Seattle were used for the analysis.

4.1.3.2 Formative assessment

Formative assessment was largely similar to what has been described for the IDU cycles above.

4.1.3.3 Recruitment and data collection

The HET cycle used RDS to recruit participants. Seeds were chosen from the census tracts in the city with the highest poverty rates. Seeds were given 3–5 coupons that they were instructed to give to other ‘friends, relatives, or people you associate with’.

4.1.3.3.1 Eligibility criteria

In addition to the general eligibility criteria as described above, there were some additional eligibility criteria:

Participants must:

- be male or female (not transgender)
- have had vaginal or anal sex with an opposite sex partner in the previous 12 months.

4.1.3.3.2 Interviewing and HIV testing

Interviewing and HIV testing were largely similar to what has been described for the IDU cycle. The questionnaire used was that for NHBS Round 3⁵. Participants were offered the possibility to receive coupons and recruit others into the study. However, only participants who were of low SES and who had not injected drugs in the previous 12 months were offered coupons. Low SES was defined as either having an income that did not exceed the Health and Human Services poverty guidelines or having an educational attainment no greater than high school. Additionally, only participants who met these criteria were counted towards the sample size.

⁵ Available from:

https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/nhbs_round3_ombapprovedquestionnaire.pdf

4.1.4 Men who have sex with men – Paper 2

Data from the 2011 MSM cycle was used for Paper 2 on MSM who exchange sex.

4.1.4.1 Study population

The study population was those who lived in one of the 20 participating cities, were born male and who reported their gender as male at the time of the interview and had had oral or anal sex with a male partner during their lifetime.

4.1.4.2 Formative assessment

The formative assessments for MSM cycles were in many ways similar to those that have been described for the IDU cycle, with some important differences due to the fact that data from MSM was collected using venue-based sampling and not RDS.

During the formative assessment, online searches as well as key informant interviews and focus groups were used to identify different venues in the city where MSM gathered and where data collection could take place (165). While bars and clubs made up the majority of venues, staff also identified and included venues such as street locations, social clubs and associations or gyms and grocery stores where 50% or more of men in attendance were MSM. Venues were then assessed for accessibility, which included seeking approval from the venues' management to recruit attendees there.

4.1.4.3 Recruitment and data collection

For each venue identified during the formative data collection, staff designated so-called 'day-time' periods where data collection could take place which is a function of when the venue was likely to be busy and when data collection was feasible. All accessible venues and possible day-time periods were then entered into a database which was used to randomly select venues and day-time periods for each month. Staff attended the venues at the chosen day-time periods and recruited men randomly who were in attendance at the venue using different predetermined strategies such as approaching any man who passed through a certain location at the venue or approaching each new man entering the venue.

4.1.4.3.1 Eligibility criteria

Men approached at the venue were, if they agreed, screened for eligibility. Eligibility criteria included the general eligibility criteria as listed above for the IDU cycle, but also some criteria specific to the MSM cycle:

Participants must:

- be male at birth
- report their gender as male
- have had oral or anal sex with a male partner during their lifetime.

4.1.4.3.2 Interviewing and HIV testing

Men who consented to the survey were interviewed face to face by a trained interviewer and tested for HIV. The questionnaire used was that for NHBS Round 3⁶. Interviewing and testing often took place inside the venue, usually in a more private part such as a back room. Some of the 20 cities used a mobile van for data collection, which enabled staff to carry out interviews and HIV testing separate from the actual venue. Men who tested positive for HIV on a rapid test at the venue were offered a confirmatory laboratory-based test immediately and the possibility of anonymously obtaining their confirmatory HIV test result at a later date. At the venue, men also received counselling and linkage to care.

At the end of this process, men received their incentive, either in cash or as a gift card. Similar to the other cycles, incentive levels were determined locally during the formative assessment, but a typical incentive would be 25 USD for taking the survey and an additional 25 USD for taking the HIV test. In some cities such as New York City, where the MSM population were more affluent, incentives were higher. Incentives also needed to be high enough to compensate them for missing out on time with their friends at the venue where they were recruited. Many participants appreciated the extra money that they could spend at the venue during the rest of the evening, and many venue owners allowed us to collect data at their venue in part because of the potential for extra spending by participants.

4.1.5 The role of the PhD student

As a team member of NHBS I worked on all aspects of the data collection and analysis. I was the main project officer for 2–3 sites at any one time – mainly Newark, Detroit and Houston. This involved weekly calls with the sites to discuss the progress of the formative data collection and to help interpret findings. I also reviewed their formative assessment reports and operational plans prior to the start of data collection. I would sometimes make a site visit during the formative data collection to help the sites interpret their findings and plan data collection. I often listen to focus groups or individual interviews and ensured these were

⁶ Available from:
https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/nhbs_round3_ombapprovedquestionnaire.pdf

carried out well. I always did site visit during data collection where I would review operations in detail and ensure staff adhered to the operations manual with regards to all aspects of the data collection including field site set-up, ethical considerations, interview technique, data management and so forth. (162-164).

I met with the other project officers on a weekly basis to discuss progress and operational issues and solutions. The purpose of this was in part to ensure that operations were standardised as much as possible across sites and also to share good ideas between sites. In parallel to this more operational work, I was working on analyses of data collected in previous years which form the basis of Paper 1 and 2 in this thesis. Papers 3 and 4 are largely based on data from years where I was involved in the process of data collection. I discussed analyses with other members of the team to ensure we had similar analytical approaches given the special consideration needed for the data we collected, and which are discussed below.

I also supported colleagues on other projects such as a new initiative to recruit young MSM using different methods including both RDS and venue-based sampling but also through Facebook. This project was led by a colleague, but I took the lead on writing some of the manuals for data collection and I also conducted site visits. These data were not included in the thesis.

4.1.5.1 The HET4-HRW cycle

After I had worked with NHBS for some time I was asked in 2016 to lead a new initiative to collect data specifically from women who exchanged sex. The idea was to, during a regular HET cycle, in five cities to specifically target only women who exchanged sex. I led the process of designing the overall strategy and adaptation of existing NHBS processes to suit this population.

I designed the formative assessment process and wrote a guide for participating sites, including detailed advice on how to liaise with sex-worker organisations, how to map out the different populations of women who exchange sex in the city and how to ask questions to understand how they were networked with each other. I also wrote the interview guides for focus groups and key informant interviews. During this process I liaised with a former sex worker who had gone on to do research with sex workers, in order to best design the formative assessment process.

It was also essential to adapt the operations manual to suit this new population. Some of this work was delegated to another team member but I did large parts myself and reviewed every change suggested. I also wrote a series of new questions to be added to the questionnaire,

specific to the population of women who exchange sex. These were discussed in detail with local project staff and with the former sex worker mentioned above.

In addition to the overall coordination and planning I was the project officer for two of the five sites and visited each of these twice during the year – once during the formative assessment and once during the data collection. I also led regular meetings with all the project officers who were assigned to one of the five sites who collected data on women who exchange sex to ensure consistency across sites.

Throughout the process it was necessary to put a significant focus on safety-related issues such as how to ensure that women who reported working under coercive circumstances could be guided to safety, and how to identify services to which women could be referred for a variety of needs. I also liaised with CDC communications and policy staff and drafted talking points should CDC be approached by the media on this sensitive project.

In summary, I led the protocol development and oversaw the data collection for Paper 3. For the other papers I participated in supervising the data collection and resolving methodological issues together with other staff throughout the data collection. For all papers I wrote the research question, analysis plan, conducted the analyses (except for the RDS weighted analysis in Paper 3 where I closely collaborated with another colleague). I also wrote the papers.

4.1.6 Sample size

NHBS is largely a descriptive surveillance system and formal power calculations, as would be done for studies designed to test specific hypotheses, were not performed when the surveillance system was originally set up (166). The target sample size of 500 per city in each cycle was arrived at by considering the presumed HIV prevalence, the desired standard error for key indicators of interest and the design effect or efficiency of the sampling method used. Salganik has presented a method to calculate sample sizes for RDS samples and NHBS also uses this for the MSM venue-based sampling (167). Analyses of NHBS-IDU data have suggested that a design effect of 4 is appropriate for RDS studies (168) and an unpublished analysis of NHBS-MSM data also suggests that a design effect of 4 is appropriate.

The criteria for having participants count towards the target sample size of 500 vary between cycles and are not always the same as the eligibility criteria:

- MSM: The target sample size for each project site was 500 completed interviews with participants who met NHBS-MSM eligibility criteria for participation *and* reported male-to-male sex in the previous 12 months.
- IDU: The target sample size for each project site, exclusive of ‘seeds’, was 500 completed interviews with participants meeting NHBS-IDU eligibility criteria.
- HET: The target sample size for each project site, exclusive of ‘seeds’, was 500 completed interviews with participants who met NHBS-HET eligibility criteria *and* had not injected drugs without a prescription in the previous 12 months *and* had low SES. Low SES is defined as having an income that does not exceed Health and Human Services poverty guidelines or educational attainment not greater than high school.
- HET4-HRW: The recruitment of women who exchange sex was in some respects nested within a regular HET cycle. While women were told to only give coupons to other women who exchanged sex, all women who met the basic HET eligibility criteria were allowed to participate. There were no eligibility questions related to exchange sex. This was a pilot study on women who exchange sex and the aim was to recruit 500 or more women if possible, but no formal sample size limit was set. A systematic review of existing studies on exchange sex in the US has suggested that a sample size of just under 400 would be adequate to estimate an HIV prevalence of 10% with a margin of error of 3% (8). This did not, however, take the design effect into account which might be needed for RDS studies. In the final analysis only women who reported exchange sex during the survey were included.

4.1.7 Ethical considerations

All study protocols were reviewed and approved by the Centers for Disease Control and Prevention (CDC). All local project sites submitted the NHBS protocol each year to an institutional review board either at the local health department or a local university if such an institution was involved in carrying out NHBS activities. No data collection activities involving human subjects could take place before approval was obtained. Informed consent was obtained from all participants prior to focus groups and key informant interviews during the formative research, and prior to taking the surveys. Consent for the HIV test was obtained separately. All NHBS activities were anonymous, including the interviews, HIV tests and linkage to care. At no point were the participants’ names obtained.

Ethical considerations include ensuring that the level of the incentive is not at a level which is coercive for participants. Formative research serves to ensure that the level is appropriate for the populations studied and for the city of implementation. For example, MSM in New York

City need a higher incentive to be motivated to participate compared to PWID in a less affluent area such as Detroit.

Ensuring that participants are linked to services in the event of a positive diagnosis is something that is given priority. Each city of implementation solves this in a different way and it may range from making an immediate call to services or providing participants with a dedicated phone number to call themselves.

Particular ethical considerations were taken into account during data collection from women who exchange sex. This included considering that they might work under coercive circumstances. Sites were advised to ensure that women could be referred to services right away from the interview room if they were to report working under coercive circumstances and in case someone was waiting for them outside the interview room. Referrals to a wide range of services were also offered to women, in particular if they reported certain needs or circumstances during the interview.

4.2 ANALYSIS

This section will describe all aspects of data analysis, including the main measures used, software and different analytical considerations.

4.2.1.1 Main variables

4.2.1.1.1 Outcomes: HIV infection and HIV-positive–unaware

HIV infection is one outcome examined in all papers. A nonreactive rapid test was considered a definitive negative result. Participants were considered HIV-positive if they had a reactive rapid test followed by a laboratory-confirmed positive HIV test result. Two of the papers look at the subgroup of HIV-infected participants that were HIV-infected unaware, defined as a positive test result, as described above, where the participant reported no previous positive HIV test results.

4.2.1.1.2 Exposures

4.2.1.1.2.1 EXCHANGE SEX

Exchange sex is the focus of three of the papers.

Exchange sex is used as a dichotomous variable in Paper 1 and Paper 1 and was defined as having received things like money or drugs in exchange for oral, anal or vaginal sex from at least one male partner in the previous 12 months.

Paper 1 on exchange sex among women who inject drugs uses data collected in 2009 where questionnaire defines partners as main, casual or exchange and these categories are mutually exclusive.

Paper 2 on MSM uses data from the 2011 cycle, where exchange partners did not form a separate category, but rather were subcategories of main and casual partners. A casual partner is ‘a man you have sex with but do not feel committed to or don’t know very well’ whereas a main partner was ‘a man you have sex with and who you feel committed to above anyone else. This is a partner you would call your boyfriend, husband, significant other, or life partner’. For the analysis, exchange sex is used as a dichotomous variable and is defined as having received money or drugs in exchange for oral or anal sex from at least one male *casual* partner in the previous 12 months.

Paper 3 on HIV prevalence among women who exchange sex for money or drugs uses data from the HET4-HRW cycle where there was an exclusive focus on recruiting women who exchange sex in five cities, four of which are included in the analysis. Exchange sex was defined as having received things like money or drugs in exchange for oral, anal or vaginal sex from at least one male partner in the previous 12 months. Data from the 2013 HET cycle among heterosexuals in the same cities is used as comparison, and the analysis of that data is limited to women who did not report exchange sex with casual partners.

4.2.1.1.2.2 PRIMARY DRUG

For Paper 4 on methamphetamine injection among MSM, the main independent variable examined is ‘primary drug’, defined as the drug the participant reported injecting most often. Participants were asked which drug they injected most often. If participants answered ‘Crystal, meth, Tina, crank, ice’ in 2012, and ‘Methamphetamine, also known as meth, crystal meth, speed, or crank’ in 2015 they were categorised as using meth as their primary injected drug. Participants who reported injecting any other drug most frequently constituted the reference category.

4.2.1.2 *Analysis strategy – general background*

The primary focus of the analyses has been to look at the association between behaviours (exchange sex or meth use) and HIV prevalence, mainly from a perspective of risk for acquisition, acknowledging the limitations inherent in cross-sectional observational data which makes it very challenging to make causal inferences. Furthermore, the behaviours and circumstances are reported for the previous 12 months are used as proxies for those that may have been present at the time of HIV acquisition. The variables to be included in the models as confounders or mediators were selected with risk for HIV acquisition in mind. However,

the prevalence of current sexual and drug-use risk behaviours are also indications of the extent to which the population is at ongoing risk for HIV acquisition *and* for transmitting the infection onward to others.

4.2.1.2.1 Directed acyclic graphs

Directed acyclic graphs or DAGs were used in Papers 1, 2 and 4 to evaluate which variables should be included in multivariable analysis as potential confounders or mediators (169). DAGs graphically represent relationships between variables using arrows to denote the direction of the relationship. DAGs are a useful tool when planning an analysis and when communicating with other researchers during the analysis process (170, 171).

The DAG below (Figure 1) shows a relationship between the exposure A and the outcome Y . The variable L is also present, which is a potential confounder, i.e. a variable that is a common cause of both the exposure and outcome. This can distort the observed relationship between the exposure and outcome unless the confounding variable is controlled for during analysis. The variable B indicates a factor that mediates the relationship between the exposure A and outcome Y . Another way of describing this is to say that B is on the causal pathway between A and Y in that A does not directly cause Y , but rather causes something else that in turn causes Y . The arrows between the variables show that we either know that there is a direct causal effect or that we are unwilling to assume that there is no such effect (172). Some factors can be confounders or mediators, and the casual relationships can be complex in particular in the settings explored in this thesis which includes human behaviours, biological factors and social contexts and challenging to study in the absence of a longitudinal design. DAGs were used in Papers 1–3 to evaluate which confounders and mediators should be included and a DAG of the final models are presented for each paper below.

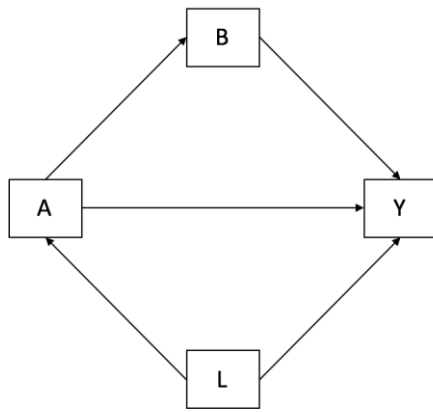


Figure 1: Generic directed acyclic graph, where *A* is the exposure, *Y* is the outcome, *L* a confounder and *B* a mediator.

4.2.1.2.2 Modelling considerations for all papers

For bivariable and multivariable analyses we used Poisson models with generalised estimating equations (GEE), in PROC GENMOD in SAS v. 9.2 or 9.3. The GEE method enables analyses of clustered data. The studies in this thesis used clustered data, either collected RDS or venue-based sampling. In clustered data, observations are groups and may be more similar to each other than to other observations in the data set (173).

The data among MSM used in Paper 2 was collected during venue-based sampling, which means that individual men who were sampled during the same recruitment event at a certain venue were probably more similar to each other compared with men sampled at the same venue at another time, or at a different venue altogether. The MSM data is in fact clustered at different levels with the highest levels being the data collection city, then venue, and then recruitment events within venues. After careful consideration it was decided to cluster the models on recruitment event which is the lowest level of clustering in the data.

RDS data is also clustered in that participants belonging to the same recruitment chain, i.e. originating from the same seed, are likely to be more similar to each other than participants in a different chain, although this similarity will be minimised the longer the chains go on. For Paper 1 on exchange sex among women who exchange sex, and Paper 3 on methamphetamine injection among MSM-PWID, models were therefore clustered on recruitment chain, i.e. where participants are grouped according to the seed which started the recruitment chains they are part of. This allowed for some adjustment of the general dependence among observations linked to one another in population networks. For the models done during the analysis of factors associated with HIV among women who exchange sex (Paper 4), Poisson regression with robust standard errors was used, clustered on individual observations as the

total number of clusters in the four cities was too small to allow for clustering on recruitment chain.

Both RDS and venue-based sampling data are also in some sense clustered by city. City of interview could also be a potential confounder, which is why a variable for data collection city was included as a covariate in all multivariable models and some bivariable models depending on the paper.

Additionally, for the paper on exchange sex among women who inject drugs, we made further adjustments to take account of the RDS sampling method. We adjusted for homophily (the possibility that people recruit other people similar to themselves) and the direct dependence between the recruiter and recruit by including the recruiter's value on the model outcome, (ie, 'yes', 'no' or 'non-applicable' if missing) as a fixed effect in the model – regardless of whether it was significant or not. Paper 1 was analysed before the other two papers that used RDS. Over time, the practice of including the recruiter's value on the outcome fell increasingly out of favour as it was found to 'overadjust' the models and obscure the association of interest.

In Paper 1, we also adjusted for the differing sample inclusion probabilities by including participants' self-reported personal network size in the model as a fixed effect. For the paper on methamphetamine injection among MSM-PWID, and the paper on HRW, we did not include network size as this variable was not significant in the models.

For bivariable and multivariable analyses of RDS data, the data was not weighted, which means that resulting estimates are sample estimates and may not be representative of the underlying population of women who exchange sex in participating cities. The reason data was not weighted was that there was at the time no reliable method that allowed for multivariable analysis of weighted RDS data and this was not done in general for other studies using NHBS data. Later evidence from the literature showed that non-weighted multivariable analysis performed better than weighted analyses (174).

4.2.1.3 Analysis strategy specific to each paper

4.2.1.3.1 Papers 1 and 2 – exchange sex and HIV among women who inject drugs and MSM

4.2.1.3.1.1 PREVALENCE OF EXCHANGE SEX

The analysis strategies for the first two papers – exchange sex and HIV infection among women who inject drugs, and among MSM, were largely similar. Firstly, the overall prevalence of exchange sex in the sample of each population was determined. Secondly, we compared prevalence of exchange sex by different socioeconomic characteristics such as age,

race, education level, homelessness and city of interview. The purpose of this part of the analysis was to understand the socioeconomic groups in which exchange sex was most prevalent. The results are presented in Table 1 of Paper 2 (women who inject drugs) and Table 1 of Paper 2 (MSM). Of note, the sociodemographic variables form the rows of the table, and exchange sex the columns. The percentages presented are row percentages, i.e. the percentage of people in each category of, for example, race/ethnicity who exchange sex.

4.2.1.3.1.2 RISK BEHAVIOURS

The second part of the analyses for Paper 1 and Paper 2 served to compare those who exchanged sex with those who did not in bivariable analysis with regards to sexual and drug-use risk behaviours. The results are presented in Table 2 of Paper 1 and Table 2 of Paper 2, where the different risk behaviours and other variables form the rows of the table and exchange sex status forms the columns. The percentages presented are column percentages.

4.2.1.3.1.3 EXCHANGE SEX AND HIV PREVALENCE

The third part of the analyses for Paper 1 and 2 focused on assessing the association between exchange sex and HIV prevalence, including HIV-positive–unaware. This was first done in bivariable analysis and then in multivariable analysis controlling for key confounders. The strategy for choosing which confounders to adjust for was slightly different between the two papers.

Paper 1

In Paper 1, the bivariable association between exchange sex and testing positive for HIV was not significant and multivariable analysis was only carried out to explore the association between exchange sex and HIV-positive–unaware. Variables that, based on previous research and the evaluation of DAGs, were considered to be potential confounders of the relationship between exchange sex and HIV were added one by one to the model, starting with the variable with the lowest P value for the association with HIV-positive–unaware in bivariate analysis. Variables examined as confounders included age, race/ethnicity, education, homelessness, arrest history, poverty, and several injection-related variables (duration, frequency of injection, receptive syringe sharing, and drug most commonly injected). For example, people who are homeless or who have a low education level are likely to live in poverty and may be more likely to exchange sex to obtain funds. People who live in poverty are also more likely to be HIV-positive. Specifically with regards to being HIV-positive but unaware, people who are homeless or have a low education level may be less likely to get an HIV test, either because of lack of health literacy or lack of access to care. Homelessness and

low education level do not of course directly cause HIV infection but may put people at risk for acquisition through a number of other pathways that are related to sexual and drug-use risk behaviours or partner risk profiles as will be described in further detail in the discussion. The DAG below (Figure 2) shows the final multivariable model.

The DAG also includes the mediator (total number of condomless vaginal and anal partners as a categorical variable) explored in a sensitivity analysis as will be described below.

We also tested for two-way interactions between exchange sex and each of the covariates in the final model but as these were not significant they were not included in the final model.

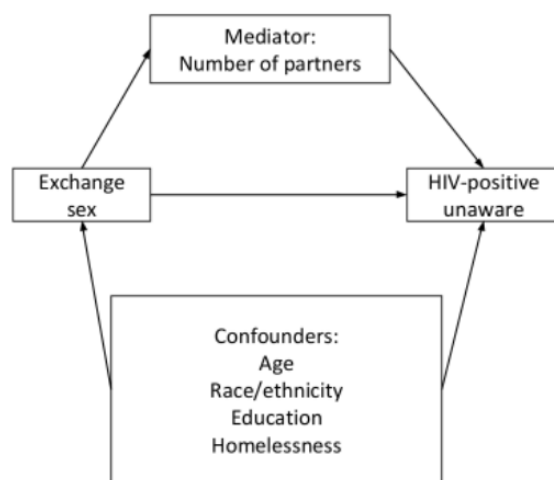


Figure 2: Directed acyclic graph (DAG) for Paper 1 on the association between exchange sex and HIV-positive–unaware among women who inject drugs. The DAG shows the confounders in the final multivariable model as well as the mediator explored.

Paper 2

In Paper 2, the bivariable associations between exchange sex and both outcomes (testing positive for HIV and being HIV-positive–unaware) were both significant. Several variables were considered to be potential confounders based on previous research and the evaluation of DAGs (Figure 3), but the strategy for which to include was slightly different. Age, race/ethnicity and lifetime history of injection drug use were all added to the model regardless of the P value in bivariable analysis as these were considered such important potential confounders that they were essential to include. Additional variables that were significant in bivariable analysis were also added but were removed if the P value was greater than 0.05 once added to the model. However, to account for income we kept poverty in the final model even though the P value was higher than 0.05, as it was considered essential to have at least

one variable related to income in the model. We also tested for two-way interactions between exchange sex and each of the covariates in the final model but as these were not significant, they were not included in the final model.

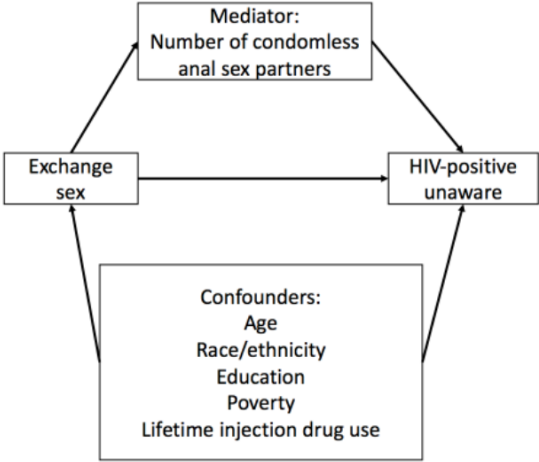


Figure 3: Directed acyclic graph (DAG) for Paper 2 on the association between exchange sex and HIV-positive–unaware among men who have sex with men. The DAG shows the confounders in the final multivariable model as well as the mediator explored.

Of note, analysis of MSM sampled in a later round of NHBS than the one used for Paper 2 revealed that almost half of HIV-positive–unaware MSM in that cycle had misreported their status as determined by testing for the presence of antiretrovirals (ARVs) in dry blood spot samples (175). The implications of these results for the findings in Paper 2 will be explored in the discussion section.

4.2.1.3.1.4 MEDIATION ANALYSIS

The final part of the analyses for both Papers 1 and 2 included the addition of the number of condomless sexual partners to explore whether the number of partners was a mediator of the association between exchange sex and HIV, as seen in Figures 2 and 3. In other words, we hypothesised that the number of condomless partners was on the causal pathway between exchange sex and HIV. Exchange sex by itself does not cause HIV infection but could do so through unsafe sexual encounters including the number of partners and the risk profile of those partners. In the analysis among women who inject drugs (Paper 1), the variable used was the total number of condomless vaginal and anal sex partners in the previous 12 months as a categorical variable. For the analysis among MSM, we used a variable for the total number of condomless anal casual sex partners as a continuous variable.

4.2.1.3.2 Paper 3 – women who exchange sex in four US cities

Paper 3 uses data from women recruited because they exchange sex in Chicago, Illinois; Detroit, Michigan; Houston, Texas, New York City, New York; and Seattle, Washington. The sample from New York City was excluded from the analysis due to particular characteristics of that sample which violated RDS assumptions (176), including strong recruitment homophily and bottlenecks for HIV status with large differences in the HIV prevalence in different recruitment chains. In addition, the sample did not reach convergence with the HIV prevalence estimates.

Analysis for the remaining four cities was restricted to women who reported receiving money or drugs in exchange for oral, vaginal or anal sex from a male partner in the previous 12 months and who had a valid HIV test.

In the first part of the analysis, we estimated the population prevalence of sociodemographic characteristics, access to care, HIV prevalence, HIV risk behaviours and exposure to violence among women who exchange sex, separately for each city.

In the second part of the analysis, we estimated the aggregate HIV prevalence across the four cities and compared it with two other populations from the same four cities: women of low SES who did not exchange sex, and women in the general population. Data collected as part of the 2013 NHBS cycle among low SES individuals was used to estimate the prevalence of HIV among low SES women aged 18–60 who did not exchange sex in these four cities (177), excluding women from the analysis who reported receiving money or drugs in exchange for sex from casual partners. Secondly, data from the US National HIV Surveillance System (NHSS) was used to estimate HIV prevalence among women aged 18–60 in the general population in the four participating cities, regardless of transmission mode. In order to account for women who are unaware of their HIV infection, the diagnosed HIV prevalence in NHSS was adjusted using the estimated proportion of women living with HIV in the US who have received a diagnosis (88.5%, 95% CI: 85.8–91.4) (178). We used 2015 census estimates for the number of women in each city aged 18–60 as the denominator when estimating HIV prevalence in the general population (179). We calculated prevalence ratios (PRs) with the 95% confidence interval comparing the aggregated HIV prevalence among women who exchange sex with the HIV prevalence in these two populations.

In the third part of the analysis, we evaluated factors associated with being HIV-infected among women who exchange sex using a Poisson model and robust standard errors, using PROC GENMOD in SAS v. 9.3. We clustered the model on individual observations, as the number of recruitment chains was too few to enable clustering at that level. We accounted for

the multi-site nature of the study by including an indicator variable for city as a fixed effect in the models. For this part of the analysis, the data was not weighted, and all results are sample estimates and may not be representative of the underlying population of women who exchange sex in participating cities.

4.2.1.3.2.1 RDS ANALYSIS SPECIFICS

For RDS weighted estimates in Paper 3 we used RDS Analyst software (version 0.7) with RDS-sequential sampler (RDS-SS) estimator to generate population proportions and 95% confidence intervals for key variables in each city. The size of social networks of women who exchange sex, used to generate RDS weightings, was estimated using the question: ‘How many women in [city where the survey took place] do you know who exchange sex?’ We included seeds in the analysis. The size of the population from which women were sampled in each city, required for the RDS-SS estimator, was obtained from the 2015 census estimates for the number of women in each city (179), adjusted using a population-based estimate of the frequency of transactional sex during the most recent partnered sexual event among women (48). To calculate aggregate HIV prevalence among women who did not exchange sex with casual partners in the 2013 NHBS cycle, we estimated the size of the population from which women were sampled by adjusting census population data by the proportion of women living below the poverty line in each city (179). To generate aggregate estimates, we used the Population Aggregate Estimate function in RDS Analyst version 0.51, where aggregated HIV prevalence is a weighted average of city-specific HIV estimates (180). In the sensitivity analysis, we excluded women who reported current or lifetime injection drug use from the analysis of HIV prevalence among women who exchanged sex.

The mean number of recruitment waves ranged from 5 in Detroit to 10 in Houston. Number of seeds ranged from 6 in Chicago to 21 in Seattle, with 13 seeds on average. Visual inspections of convergence plots indicate that for all four sites estimates for HIV prevalence stabilized before the end of data collection. Inspection of recruitment network graphs indicate that there was no clustering in the recruitment process based on the HIV status in any of the four sites.

4.2.1.3.3 Paper 4 – men who have sex with men and inject drugs

The fourth paper of this thesis examines whether HIV infection is associated with reporting methamphetamine as the primary drug injected among MSM who inject drugs. Only cities where at least 10 individual MSM in either 2012 or 2015 reported injecting meth as their primary drug were included. As the objective was to examine the potential risk of HIV acquisition associated with primary drug injected, participants who reported being diagnosed

with HIV in the same year or prior to the year that they first injected drugs were excluded. Participants with a missing date of HIV diagnosis were also excluded.

Participants were categorised into two groups. Of 961 MSM included in the final analysis sample, 324 (33.7%) reported injecting meth most often and constituted one group. The remaining participants constituted the reference group. Of these, 429 (44.6% of the full sample) most often injected heroin, 74 (7.7%) most often injected cocaine, 98 (10.2%) most often injected 'speedball' (heroin and cocaine together), and 36 (3.8%) most often injected some other drug.

The first part of the analysis examined primary drug injected by sociodemographic characteristics and city of interview. We furthermore compared the prevalence of sexual and drug-use risk behaviours, HIV infection, and use of prevention and testing services by primary drug injected.

The bivariate association between primary drug and HIV infection was also examined. We used previous research and evaluation of directed acyclic graphs to inform the selection of potential confounders of the association between primary drug and HIV infection for multivariable analyses (Figure 4). Variables that were significantly associated with both primary drug and HIV infection were added one by one, starting with the variable with the lowest P value for the association with HIV infection. Variables with $P < 0.05$ were retained in the model. Race has been shown to be associated with HIV infection in the US and, despite the lack of a significant association with the outcome in this sample, was included in the model. We also retained education in the model for similar reasons. Sexual identity was included as a two-level variable: gay-identified and non-gay-identified. We evaluated whether there was an interaction between region (West Coast and Denver vs East) and primary drug.

To evaluate whether the association between primary drug and HIV infection was mediated by sexual risk behaviours (number of condomless anal sex partners in the previous 12 months) and/or injection-related risk behaviours (syringe sharing in the previous 12 months), we added these variables to the confounder-adjusted multivariable model one by one. In a sensitivity analysis, multivariable analysis was repeated with a sample that excluded men who injected meth in addition to primarily injecting another drug.

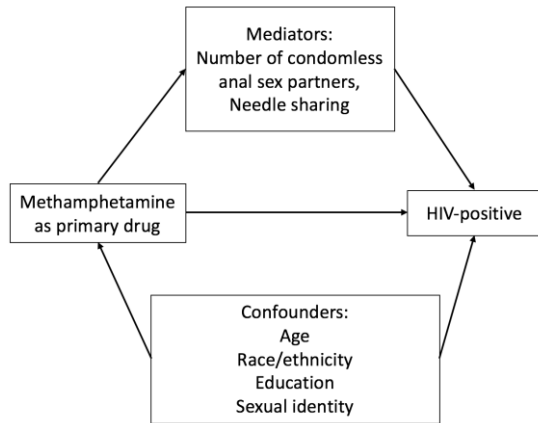


Figure 4: Directed acyclic graph for Paper 4 representing the confounders in the final multivariable model as well as the mediators explored.

5 RESULTS

This section will first report the results from the first three papers, which focus on exchange sex, starting with the results of the main research question on whether HIV infection is more prevalent among those who exchange sex in comparison with other members of similar populations who do not exchange sex. This will be followed by the key results highlighting the differences in socioeconomic characteristics and risk behaviours among those who exchanged and those who did not and which offer a degree of insight into the drivers of HIV prevalence among those who exchange sex as well as highlight their ongoing risk for HIV acquisition and transmission.

Thereafter, Paper 4 on MSM who inject drugs will be presented. This paper discusses the differences in demographic characteristics, sexual and drug-use risk behaviours, and HIV prevalence between MSM who primarily inject meth and MSM who primarily inject other drugs, and possible drivers of HIV risk.

5.1 EXCHANGE SEX – PAPERS 1–3

Exchange sex was very common among women who injected drugs, with 903 out of 2305 (39%) reporting having exchanged sex in the previous 12 months (Paper 1, Table 1). Among MSM this proportion was lower, at 7% (585 out of 8 411; Paper 2, Table 1). Among women who injected drugs and exchanged sex, 31% had had 10 or more and 9% had had 100 or more exchange partners in the previous 12 months. Among MSM, this distribution was skewed more towards a higher number of partners, with only 32% having had a single exchange partner and 19% having had 10 or more exchange partners in the previous 12 months.

5.1.1 HIV infection and exchange sex

Among women who injected drugs (Paper 1), 10.0% of those who exchanged sex tested positive for HIV. There was no statistically significant difference in HIV prevalence between those who exchanged sex and those who did not (10.0% vs 7.4%, $P = 0.33$, Paper 1, Table 2). Among those who exchanged sex, five percent were HIV-positive-unaware, compared to 2.6% among those who did not report exchange sex ($P = 0.01$; Paper 1, Table 2). In bivariable analysis, exchange sex was associated with being HIV-positive-unaware (PR 1.80, 95% CI 1.3–2.5). In multivariable analysis, controlling for age, race/ethnicity, education, homelessness and city of interview, the association between exchange sex and HIV-positive-unaware remained significant (aPR 1.97, 95% CI 1.31–2.97; Paper 1, Table 3).

Among MSM who exchanged sex (Paper 2), 29% tested positive (Paper 2, Table 2). In bivariable analysis there was a statistically significant difference in prevalence compared with those who did not exchange sex (29% vs 18%, $P < 0.001$; Paper 2, Table 2). However, this difference became non-significant when controlling for race/ethnicity, having ever injected drugs and city of interview in multivariable analysis. Among those who exchanged sex, 13.2% were HIV-positive-unaware, compared with 5.6% among MSM who did not report exchanging sex ($P < 0.001$; Paper 2, Table 2). Exchange sex was associated with being HIV-positive-unaware in bivariable analysis (PR 2.16, 95% CI 1.68–2.77). This association remained significant in multivariable analysis controlling for age, race/ethnicity, poverty, education, lifetime injection drug use and city of interview (aPR 1.34, 95% CI 1.05–1.69; Paper 2, Table 3).

In Paper 3, 4.9% (95% CI 2.7–7.1), of women who exchanged sex tested positive for HIV. The HIV prevalence among women of low SES who did not exchange sex with casual partners was 1.6% (95% CI 0.3–2.8), and among women in the general population 0.55% (95% CI 0.54–0.57; Figure 5). Women who exchanged sex had 3.1 times the prevalence of HIV compared to women of low SES who did not exchange sex (95% CI: 1.6–5.9). Compared with women in the general population, women who exchanged sex had 8.8 times the prevalence of HIV (95% CI 7.0–11.1) (Figure 5). Excluding women with any history of injecting drugs from the sample of women who exchange sex in sensitivity analysis did not result in a lower HIV prevalence (4.9%, 95% CI 2.8–7.0). Neither did we observe a large change in HIV prevalence after age standardisation (4.6%).

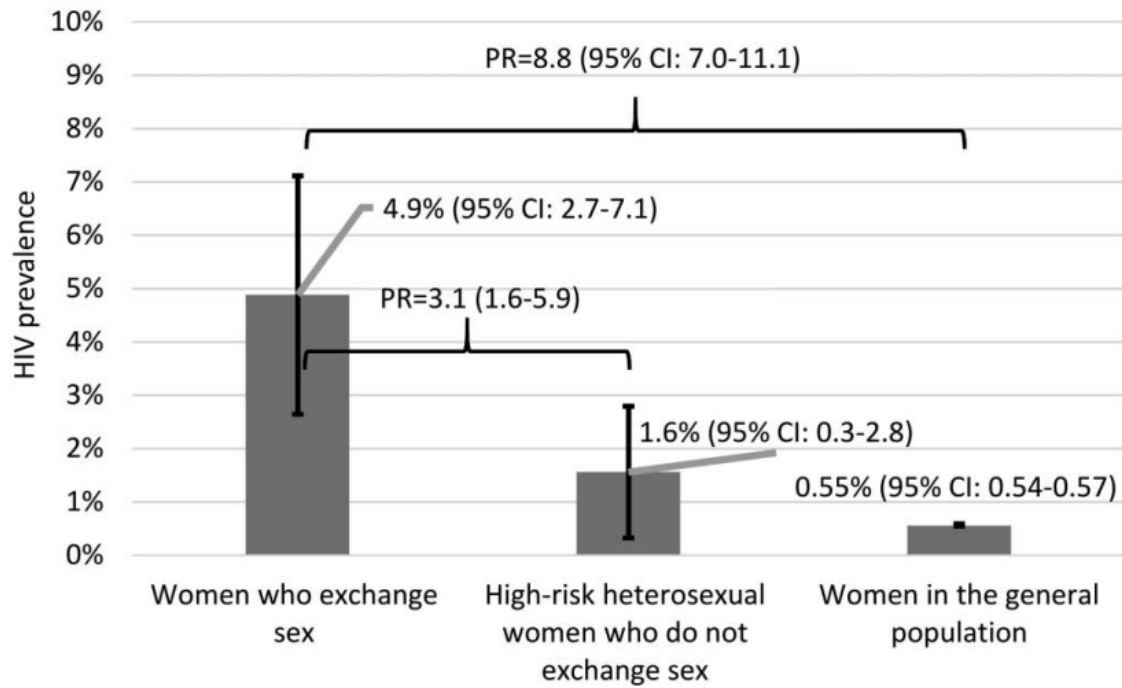


Figure 5: HIV prevalence among women who exchange sex for money or drugs (2016), among high-risk heterosexual women who do not exchange sex (2013), and among women in the general population (2014) – Chicago, Detroit, Houston, Seattle. Paper 3.

5.1.2 Characterising the populations who exchange sex

Sociodemographic disadvantage, sexual and drug-use risk behaviours were associated with exchange sex or common among the populations who exchanged sex.

5.1.2.1 Association between exchange sex and sociodemographic characteristics

Exchange sex was associated with socioeconomic disadvantage both among women who inject drugs and among MSM in Papers 1 and 2, and among women who exchange sex in Paper 3.

Among women who inject drugs, 42% of those with less than a high-school education exchanged sex, compared with 35% of women with at least some college education ($P = 0.03$; Paper 1, Table 1). Exchange sex was more common among those who were unemployed (41% vs 27% for those employed, $P < 0.001$), those who had been incarcerated in the past 12 months (50% vs 34% for those who had not; $P < 0.0001$) or homeless (49% vs 25% for those not homeless, $P < 0.0001$), (Paper 1, Table 1).

Exchange sex was more common among MSM who were black (11%) compared with MSM who were white (5%) or Hispanic (6%), ($P < 0.001$; Paper 2, Table 1). Twenty-five percent of MSM who had less than a high-school education reported exchange sex, whereas only 2% of those with a college or postgraduate education did. Exchange sex was also more common among MSM who were unemployed (13% vs 4% for those employed; $P < 0.001$), homeless (31% vs 5% for those not homeless; $P < 0.001$), lived in poverty (15% vs 5% of MSM who did not live in poverty; $P < 0.001$) and among those who had ever been incarcerated (19% vs 4% for those never incarcerated; $P < 0.001$) (Paper 2, Table 1).

The analysis of data on women who exchange sex in Paper 3 shows that socioeconomic disadvantage was common in this population. Around a third of women in Detroit, Houston and Seattle reported having less than a high-school education, and in Chicago this proportion was 48%. More than 80% of women in all four cities lived below the federal poverty line and between 42% and 65% across cities reported having been homeless in the previous 12 months (Paper 3, Table 1).

Across cities in Paper 3, the proportion of women who reported having been exposed to physical or sexual violence in the previous 12 months ranged from 33% to 56% and the proportion who had been arrested in the previous 12 months because they exchanged sex ranged from 3% to 14%. The proportions who had been incarcerated for any reason in the

previous 12 months ranged from 9% to 25% in addition to the proportion of women who reported having ever been incarcerated which ranged from 35% to 63% (Paper 3, Table 1).

In paper 3, the ways in which women most commonly found clients varied by city. Finding clients in the street, public places, drug-related settings, or through a pimp were the most common ways reported in Chicago, Houston, and Seattle whereas the most common ways reported in Detroit were “through my boyfriend or husband,” “through friends, family or neighbors,” or some other informal way. The reported median income from exchange sex ranged from 300 to 500 USD across cities during the past 30 days (Paper 3, Table 1).

5.1.2.2 Sexual risk behaviours are common among people who exchange sex

Sexual risk behaviours were common among people who exchanged sex. In Paper 1, women who injected drugs and exchanged sex reported a mean of 63.3 male oral, vaginal or anal sex partners in the previous 12 months, compared with 2.6 among women who did not exchange sex ($P < 0.001$; Paper 1, Table 2). Among women who exchanged sex, 19% had had 10 or more condomless vaginal sex partners in the previous 12 months whereas this was the case for only 1% of women who injected drugs and did not exchange sex. Anal sex without a condom was also more common among those who exchanged sex, with 13% having had more than one partner in the previous 12 months compared with 3% of women who did not exchange ($P < 0.0001$). Women who exchanged sex were also more likely to report not knowing the HIV status of their most recent partner (67% vs 34%; $P < 0.0001$) and to report having been diagnosed with an STI in the previous 12 months (20% vs 9%; $P < 0.0001$).

In Paper 2, MSM who exchanged sex had had a higher number of male and female oral, anal or vaginal partners in the previous 12 months compared with MSM who did not exchange sex (mean 19.4 vs 8.6; $P < 0.001$) This was also the case for male condomless anal sex partners (mean 4.3 vs 1.8; $P < 0.001$) (Paper 2, Table 2). Among MSM who exchanged sex, the most recent male partner was more likely to be of unknown HIV status (61% vs 38% for MSM who did not exchange; $P < 0.001$) and had ‘definitely’ or ‘probably’ ever injected drugs (20% vs 7% for MSM who did not exchange; $P < 0.001$) (Paper 2, Table 2).

In Paper 3, among women who exchange sex, the median number of both exchange and non-exchange partners reported in the previous 12 months ranged from 5 to 8 between cities, and the median number of clients ranged from 4 to 6 (Paper 3, Table 2). The mean number of clients ranged from 17 to 56. The median number of clients with whom the participant reported having had condomless vaginal sex in the previous 12 months ranged from 2 to 3, whereas the means were substantially large across cities (7 to 19). The median number of

condomless sex *acts* in the previous three months with any partner ranged from 4 to 10 for vaginal sex and 0 to 2 for anal sex (Paper 3, Table 2).

5.1.2.3 Drug use and associated risk behaviours among people who exchange sex

Drug use and related risk behaviours were more common among those who exchanged sex than those who did not. In Paper 1, women who exchanged sex were more likely to report having receptively shared syringes in the previous 12 months (56% vs 33%; $P < 0.0001$) and to have used non-injection crack cocaine (69% vs 52%; $P < 0.0001$) (Paper 2, Table 2). In Paper 2, among MSM we found that drug use was more common among MSM who exchanged sex compared with those who did not, including a lifetime history of injection drug use (27% vs 5%; $P < 0.001$), use of non-injection crack cocaine (27% vs 3%; $P < 0.001$) and non-injection methamphetamine (24% vs 5%; $P < 0.001$) in the previous 12 months (Paper 2, Table 2).

In Paper 3 there were large variation in the proportion of women who had a history of injection drug use between cities. More women reported previous 12-month injection drug use in Seattle (61%) and Chicago (26%) than women in Detroit (8%) and Houston (4%). The pattern of non-injection crack use was similar, with more women reporting previous 12-month use in Chicago (61%) and Seattle (58%) but fewer in Detroit (23%) and Houston (25%) (Paper 3, Table 2).

5.1.2.4 Factors associated with or mediating the association between exchange sex and HIV prevalence

In both Papers 1 and 2 we explored whether the number of partners mediated the association between exchange sex and HIV-positive–unaware. Among women who inject drugs, after we added a variable for the total number of condomless vaginal and anal sex partners to the final model, the association between exchange sex and HIV-positive–unaware remained significant, although somewhat weakened (aPR 1.78, 95% CI 1.13–2.81). Likewise, the association between exchange sex and being HIV-positive–unaware among MSM remained significant (aPR 1.30, 95% CI 1.03–1.65) when adding the number of casual male condomless anal sex partners in the previous 12 months to the final model.

In Paper 3 we evaluated factors associated with HIV prevalence in the sample of women who exchange sex in a bivariable analysis. Women who had been arrested in the previous 12 months because they exchanged sex were more likely to test positive for HIV than those who had not (PR 2.1, 95% CI 1.1–3.8) (Paper 3, Table 3). However, having been arrested for any reason was not associated with testing positive for HIV (data not shown). Non-injection use

of crack was associated with testing positive for HIV (PR 1.9, 95% CI 1.1–3.4), but current or lifetime injection drug use was not.

5.1.2.5 HIV testing and access to care

In Papers 1 and 2, we found that over 70% of people had visited a health care provider in the previous 12 months, even though the proportions were slightly higher among those who did not exchange compared with those who did. In neither paper did we see significant differences in the proportion of people who had had an HIV test in the previous 12 months (excluding participants who were diagnosed with HIV more than 12 months ago) between those who exchanged sex and those who did not: around half of the women who injected drugs and around 65% of MSM had been tested for HIV (Paper 1, Table 2 and Paper 2, Table 2).

In Paper 3, we found that more than 80% of women had health insurance in all cities except Houston, where only 52% had insurance (Paper 3, Table 1). Over 70% of women had seen a health care provider in the previous 12 months – even in Houston. The proportion of women who had been tested for HIV in the previous 12 months ranged from 33 to 50% across cities (excluding participants who were diagnosed with HIV more than 12 months ago). Some women reported that they had avoided going to health care services because they exchanged sex – ranging from 10% in Detroit to 20% in Houston.

5.2 MSM WHO INJECT DRUGS – PAPER 4

In this paper we found that sociodemographic characteristics, sexual risk behaviours, drug-use risk behaviours and HIV prevalence varied between MSM who primarily injected meth and MSM who primarily injected other drugs. The very high HIV prevalence among MSM who primarily injected meth was largely mediated by sexual rather than drug-use risk behaviours. The results are discussed in detail below.

5.2.1 HIV prevalence

Among MSM who primarily injected meth HIV prevalence was 29% compared with 16% among MSM who primarily injected other drugs ($P < 0.0001$) (Paper 4, Table 1) with an unadjusted PR for this association of 2.06 (95% CI 1.52–2.78). In multivariable analysis, MSM who primarily injected meth were significantly more likely to be HIV-positive compared to MSM who primarily injected other drugs (aPR 1.48, 95% CI 1.08–2.03) (Paper 4, Table 3), adjusting for age, race, education, sexual identity and city.

5.2.2 Characterising the population by drug most commonly injected

5.2.2.1 Demographic characteristics

Meth users were more likely to be younger, with a lower proportion (39%) aged 45 or older among those who injected meth compared to 59% of those primarily injecting other drugs ($P = 0.005$). Almost 60% of those who injected meth were white compared with around a third of those reporting primarily injecting other drugs ($P = 0.04$). Forty-eight per cent of participants who primarily injected meth compared with 35% of those who primarily injected any other drug had some college education or above ($P = 0.02$). Those who injected meth were less likely to report having been homeless in the previous 12 months even though the proportion was still high (71% vs 82%, $P = 0.02$). Primary drug was associated with self-reported sexual identity with a higher proportion of those injecting meth identifying as homosexual or gay compared others (44% vs 15%, $P = 0.0002$) Paper 4, Table 1.

5.2.2.2 Sexual risk behaviours

Sexual risk behaviours were common among MSM who primarily injected meth compared with other MSM who injected drugs. Twenty-nine per cent of MSM who primarily injected meth reported five or more condomless anal sex partners in the previous 12 months compared with 9% among MSM who primarily injected other drugs ($P = 0.0004$). This group was also more likely to report a diagnosis of gonorrhoea or chlamydia (13% vs 5%, $P = 0.0003$) or syphilis (11% vs 2%, $P = 0.0008$) in the previous 12 months (Paper 4, Table 1).

5.2.2.3 Drug-use risk behaviours

MSM who primarily injected meth were less likely to report a variety of drug-use risk behaviours compared with those who primarily injected other drugs. These behaviours include receptive syringe sharing (26% vs 51%, $P = 0.0005$), and the number of syringe-sharing partners (mean 1.5 vs 3.2) (Paper 4, Table 1). Forty-six per cent of meth users reported injecting one or more times per day compared with 66% of MSM who primarily injected other drugs ($P < 0.0001$).

5.2.2.4 Factors mediating the association between primary drug and HIV prevalence

Syringe sharing in the previous 12 months was explored as a potential mediator of the association between meth use and HIV infection but did not alter the association (aPR 1.44, 95% CI 1.07–1.95). However, the association between meth use and HIV became not significant when the total number of condomless anal sex partners in the previous 12 months

was added to the model as a potential mediator (aPR 1.30, 95% CI 0.94–1.79) (Paper 4, Table 3).

5.2.2.5 *HIV testing and access to care*

MSM who injected meth were more likely to have tested for HIV in the past 12 months (excluding participants who were diagnosed with HIV more than 12 months ago) compared to those who injected other drugs (65% vs 54%, $P = 0.03$)

The proportion of HIV-infected MSM who were being treated with ARVs were around three-quarters with little difference by primary drug.

6 DISCUSSION

6.1 SUMMARY OF FINDINGS

I have shown in this thesis that HIV prevalence was generally high among people belonging to more than one key population or within subgroups of key populations in the US. Women who injected drugs and exchanged sex and MSM who exchanged sex were more likely to be HIV-positive but unaware of their status than other members of the same populations who did not exchange sex. Women who exchanged sex were more likely to be HIV infected than women recruited from the same low-income communities and substantially more likely to be HIV infected than women in the general population. MSM who injected methamphetamine had very high HIV prevalence even in comparison to other MSM who inject drugs. Among those who exchanged sex, both sexual and injection risk behaviours were prevalent, and this was also the case among MSM who injected methamphetamine. A common theme across the populations was that exchange sex was associated with socioeconomic disadvantage.

The factors that may influence risk of HIV acquisition and transmission in different populations occur at the level individual level such as sexual and drug use behaviours as well as higher-order factors beyond the individual including sexual contact patterns, structural factors and laws and policies (181-184). The populations in this thesis belong to more than one key population or vulnerable group and different types of individual and higher-order risk factors intersect which is important to take into account when considering where and how to target interventions.

In this discussion I will first discuss the findings in the thesis specifically with regards to HIV prevalence with reference to existing literature. I will then discuss the overall findings in the context of a modified social ecological model (184).

6.1.1 HIV prevalence

6.1.1.1 HIV prevalence among women who exchange sex

We found a prevalence of HIV of 4.9% among women recruited specifically because they exchange sex and 10% among women who inject drugs and exchange sex. The difference between these two estimates is not surprising given that the higher estimate comes from a population of women who all inject drugs. These estimates are both lower than the pooled estimate of 17.3% (95% CI 13.5–21.9) provided in a systematic review of HIV prevalence among US women who exchange sex – some of whom also injected drugs (8). Another review estimated the regional prevalence in Western and Central Europe and North America at 7.4% (95% CI 4.9–10.4) which is more similar to our estimates (7). In both review articles

there was however substantial heterogeneity among the studies included. Many studies are decades old, and a possible explanation for the higher prevalence in some of the older studies could be survival bias whereby people with HIV have since passed away and overall prevalence is lower. The study with the most comparable sample used data from the LA county 2003–4 HIV Testing Survey, a venue-based interview study initiated by the CDC (69) which found a prevalence of 6% among those ever tested. A San Francisco study among sex workers attending care at a peer-based clinic found a self-reported HIV prevalence of 8.7% among those ever tested. However, both of these studies only measured self-reported HIV prevalence which relies on participants having been tested and being willing to disclose a positive result in the survey. Additionally, by not testing participants for HIV, the reported prevalence is likely to be an underestimate.

We found a prevalence ratio of 8.8 (95% CI 7.0–11.1) of the HIV prevalence among women who exchange sex relative to women in the general population. Among women who inject drugs, there was however no difference in HIV prevalence between those who exchange and those who did not.

A study with data from low- and middle-income countries report that female sex workers had 13.5 times the odds of being HIV-infected compared with all women of reproductive age. The comparability to our findings is limited however as that study did not include high-income countries and furthermore presents an odds ratio (OR) which is a measure that cannot be directly compared with a PR (185, 186). Shannon et al. compared the estimated prevalence among sex workers in Western and Central Europe and North America (7.4%) with the HIV prevalence of all adult women and found it to be significantly different (Figure 6) although no measure of association is reported (7).

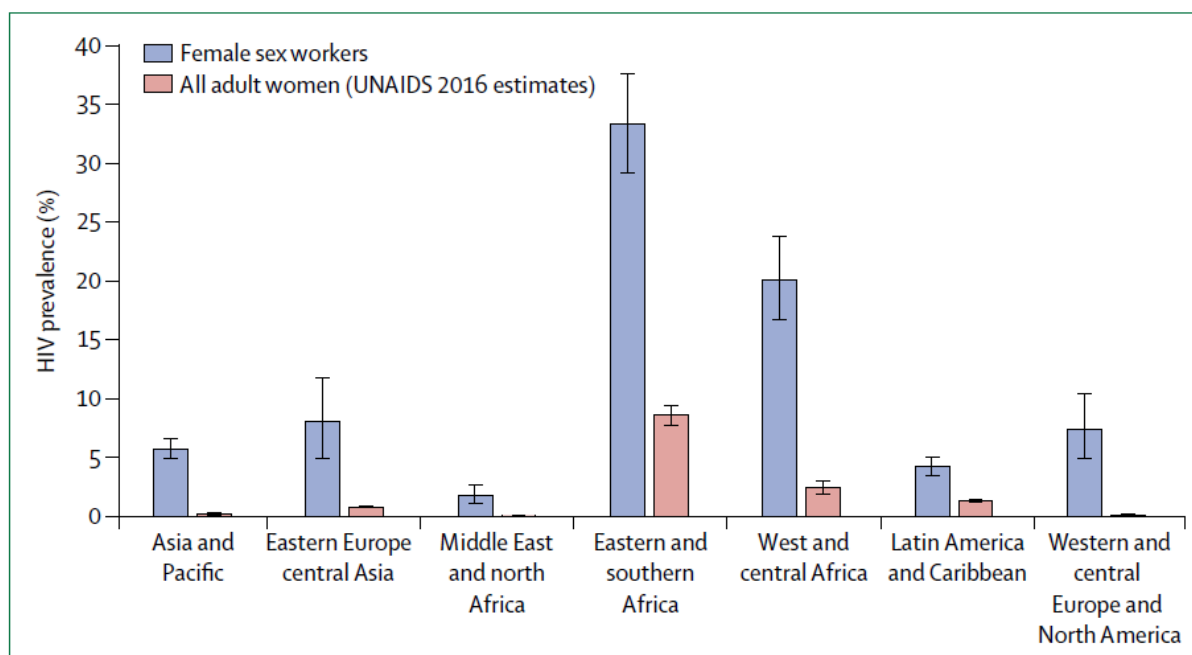


Figure 6: Regional HIV prevalence estimates among female sex workers and all adult women (7). Error bars show 95% confidence intervals (reproduced with permission).

6.1.1.2 HIV prevalence among MSM who exchange sex

The estimated HIV prevalence among MSM who exchanged sex was 29% which is close to the upper range of estimates of HIV prevalence among male sex workers from other studies. The most rigorous of these found an HIV prevalence of 18.7% among those who had ever traded sex and involved more than 2500 men that were tested for HIV, although the sample was limited to men recruited from shelters, meal programmes and low-cost hotels, which limits the comparability with our sample (60). A sample of street-recruited MSM in San Francisco is closer to our study in terms of recruitment strategy and the fact that they tested participants, although they only recruited participants below the age of 30 which limits the comparability and which may explain the lower prevalence of 12% (59). This study is also one of the few that reports on the proportion who are unaware of their infection (42%) which is a higher proportion than we found - 31%. Two of these studies found an association between exchange sex and HIV prevalence. Robertson et al. found an odds ratio (OR) of 3.2 (95% CI 2.5–4.2) although the use of an OR limits comparability with the findings in this thesis given that the outcome (HIV prevalence) was well above 10%. Bacon et al. found that HIV prevalence was associated with a larger number of paying male partners (59, 60). They did not look at the association between exchange sex and being unaware of being HIV-positive, however.

6.1.1.3 *HIV prevalence and HIV-positive–unaware*

In multivariable analysis of the association between exchange sex and HIV prevalence among women who inject drugs and among MSM the association between exchange sex and HIV-positive–unaware was significant. This finding is important given that people who are unaware of being infected cannot be linked to care and treatment, which puts their long-term health at risk. Not knowing their HIV-positive status also puts them at risk of transmitting the infection to others (89).

There are several possible explanations for why an association was seen between exchange sex and HIV-positive–unaware but not overall HIV prevalence. One possible explanation for this finding could be that people who exchange sex and are diagnosed with HIV stop exchanging sex. This is consistent with data that show people who become aware of being HIV-positive change their risk behaviours after learning about their status (89). People who become diagnosed with HIV may also stop exchanging sex due to fear of laws that criminalise potential HIV exposure – in particular in the context of prostitution law (187). If people who have only recently started exchanging sex and have become infected with HIV but not yet been diagnosed, this could lead to a higher overall proportion HIV-positive–unaware among those who are HIV-positive and exchange sex. We were however only able to measure exchange sex in the previous 12 months and it was not possible to stratify analyses by how long people had been exchanging sex. Prevalence of HIV testing in the previous 12 months was similar between those who exchanged and those who did not exchange, but it is possible that those at highest risk for HIV among those who exchanged sex were the ones who had not been tested.

6.1.1.3.1 Misreporting

It is also possible that the findings are the result of misreporting. While people may stop exchanging sex due to fear of laws that criminalise potential HIV exposure, these same fears may have resulted in people who were in fact aware of being HIV-positive not volunteering this information in the interview (187). Thus, our study may have overestimated the number of people who were HIV-positive–unaware among those who exchange sex. Likewise, for similar reasons people who are HIV-positive may have been less likely to disclose that they exchange sex, which could have biased the association between exchange sex and HIV prevalence toward the null.

There is evidence that, at least among MSM, there could have been misreporting of HIV status. Analysis of a MSM sampled in a later round of NHBS (MSM4 in 2014) than the ones used in this thesis (MSM3 in 2011) revealed that a substantial proportion of HIV-positive–

unaware MSM had misreported their status (175). This was based on testing for the presence of ARVs in dry blood spot samples from 299 MSM who self-reported being HIV-negative or having unknown HIV status. Of these, 49% were considered to have misreported their status based on ARVs being detected in their dry blood spot samples suggesting they were HIV-positive on antiretroviral therapy. There are several possible reasons as to why MSM may have misreported their status. The questionnaire asks when they were last tested for HIV and what the result of that test was, and it is possible that MSM who were taking ARVs and had an undetectable viral load at their last test would report this test as ‘negative’. It is also possible that MSM did not report having had a positive HIV test due to stigma and social desirability bias in the interview.

6.1.1.3.2 Implications for validity

The findings from the 2019 study give cause to question the validity of the results with regards to the association between exchange sex and being HIV-positive–unaware, in particular among MSM and possibly also among women who inject drugs. However, as the MSM data used in this thesis was from a different round of data collection, three years later than when the data were collected for the analysis for the 2019 study, it is not possible to determine the extent to which the misreporting occurred at that point. There may be factors that are different between the two data collection cycles, such as overall prevalence of ART in the MSM population. As regards the data on women who inject drugs it is not clear to what extent the findings from the MSM data collected in 2014 would apply to this very different population recruited five years earlier – probably with different proportions treated with ARVs, different levels of education and different concerns about stigma.

If, however, a substantial proportion of MSM or women who inject drugs in this thesis also misreported their HIV status, the way in which it could have impacted the results would depend on whether those who exchanged sex and those who did not exchange sex misreported their HIV status to the same extent. If they did, the prevalence ratio of the association between HIV-positive–unaware and exchange sex would not be biased. It may, however, be a problem for precision of the estimates given that the effective sample size would be smaller and might have rendered the results of the association between HIV-positive–unaware and exchange sex not significant.

If, on the other hand, those who exchanged sex misreported their status to a larger extent than those who did not exchange sex, this would bias the results away from the null and could be an explanation as to why we did not find a significant difference in HIV prevalence in

multivariable analysis although the difference in prevalence of HIV-positive–unaware was significantly different.

It is not possible to say whether the degree of misreporting was higher or not among those who exchanged sex compared with those who did not exchange sex. The 2019 paper found that in comparison with MSM who self-reported as being HIV-positive, those who misreported their status were more likely to be black. The results presented in this thesis found that a higher proportion of black MSM exchanged sex, and black MSM were also more likely to be HIV-infected–unaware. This could mean that the degree of misreporting might be higher among MSM who exchanged sex. Future research repeating the same analysis on the later round of MSM data, excluding those who misreported their status, would be able to shed more light on this issue.

Taken together, there is reason to be cautious when interpreting the findings on the association between exchange sex and HIV-positive–unaware, in particular with regards to MSM. However, despite the potential biases in the self-reported status, my analyses also found that those who exchange sex had high overall prevalence of HIV, not just HIV-positive–unaware. While there were no significant differences in prevalence with those who did not exchange, those who exchanged sex more commonly reported sexual and drug use risk behaviours which is a concern for HIV transmission. While some would have been diagnosed and adequately treated, many would not, and targeting testing for this group is still relevant and recommended. Furthermore, those not infected with HIV are at risk for HIV acquisition and should be targeted with preventive services including PrEP.

6.1.1.4 HIV prevalence among MSM who inject methamphetamine

MSM who inject methamphetamine is an example of a subpopulation where several factors that put people at risk for HIV intersect, including male-to-male sex, injection drug use and use of methamphetamine. The HIV prevalence in this group was found to be high – 20%, and almost 50% higher than the prevalence found among MSM who injected other drugs even though this comparison group is itself a very high-risk population. Of note, non-injection meth use was significantly more common among MSM who exchanged sex compared to other MSM.

In the literature there is limited data specifically on HIV among MSM who inject meth. A significant association was found between MSM between meth or amphetamine use by any route versus no use and HIV infection was found in a meta-analysis (188) with the limitations that none of the studies included looked at injection of methamphetamine. Among young MSM those who injected meth had higher HIV prevalence compared with those who used through

other routes, or who injected other drugs (189). Finally, a recent cohort of MSM in the US recruited through apps found that those who used meth were significantly more likely to seroconvert than those who did not, although they did not measure by which route meth was administered which limits the comparability (138).

Of note, the prevalence among MSM who exchanged sex was higher than among MSM who inject meth. This is not surprising given that the overall HIV prevalence among MSM is known to be higher than among PWID. The men included in the study on exchange sex were specifically recruited through targeting MSM venues and it could be that they were more likely to identify as gay and were more connected to high risk sexual MSM networks. By comparison, people in the IDU cycles – used for the analysis on meth injection – were recruited mainly because they injected drugs and might be less likely to identify as MSM and to be part of MSM sexual networks to the same extent.

The findings of this thesis indicate that MSM who inject meth have very high HIV prevalence, in particular in comparison to other MSM who inject drugs.

6.1.1.5 Summary

In summary, HIV prevalence is high among people who exchange sex and among MSM who inject meth. In order to target interventions to prevent HIV acquisition and transmission appropriately it is important to consider the various factors that might influence the risk of acquisition and transmission. These include not only sexual and drug use risk behaviours but sexual contact patterns, socioeconomic characteristics, and laws and policies. For the populations studied in this thesis who belong to more than one key population or vulnerable group, several risk factors intersect which needs consideration when designing interventions. The next section of the discussion will present discuss the findings of the thesis in relation to the existing literature.

6.2 DETERMINANTS OF HIV RISK

A widely used model for looking at determinants of HIV risk is the modified social ecological model (184). This model looks at several domains of HIV infection risks including individual factors as well as factors beyond the individual at four other levels: network, community, public policy and stage of epidemic (Figure 7). It provides a framework for considering how these factors interact to influence HIV risk. I will now discuss the findings of the studies included in this thesis using this model. The primary perspective is that of the US, but where relevant other literature is included.

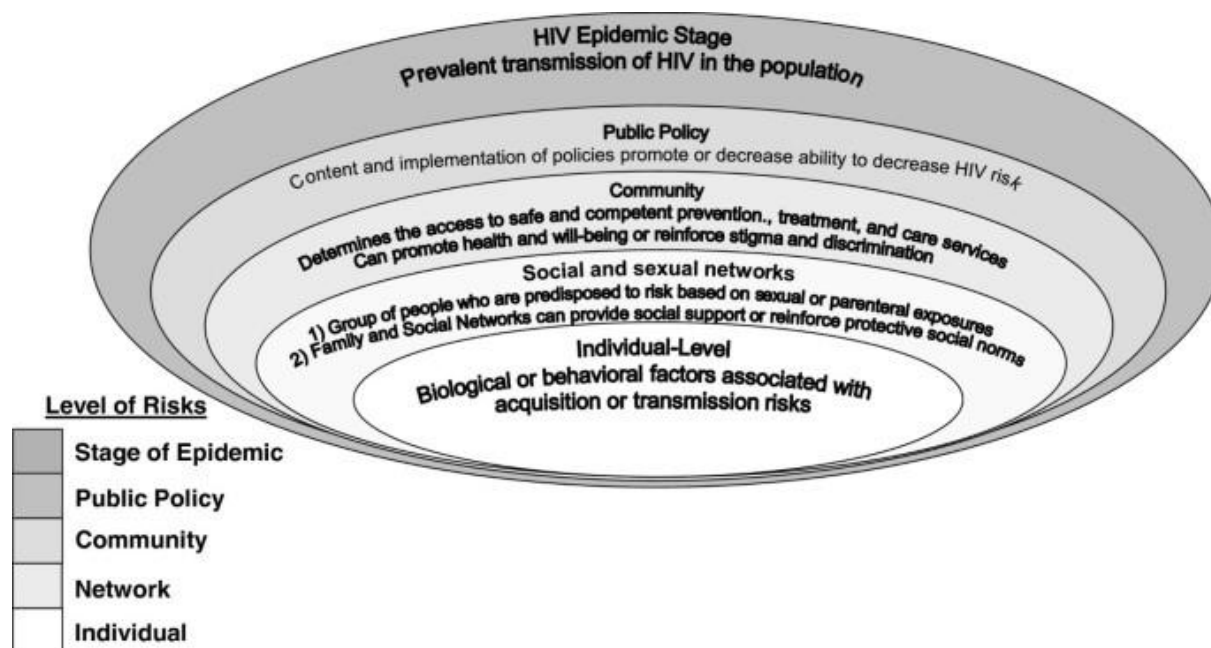


Figure 7 Modified social ecological model for HIV risk in vulnerable populations (184) – reproduced with permission.

6.2.1 Individual

Factors that affect risk for acquisition and transmission at the individual level include sexual and drug use risk behaviors (184). In this thesis, the populations studied are defined by their behaviour – specifically exchange sex, injection drug use in general and meth use in particular. While these are risk behaviours they do not necessarily put people at risk for HIV directly but through other behaviours including condomless sex and needle sharing.

6.2.1.1 Sexual risk behaviours

A consistent finding across all populations who exchange sex was that sexual risk behaviours were common. Among women who inject drugs and among MSM, those who exchanged sex reported more condomless partners than those who did not exchange sex. Women specifically recruited because they exchange sex also reported multiple condomless partners and clients over the previous 12 months. The findings that people who exchange sex have multiple partners is not surprising and is consistent with existing literature (21, 56, 91, 96, 102, 190, 191) and is a concern for both HIV acquisition and transmission.

MSM who primarily injected meth were substantially more likely to report sexual risk behaviours, including a higher number of condomless anal sex partners, than MSM who primarily injected other drugs. As discussed earlier, meth is used to increase sexual desire, to prolong sex and to make sex more pleasurable (139-141). Existing literature shows that men using meth are more likely to have condomless anal sex and sex with multiple partners (144, 145, 192). Meth use is therefore one individual level behaviour that influence the likelihood of another individual behaviour that increases the risk for HIV acquisition and transmission.

6.2.1.2 Sexually transmitted infections

STIs increase the risk of HIV acquisition and transmission (99, 193) and is an individual level factor that influences the likelihood of HIV acquisition and transmission associated with sexual risk behaviours. Among women who inject drugs and among MSM, those who exchanged sex were more likely to report STIs, compared with those who did not exchange sex. MSM who injected meth were more likely to have been diagnosed with an STI in the previous 12 months than MSM who primarily injected other drugs. There may be a multitude of reasons as to why the prevalence of STIs is higher among those who belong to more than one key population or vulnerable group although the high prevalence of sexual risk behaviour is likely a factor. Other factors may also be important such as sexual contact patterns which will be discussed below.

6.2.1.3 Drug-use risk behaviours

Drug-use risk behaviours were common among all the populations who exchanged sex in this thesis. In the literature, injection drug use has been shown to intersect with exchange sex: exchange sex is common among women who inject drugs (52, 53, 120, 194) and injection drug use is more common among women who exchange sex than among other women (92, 103, 121). Women may also choose riskier situations or behaviours out of desperation to avoid withdrawal (93), illustrating how drug use could influence sexual risk behaviours. With regards to MSM, several studies in the US and Australia have shown both injection and non-injection drug use to be more common among MSM who exchange sex compared with those who do not (56, 58, 91, 122). While sexual transmission has been shown to be an important risk factor for HIV transmission among PWID (77) exchange sex may be associated with additional risk. Hence, populations who inject drugs and exchange sex are at risk for HIV acquisition and transmission through both drug use and sexual risk behaviors and that services need to address both.

MSM who primarily injected meth were, however, less likely to report injection-related risk behaviours compared with MSM who primarily injected other drugs. In the literature there is

not clear evidence as to whether injection risk behaviours differ by drug injected. Lorvick et al. found that women who injected methamphetamine were more likely to report receptive syringe sharing and sharing with more than one person in the previous six months (195). Molitor et al. found that PWID who injected methamphetamine were more likely to share needles, but Ropelewski et al. found that this was not the case (196, 197). None of these studies were among MSM who inject drugs, however. In this thesis, MSM who primarily injected meth injected less frequently than other MSM which is consistent with a previous study which found that of MSM who injected meth, only 20% reporting injecting at least once a week compared with 43% of those who injected heroin (Bull et al., 2002). It is possible that the need for syringes is lower, reducing the need to share needles. It could also be that as MSM who injected meth were more affluent they had better access to clean needles.

With regards to the relative roles of sexual and drug-using risk behaviour among MSM who inject meth we found that the association between meth as primary drug injected and HIV infection was in part explained by the number of condomless anal sex partners. This indicated that sexual risk behaviours may have a role in acquisition even though the interpretation is limited by the fact that behaviours were only reported for the previous 12 months. Syringe sharing did not mediate the association between primary drug injected and HIV infection; not surprising given that MSM who injected meth were less likely to share needles, further suggesting that HIV prevalence may be driven by sexual risk behaviours rather than injection risk behaviours in this subpopulation of MSM who inject drugs. This is an important finding in that while MSM who inject drugs are at risk for HIV due to both injection and sexual risk behaviours, this may not be as much of a concern for MSM who inject meth.

6.2.2 Network

The next level of the modified social ecological model concerns social and sexual networks and how they relate to HIV risk (184), Figure 7. Network level factors influence the probability of exposure to HIV of individuals and include both biological factors such as HIV prevalence as well as sexual contact patterns. This level is also concerned with supportive social networks although these were not studied in this thesis.

6.2.2.1 Partner risk profile

The risk profile of the partner could be important in determining the risk of HIV acquisition or transmission associated with condomless sex and needle sharing. This includes whether the partners themselves engage in risk behaviours or are part of communities or networks with high HIV prevalence (198). In this thesis we found that those who exchanged sex had more condomless partners than their counterparts who did not exchange sex but in mediation

analysis these sexual risk behaviours did not explain the association seen between exchange sex and being HIV-positive–unaware. This suggests that factors other than the number of partners may explain some of the association between exchange sex and being HIV-positive–unaware, such as such as the risk profile of the sexual partners. It is possible that people who exchange sex have partners that are more likely to be HIV-positive, either because they are ‘customers’ who in turn have more condomless sex with others who exchange sex, or because they are non-exchange partners that themselves are part of a broader risk environment and with higher-risk sexual contact patterns. We were not able to formally test these hypotheses, but among women who inject drugs and among MSM, those who exchanged sex were more likely to have had a most recent partner whose HIV status was unknown. MSM who exchanged sex were also more likely to report that their most recent partner injected drugs.

An example from the literature of a similar situation is what has been observed among black MSM, where a difference in risk of HIV acquisition persists even after controlling for the number of condomless partners and the variable that best explains excess risk is race of the sexual partner. With HIV prevalence high among black MSM, any one condomless sexual encounter with another black MSM is more likely to result in exposure to HIV than if the partner had been of another race. The more segregated sexual contact patterns become – not unlikely in the southern US where this study was done – the more risk is concentrated. As the authors put it: ‘partner pool risk is a driver of disparities’ (198). Similarly, Hallfors et al. found that differences in rates of STIs and HIV rates between white and African-American young people were not explained by differences in sexual behaviours, indicating that HIV risk is related to factors other than sexual behaviours in this group (199).

There may be other factors in the community that determine the level of risk associated with individual sexual behaviours (200). Some of these will be discussed below, but relevant to the ‘network’ level is the presence of concurrency. Concurrent sexual partnerships in a population are associated with the spread of HIV infection and this is an important determinant of individual HIV risk. These partnerships, as opposed to sequential partnerships, carry a higher risk of HIV transmission as all partners – not just the last partner – are at risk for HIV acquisition from the other partners (201, 202). Frew et al. found that 38% of women in low SES areas reported having a male partner who had multiple relationships (183). Concurrency is also associated with exchange sex. Dunkle et al. showed that women who reported having stayed in relationships for economic reasons and women who reported transactional sex with non-regular partners were more likely to also report sexual concurrency (26). Other community level factors that could influence whether concurrency occur as well be discussed below.

Among MSM who inject drugs the association between meth injection and HIV infection was mediated by the number of partners given that the association between primary drug and HIV became not significant when a variable for total number of condomless anal sex partners was added to the model in mediation analysis. While the number of partners appears to a key factor associated with HIV infection, this variable may also be a proxy for other sexual risk factors. MSM who inject meth may have more risky sexual encounters such as having sex for longer durations and having rougher sex which may increase the risk for HIV acquisition. The nature of sexual contact patterns may also play a role. In the context of meth use among MSM group sexual activity may occur where condomless sex is common (136, 143, 203, 204). It may be that HIV prevalence is high in these groups, increasing the risk that any one sexual encounter may result in HIV transmission.

In summary, the findings from the studies included in this thesis suggest that sexual contact patterns and partner level risk could be factors in determining individual level risk among populations who exchange sex and among MSM who inject meth.

6.2.2.2 Violence

Violence can be another factor that influences the likelihood that people engage in risk behaviours. Violence is perpetrated between people and that is why I have included it at the network level, although the determinants of violence can be found at the other levels of the model – community and laws and policies (20).

Experiences of violence in the past could be a determinant of risk behaviours – adverse childhood events have been linked to risk behaviours in adulthood such as sex work and injection drug use (58, 205, 206). We did not collect data on past violence however so it is not possible to comment on its relevant to the population studies in this thesis.

The high prevalence of current physical and sexual violence victimization among women who exchange sex seen in this thesis and reported elsewhere (93) is a major concern for women's health and safety in a general sense but it is also important for HIV risk specifically. It is well-documented that women who exchange sex are at risk of sexual and physical violence from clients, pimps and law enforcement, as well as from regular partners who may also serve as pimps (20). There is evidence that women who are homeless or who work on the street and in public places are more exposed to violence (207, 208), although some women who work indoors, for example in their own home or hotels, are also at risk as they are isolated (27). Violence is underreported among women who exchange sex due in part to how normalised these experiences of violence are; therefore true experiences of violence in our sample could be higher (93). Although violence was not associated with HIV prevalence in this thesis,

previous work has shown that violence against women who exchange sex has been linked to HIV risk behaviours as it limits women's negotiating power, and mathematical modelling suggests that eliminating sexual violence against sex workers in Canada, together with measures to support sex workers in dealing with the effects of past violence, would lead to a 20% reduction in HIV prevalence among sex workers and their clients (20). The high prevalence of violence reported in this thesis remains a concern for the safety as well as HIV risk of women who exchange sex.

6.2.3 Community

There are a multitude of factors at the community level that could be important for HIV risk including socioeconomic factors such as poverty, deprivation, and disadvantage. Also included here are more practical factors around access to services for treatment and prevention. These may, in turn, be affected by stigma and community norms (184).

6.2.3.1 Community factors that affect network level HIV risk

Community factors could affect HIV risk at the lower network level through, for example, prevalence of STIs, sexual partner concurrency and access to HIV testing and treatment (209). A neighbourhood where a high proportion of people lack health insurance and access to care will likely be a community with a higher prevalence of STIs. An STI at the individual level increases the risk that that person will acquire HIV, but a high population prevalence of STIs could increase transmission risk of HIV in the community and therefore the risk that someone will encounter a partner who is HIV-infected (210). Access to PrEP testing and treatment for HIV may also be relevant to burden of HIV in some communities. Sullivan et al. found that many of the census tracts with high HIV burden are in US states that did not expand Medicaid although this is only an ecological correlation and there may be alternative explanations. Other barriers include access to PrEP and access to transportation to meet medical appointments (211).

High rates of incarceration can affect HIV risk in different ways through disrupting existing relationships and affecting sex ratios in communities which may result in concurrency. The incarcerated partner may also face a higher risk of HIV in prison through, sometimes coercive, sexual relationships with people at high risk of infection. The partner that is left in the community may have other relationships, and this phenomenon is referred to as separational concurrency (37, 183, 202, 212). Repeated, short incarceration episodes can cause disruption not only at the individual and family level but also at the community level and contribute to ongoing health disparities (213).

Residential segregation in the US context is another factor that may influence HIV risk of individuals through their sexual contacts, as people vulnerable to HIV are concentrated in low-income neighbourhoods. Concentration of risk in neighbourhoods means that a particular person's HIV risk is increased regardless of their individual risk behaviours (200). A neighbourhood study in Massachusetts found that the incidence of AIDS increased with the levels of economic deprivation of the neighbourhood, being seven times higher in places where 40% of people lived in poverty compared with neighbourhoods where 2% lived in poverty (214). An analysis of more recent data shows that among women in the US who did not inject drugs and who lived in areas with high prevalence of poverty, the HIV prevalence was 2.2% – 20 times greater than women in the general US population (215). New diagnoses of HIV as well as HIV prevalence in the US intersect with areas with poverty and low educational attainment, as found by ecological analyses and work with mapping at the census tract level (211).

Concentration of risk have relevance for people who exchange sex. Inciardi et al. showed that in Miami HIV is concentrated in neighbourhoods that historically have a high proportion of African-American residents. African-American women who exchange sex were found to recruit clients largely in these areas as they were local residents. White and Hispanic women on the other hand recruited clients in areas with a lower prevalence of HIV (102). In this thesis, women who exchanged sex were almost nine times as likely to be HIV-infected as women in the general population, but only three times as likely compared with women of low SES from the same communities. This suggests that part of the high HIV prevalence seen among women who exchange sex could be related to factors that they share with other women of low SES. Some of these may be related to the HIV risk in the surrounding community or in their sexual contact patterns – including with both clients and non-clients.

6.2.3.2 Socioeconomic factors influencing individual behaviours

Socioeconomic factors do not only influence the HIV risk associated with sexual contact patterns at the network level but could also influence individual level risk behaviours such as for example whether people engage in exchange sex and what sexual risks are taken in that context.

Indicators of socioeconomic hardship were associated with exchange sex or common among those that exchanged sex in the studies included. Among women who injected drugs exchange sex was more common among those with low educational attainment, unemployment and homelessness. Among other women who exchanged sex studied in this thesis, socioeconomic disadvantage was also common. These findings are largely consistent with previous research

(26, 103). Among MSM, exchange sex was also more common among those with low education level, unemployment, homelessness, poverty and a history of incarceration. These findings are largely consistent with existing data, also showing that MSM who exchange sex are more likely to be affected by poverty, low educational attainment, homelessness and previous incarceration (22, 58, 216). In contrast to the findings for people who exchange sex, MSM who primarily injected meth were more likely to have attained a higher level of education and less likely to be homeless compared with MSM who primarily injected other drugs, but they were more likely to be HIV-infected, indicating that socioeconomic disadvantage is less likely to be an upstream driver of risk in this population.

Poverty has been associated with HIV infection both at individual and community levels (100, 209, 214). A case–control study comparing African-American men and women who had been diagnosed with HIV with age and gender-matched controls found that cases were more likely to have low income, be homeless, food insecure and have a history of incarceration (100). Socioeconomic factors could influence the likelihood that people engage in exchange sex. In a survey of low-income women in Baltimore, German et al. found that the odds of having multiple partners or exchanging sex were significantly reduced with each additional characteristic of stability as measured by income, an absence of homelessness, and an absence of recent incarceration (101). In a case–control study of African-American men and women diagnosed with HIV, Adimora et al. found that those with HIV were not only more likely to have markers of poverty such as being homeless, not having insurance, and having a low level of education, they were also more likely to exchange sex, have riskier partners and to use crack than those where not HIV-infected. The authors also looked at a subset of cases that were ‘lower risk’, as defined by the absence of a number of risk behaviours, including exchange sex. Also in this subset, low income and low education and food insecurity were associated with HIV infection (100).

Socioeconomic factors could also directly influence specific sexual risk behaviours as risk-taking around condom use may be related to people being in positions of economic hardship (22, 37, 92, 93).

6.2.3.2.1 Arrest and exchange sex

People who exchange sex are at risk for being arrested on prostitution-related charges but also on other charges – in particular, drug-related – illustrating one of the ways which exchange sex, drug use and risk of arrest appear to interact. Among women who inject drugs and among MSM, we found that exchange sex was more common among those with a history of incarceration. Among women recruited specifically because they exchange sex, incarceration

and having been arrested because they exchange sex were commonly reported, with the latter being associated with HIV infection.

Our findings are consistent with previous literature. A survey of 30 street-based women who exchange sex in New York City found that 28 had been arrested in the previous 12 months, and of those, 43% were arrested for prostitution-related charges (217). A study in Canada found that 24% had been incarcerated in the previous 44 months (218). Arrest has also been shown to be associated with HIV infection. A systematic review of research on policing practices and HIV risk among female sex workers worldwide found that between 6 and 45% of sex workers reported having ever been arrested (219), and that history of arrest was associated with HIV infection. However, most studies in that review looked at arrest for any reason, and only one study, from Argentina, looked specifically at arrest related to sex work activity (220). An ecological analysis focused on Europe found a linear relationship between the number of people imprisoned and HIV prevalence among sex workers (182) which gives some indirect evidence. People who exchange sex and who find clients on the street and in public places are more visible which may mean they are more likely to be arrested (218, 221) and several studies have shown an increased risk for HIV among women working on the street (182). High prevalence of prior arrest reported in this thesis is therefore a concern given the evidence of the association with HIV risk in the literature.

Police arrest for exchange sex might be an indication for general police activity, as has been shown elsewhere (218) and which could result in people who exchange sex choosing less safe areas. Their negotiating power with clients around condom use may also be compromised and people who exchange sex might also not carry condoms as it could be taken for evidence for sex work (20, 219, 222). This illustrates how community police activity could influence whether individual sexual risk behaviours occur.

6.2.3.2.2 Homelessness

Among women who inject drugs and among MSM, exchange sex was more common among those who had a history of homelessness compared with those who did not. A history of homelessness was also common among the other women who exchange sex studied in this thesis. Living in unstable housing conditions has also been shown to be associated with incarceration among sex workers in Canada (218). Women who are released from prison face barriers to re-entering the community and to finding housing, and homelessness can be a main reason for recidivism (213, 218). Women who exchange sex and live in unstable housing conditions may also be more likely to solicit in public, thus being at increased risk of arrest (223, 224).

6.2.3.3 *Stigma*

Stigma, including perceived, anticipated or enacted stigma may affect behaviour as well as access to services. Stigma may be related to sexual orientation, HIV status and to exchange sex and drug use and the populations in this thesis may therefore be subject to multiple stigmas – referred to as layered or intersectional stigmas (225). MSM who exchange sex could be affected by stigma around both sexual orientation, exchange sex and HIV status. Even those who are not HIV infected may be subject to HIV-related stigma which may be a barrier to accessing PrEP (226).

Stigma against people who exchange sex have multiple manifestations including a reduction in negotiating power with clients around condom use which is another way in which stigma could affect specific sexual risk behaviour (227). Stigma may also affect access to both drug treatment and harm-reduction services, and to services for women who exchange sex (228). In this thesis, between 10 and 20% of women who exchanged sex reported that they avoided going to health care services because they exchange sex which indicates that this particular stigma might not be such a concern. We did not collect this data among women who inject drugs and exchange sex, or among MSM however.

Stigma around sexual orientation might influence the decision to inject meth and MSM who primarily inject meth may have started using meth to help deal with negative emotions associated with being gay (229, 230) illustrating one way in which stigma can be a factor that affect behaviour. In this thesis, sexual identity was found to be associated with primary drug.

6.2.3.4 *Access to prevention and care services in the community*

Access to prevention and care service are a community level factor that may influence the likelihood that people engage in risk behaviours as well as the transmission risk associated with individual behaviours.

6.2.3.4.1 *Drug treatment and harm reduction*

Harm reduction refers to a set of measures to minimise the harmful effects of drug use, ranging from safer use to managed use to abstinence (231). The availability of, and access to, services designed to help people transition out of drug use, such as counselling for substance abuse and medication-assisted therapy, can be a determinant of risk behaviours and it could affect the likelihood that people are able to transition out of drug use, thus reducing risk behaviours such as needle-sharing, or sexual risk behaviours such as exchange sex that people may engage in in order to gain access to drugs (40, 58, 232-236). In this thesis only a third of

women who injected drugs and exchange sex reported receiving alcohol or drug treatment in the previous 12 months.

Access to sterile injection equipment through needle-syringe exchange programmes is another community level factor that influence individual risk for HIV acquisition and transmission (237). Among women who inject drugs in this thesis, less than half had received free needles and syringes in the past 12 months, indicating a substantial shortfall. Access to these is largely influenced by factors at the level of laws and policies which will be discussed below.

6.2.3.4.2 Pre-exposure prophylaxis

Access to and use of PrEP is a factor that modifies the risk of HIV acquisition associated with condomless sex or needle-sharing (22, 238, 239). PrEP involves taking a specific combination of HIV medicines daily and is a way for HIV-negative people at high risk of HIV infection to reduce their risk of acquiring the infection. Among MSM who exchange sex in this theses, only about a quarter had heard of PrEP, although this proportion may have been higher with a more recent sample given the rapid increase in use of PrEP since data were collected (240).

The US Government Plan for Ending the HIV Epidemic identifies increasing use of PrEP as an important strategy (241). Based on current US federal guidelines (242), people who are at ongoing substantial risk of acquiring HIV should be offered PrEP. This includes MSM who have had anal sex without a condom or been diagnosed with an STI in the past 6 months, and women who infrequently use condoms during sex with one or more partners of unknown HIV status or who have been diagnosed with an STI in the past 6 months. For PWID the sexual risk criteria also apply as an indication for PrEP, in addition to having shared injection equipment in the past 6 months. Large proportions of the populations that are the focus of this thesis would be eligible for PrEP based on these guidelines. There are multiple factors that affect the access to and use of PrEP in the US, including access to health insurance, levels of health literacy and the presence of stigma related to sex, HIV and sexual orientation (240). For the populations studied in this thesis, several possible stigmas may intersect which could limit the uptake of PrEP, including exchange sex and injection drug use, or sexual orientation and exchange sex.

6.2.3.4.3 Testing and treatment

Access to testing and linkage to care and treatment is a key community level factor that modifies the individual level risk of HIV transmission from condomless sex and needle sharing given that HIV-positive people who are adequately treated and who have an undetectable viral load have been shown to not transmit infection (86, 87). This is of

importance with regards to the populations in this thesis. While in some of the studies it was not possible to conclude that the HIV prevalence was significantly higher among those who exchanged sex compared to those who did not, the finding that absolute HIV prevalence was high and sexual and drug use risk behaviours were common among those who belonged to more than one key population or vulnerable group is still of concern. Ensuring access to treatment is key to ensuring that onward transmission of HIV is limited.

Testing is the first step in ensuring that people are linked to care. Current CDC HIV testing guidelines recommend that people at high risk for HIV infection, which include those who inject drugs as well as those who exchange sex for money or drugs, are tested for HIV every 12 months. MSM should also be tested every 12 months (243, 244). In the populations studied in this thesis the proportions of people who had been tested for HIV in the previous 12 months were not as high as recommended. Around half of women who inject drugs and two thirds of MSM had been tested in the previous 12 months. Among other women who exchanged sex, between half and two thirds had been tested in the previous 12 months. Among MSM who inject drugs, a higher proportion – around two-thirds of those who injected meth, had been tested in the past 12 months compared to others. Still, given that the prevalence of HIV was substantially higher among MSM who injected meth, this indicates that more frequent testing may be needed.

In the populations studied in this thesis, relatively high proportions of people had health insurance or had visited a health care provider in the previous 12 months, indicating that there are missed opportunities for offering HIV tests. Those who test positive for HIV should be offered linkage to care and support for retention in care, something that may be challenging for many people who belong to key populations or vulnerable groups. Prevalence of treatment was not examined with regards to the populations in this thesis who exchange sex but is included as key recommendation for future analyses. Among MSM who injected meth, however, around three-quarters of those who reported a previous positive HIV result also reported being on treatment. While this is a relatively high proportion, it still falls short of the UN target of 90% of those diagnosed being on treatment (245).

6.2.4 Public policies

Laws and policies act to influence risk at lower levels including community level and ultimately individual behaviour. To illustrate the relevance of laws and policies however, a few examples are provided how it is relevant to the populations studied.

Laws that criminalise prostitution together with policing practices may result in people who exchange sex choosing to do so in less safe locations and the risk to individuals who exchange

sex is therefore influenced by whether sex work is legal and relates to factors including their risk of arrest and incarceration and whether they are able to carry condoms (114). Criminalising sex work also results in inadequate access to HIV prevention and treatment services, thus influencing HIV risks at the individual level (20). The criminalisation of sex work can interact with other structural factors – as discussed in the introduction, people may have begun exchanging sex as a result of a lack of other ways to earn an income (31, 36) and people who engage in these practices face increased rates of incarceration. With a criminal record people could face barriers to finding employment, housing or social benefits (110, 111) potentially resulting in difficulties leaving sex work.

In the US today, needle-syringe exchange programmes are illegal in many states (116) which is a key barrier to access for people who inject drugs. Women who inject drugs and exchange sex face challenges associated with two sets of laws and policies – those around sex work and those around needle-syringe exchange programmes, potentially negatively impacting HIV risk.

Health insurance policies are also relevant to HIV risk as it could impact access to care and treatment. In this thesis, over 80% of women who were recruited because they exchanged sex had health insurance, except for Houston where the proportion was 52%, likely because Texas is one of the states that chose to not expand access to Medicaid under the Affordable Care Act enacted under the Obama administration⁷.

6.2.5 HIV epidemic stage

The final level in the modified social ecological model (184) concerns the HIV epidemic stage in terms of incidence and prevalence which ultimately influences the risk of HIV acquisition and transmission. In terms of the groups studied in this thesis, these belong to populations in the US where prevalence is known to be high and where large proportions of new HIV diagnoses occur (12) which would influence HIV risk of individual members of these populations. It was in fact because of the burden of HIV in these populations was so high that I was interested in exploring whether it was even higher among those who belonged to more than one key population or vulnerable group.

⁷ <https://www.healthinsurance.org/medicaid/> Accessed April 23, 2022

6.3 RECOMMENDATIONS FOR INTERVENTIONS

Interventions to prevent HIV acquisition and transmission can be targeted at the different factors that directly or indirectly affect the risk for HIV acquisition and transmission as outlined above. This includes addressing individual risk behaviours through improving access to drug treatment services that can help people refrain from injecting drugs and improving access to needle-syringe exchange services reduced the harm associated with needle sharing. Other measures modify the risk of HIV acquisition and transmission of different behaviours such as improving access to STI treatment, PrEP and testing and linkage to care with ART. Expanding access to these services could also address risks at the network level; those concerning partner risk profile and sexual contact patterns. If people are treated for STIs, on PrEP, test regularly and are linked to care and treatment this may likely result in a lowered overall risk that sexual and drug-using partners are able to transmit HIV, although evidence show that expanded use of ART does not necessarily result in lower incidence at the population level, likely because of heterogeneity of risk where a smaller group of higher risk individuals sustain transmission (246). This is an argument for targeting some of the populations with high HIV prevalence and frequent risk behaviours described in this thesis. Many of the higher-order factors that affect whether behaviours occur are important but more complex to address including stigma, poverty, homelessness and unemployment and the legal or policy environment. These require interventions beyond the scope of public health, but where advocacy using public health data could play an important role.

6.3.1 Targeting interventions to populations with intersecting risk

The focus of this thesis is the intersection of risk among people that belong to more than one key population or vulnerable group. This section outlines some considerations with regards to addressing risk for HIV acquisition and transmission in populations where risks intersect.

6.3.1.1 Exchange sex, low SES and drug use

People who exchange sex and inject drugs face different challenges to those who only inject drugs, and services should take this into account and address sexual as well as injection-related risk. HIV prevention interventions for PWID are often largely focused on injection-related risk, whereas an increased focus on sexual transmission may be needed, in particular for those who exchange sex.

While use of male and female condoms should be promoted (111), condom use may be difficult to negotiate if people are offered additional money to not use a condom when they are in a position of drug dependency or economic hardship (22, 37, 92, 93). These same

factors are likely barriers to a reduction in the number of partners among those who exchange sex. This illustrates how additional factors such as drug use or low SES affect the risk of HIV acquisition and transmission among those who exchange sex and they need addressing accordingly. Interventions for people who exchange sex need to address the broader context and structural factors and consider needs around housing, and alternative ways of earning an income (93, 111). Services should also recognise that some people may have started exchanging sex to be able to finance a substance use disorder, whereas others may have first exchanged sex and then started using drugs. For them, using drugs may be a way to cope with the sex trade or are initiated to drug use as a means of control by pimps (247-251). Helping people to stop using drugs and leave the sex trade may require different approaches depending on the individual person's trajectory into drug use and exchange sex.

6.3.1.2 MSM who inject meth

As sexual and injection related risks are seen as distinct transmission categories HIV prevention services may focus on one or the other, such as services for MSM and PWID. This approach might not be adequate for populations that face intersecting risks such as MSM who inject methamphetamine (252, 253). Furthermore, depending on the drug injected different strategies are needed to address HIV risk. Methamphetamine is associated with sexual disinhibition and MSM who inject these face challenges different from those who inject heroin or other drugs. While medication-assisted treatment (MAT) is commonly offered to PWID it is not an intervention to address meth addiction, and no medications are approved for treatment of meth dependence (118, 254). Even though MSM who inject meth were less likely to share syringes than others and that sexual transmission appears to be more closely linked to their HIV risk, SSP services should still be available for this group. It would be best to combine sexual and harm reduction services given the relationship between meth use and sex among MSM (136, 203, 255-257).

6.3.1.3 Testing frequency

Targeting testing interventions towards people who exchange sex is a way to reach populations with a high prevalence of HIV and who have significant sexual and drug-use risk behaviours.

As mentioned above, current CDC HIV testing guidelines recommend that people at high risk for HIV infection are tested every 12 months (243, 244). Ensuring that all people who exchange sex are offered testing in line with these recommendations would be a good first step, but it is possible that even more frequent testing may be necessary, in particular in view of the finding that people who exchange sex were more likely be HIV-positive-unaware than

members of the same populations who did not exchange sex. A recent review of the guidelines for MSM concluded that there was insufficient evidence to recommend more frequent testing but that more frequent screening could be considered by clinicians for MSM based on individual risk factors. Exchange sex could be one such factor to consider (244) as could the type of drug used, given the very high prevalence of HIV seen among MSM who inject meth in this thesis.

It is also important to ensure that those who are aware of their HIV-positive status are adequately linked to and retained in care and treated in order to achieve viral suppression. Given transmission does not occur from those who are virally suppressed ensuring that the groups studied in this thesis are on treatment is key in light of the fact that sexual and drug used risk behaviors were commonly reported.

6.3.1.4 Adequately targeted, accessible and stigma-free services

Prevention and care services should be integrated to serve the multitude of needs of people who belong to one or more key population or vulnerable group. Services should be accessible and acceptable to the target population, which includes non-judgemental attitudes from staff. Previous work has shown that people who exchange sex are sometimes treated poorly by the health care system, and fear of stigma as well as real or perceived mistreatment of women who exchange sex could affect their access (111). With regards to MSM who exchange sex, multiple stigmas may be at play, including both sexual orientation and stigma related to exchange sex, and create barriers to accessing care (258).

Similarly, if services are targeted at homeless people, or people who are released from prison, or those who use drugs, in order to address HIV risk appropriately it is important consider that a proportion of people in these populations may also exchange sex.

Services that specifically target one key population such as PWID or MSM may not adequately cater to the needs of people who are at the intersection of different groups. For example, services targeted at MSM should not have an exclusive focus on gay men as many MSM who exchange sex identify as bisexual or straight (22, 259). It is important to consider how services can be targeted to various subpopulations of people who exchange sex. Those who only exchange sex occasionally may not access services targeted at sex workers as they may not identify as such, and the methods to target women who find clients in public places will likely have to be different compared to those needed for women who find clients online. Additionally, MSM who inject drugs may not consider themselves PWID and therefore may not feel comfortable accessing services targeted to this population. However, given the small size of the population of MSM who inject meth, services would be better focused not only on

injection of meth but rather all meth use, as non-injection meth is frequently used by many MSM (130-132, 134).

6.3.1.5 Structural interventions

Given the importance of socioeconomic factors in determining HIV risk, prevention interventions need to address the broader context and structural determinants (184). While addressing these is challenging and require interventions well beyond the scope of public health and social services, some interventions for individuals could include help with employment those who wish to exit the sex trade and access to education and assistance with housing. Adequate mental health services and interventions against stigma and discrimination are also important (93). It is also important to understand the reasons people start exchanging sex or start to inject drugs and work preventively with, for example, victims of child sexual abuse and to provide services for mental health (58, 205, 206).

Empowering people who exchange sex, both at the individual and community level is another way to reduce vulnerability. This can include improving self-esteem, negotiation skills including the ability to use condoms and refuse clients, and ways to recognise, avoid, and escape violence (111). Working with law enforcement through education, training, and lobbying can improve relations and help sex workers to view the police as supportive (110, 260, 261). Involving sex workers themselves through community-based organisations is key to the success of many of these proposed interventions (93, 111).

As we have seen, many socioeconomic factors such as poverty, history of arrest and homelessness relate to exchange sex and to each other in complex ways at individual as well as community levels. Disentangling these relationships becomes challenging and it may be impossible to determine the ‘pure’ causal association between exchange sex and HIV. But is it even necessary? The purpose of many analyses in public health is to determine target populations for interventions and decide which subpopulations are more at risk. If we find that people who exchange have high HIV prevalence, does it matter that some of this association is explained by arrest or homelessness? It may be enough to determine that those who exchange sex have high HIV prevalence and then target services accordingly.

6.4 LIMITATIONS

This section will describe the limitations of the analyses and findings of the papers included by discussing factors that affect their internal and external validity, including different types of biases, how these may have affected the findings and what was done to mitigate any biases.

Internal validity concerns whether the exposure caused a difference in the outcome or whether such findings are the result of biases or systematic error in the study – in other words whether the inferences made from the study are valid. Internal validity is therefore a prerequisite for external validity. External validity refers to the extent to which the findings from the study can be generalised to a wider population. If the study population is not representative of the wider population, external validity is compromised. The inferences made from the study population may be internally valid, but not generalisable to the wider population of interest (262, 263).

6.4.1 Random error

One factor that can affect the precision of the estimates is random error, which is an error due to chance. Sample size affects the risk of random error – the larger the sample the lower the risk of such an error. In the studies concerned, sample size was met for most cities in the main IDU and MSM samples used for Papers 1, 2 and 4. However, in Paper 1 and Paper 4 we only used a subset of the total sample – women who inject drugs and MSM who inject drugs. As the size of this subsample is smaller this may have affected precision. In the sample for women who exchange sex in Paper 3 the target sample size of 384 was only reached in Chicago, although Detroit and Houston were close at 379 and 344, respectively. However, only 293 women who exchange sex were recruited in Seattle. This will have affected the precision of our estimates.

6.4.2 Systematic error

Systematic error or bias may affect both internal and external validity and refers to errors that are a result of the methods used by investigators to recruit participants, factors that affect study participation or systematic errors in measuring exposures and outcomes.

6.4.2.1 Selection bias

Selection bias can be one form of systematic error and refers to factors that are related to participation in the study. It has been described as ‘Distortions that result from procedures used to select subjects and from factors that influence participation in the study’ (264) or ‘Error introduced when the study population does not represent the target population’ (265). Selection bias occurs when selection probabilities and/or participation are related to or influenced by exposure status (for example, exchange sex in our studies) or the outcome (HIV status). There are several kinds of selection bias: *non-participation bias* may arise if there is bias in terms of who is invited or recruited into the study, and *non-response bias* describes bias in who participates once they are invited. Selection bias becomes an issue for internal

validity when participation or response rate is associated with the exposure and, independently, to the outcome. The concern here is that the relationship between exposure and outcome may be different in the people who participated in the study compared with those from the source population who did not, thus compromising internal validity. Selection bias is also an issue in terms of external validity in that the people who participated in the study are not representative of the wider population and, for example, an estimate of HIV prevalence is not representative of the HIV prevalence in the wider population.

In RDS studies, selection bias can occur at two levels. Firstly, there may be bias in who receives coupons (*participation bias*) and secondly, in terms of who participates (*non-response bias*). In Paper 2, using venue-based sampling, participation bias may be affected by who attends venues and non-response bias by who agrees to participate once approached at the venue.

6.4.2.1.1 Participation bias

People with smaller networks are less likely to receive a coupon, but network size is measured as part of the survey and adjusted for as far as possible. In Paper 3 we used full RDS weighting, but in Papers 1 and 4 we only partly adjusted for the RDS design in multivariable analysis. This is a limitation. In Paper 3, focused only among women who exchange sex, there may also be a bias in terms of who received coupons. We were, for example, unlikely to reach women working under coercive circumstances such as those who had been trafficked or worked under a controlling pimp. These women would be unlikely to receive coupons from other women who exchange. Another example is women who reported finding clients online and who constitute only a small proportion of the total sample even though the real proportion of women who find clients online is likely to be much larger (42). One study suggested that some women who recruit online are more isolated than women who work on the street (36) which means that they may have smaller networks of other women who exchange. Women who find clients online might also only be networked with other women online and they may not meet in real life. We attempted to mitigate this by introducing the option of electronic coupons.

RDS weighting addresses some of these biases by assigning greater weightings to participants who might be isolated from the rest of the population due to their smaller network size but this adjustment is limited if there are too few women from that subpopulation in the sample. Our results may be biased in either direction if women from these populations have higher or lower HIV prevalence than the women who participated.

In Paper 3, women were asked to recruit other women who exchange sex and it is possible that women who did not exchange sex may have lied about exchanging sex in order to get to participate in the survey and obtain the incentive. This would be a form of recruitment bias. However, the question through which we ascertained whether women exchanged or not was asked in the middle of the survey, as part of the questions around behaviours. This placement of the question reduced the risk that women lied, compared with using an upfront question before starting the survey.

With regards to the paper on MSM who inject meth it is possible that there might have been bias in the recruitment of MSM who inject meth. When doing formative work and selecting seeds for the start of recruitment, NHBS staff commonly work through community-based organisations to reach PWID; however, MSM who inject meth may not identify as regular PWID, nor access services like other PWID. As a result, local staff may not have explored MSM who inject meth as a potential target population during the formative assessment or added seeds in this population. This may have led to under-recruitment of MSM-PWID who inject meth. This would probably not have biased our findings in any particular direction; only reduced sample size and therefore precision.

Paper 2 uses venue-based sampling, and different factors are at play here in terms of potential causes of participation bias. The survey population is limited to MSM who attend venues; MSM who do not attend venues may differ from the survey population which could affect external validity. It is possible that those who attend venues are more likely to have multiple partners, exchange sex or be HIV-positive. This would bias our results in terms of assessing the prevalence of exchange sex but may not bias the association between exchange sex and HIV in which case external validity would not be compromised.

6.4.2.1.2 Non-response bias

The second potential source of selection bias in RDS studies occurs if there is a bias in terms of who participates once they received a coupon. In Paper 3, women who worked under coercive circumstances would probably not even receive a coupon, but if they did they would not be likely to be able to come to the study site and participate. Women may also have been differentially motivated by the incentive which would have determined probability of participation. The majority of women who participated were African-American and older. In addition, a high proportion of women were of low SES and may have been particularly motivated by our incentive to participate (102). As women of low SES and African-American women are more likely to be HIV-positive (266) than women of higher SES and white

women (100, 214), we may have overestimated the true prevalence of HIV among all women who exchange sex.

In Paper 1 and Paper 2 it is possible that those who exchange sex were less likely to participate than those who did not exchange. Those who exchange sex may be less motivated by the incentive as they have alternative means of income. However, as long as the HIV prevalence was similar among those who exchange sex and participated was similar to that among those who exchanged sex but did not participate, our results in terms of the association between exchange sex and HIV prevalence would not be biased.

In Paper 4 it is possible that MSM who use methamphetamine were more or less likely to participate in the survey than MSM who injected other drugs, even if they got a coupon. We found that MSM who injected meth generally had higher SES and it is possible that this population was less motivated by the incentive. However, as long as the HIV prevalence among the MSM who injected meth and participated was similar to that among those who injected meth but did not participate, our results in terms of the association between exchange sex and HIV prevalence would not be biased.

A further source of non-response bias across all studies is that we were not able to survey people who did not speak English or Spanish; hence they could not participate. This affects the extent to which the findings are generalisable to all members of the risk group sampled in participating cities.

6.4.2.1.3 Survivorship bias

A particular form of selection bias may apply to all papers – survivorship bias. This refers to the possibility that some people may have died before having gotten the opportunity to be sampled during the study (267). For example, people infected with HIV may have been more likely to die in the years preceding data collection. This would result in an underestimation of the true burden of HIV in the study population. For Papers 1, 2 and 4, which look at the relative prevalence of HIV between two groups, this survivorship bias should not affect the *relative* prevalence of HIV between the two groups, unless there is difference in mortality due to HIV by exposure category. If people who exchange sex are more likely to die from HIV than people who do not exchange sex – perhaps due to worse socioeconomic status or access to health care, then such bias would have resulted in our study underestimating the magnitude of the association between exchange sex and HIV.

6.4.2.2 *Information bias*

Information bias is another aspect of systematic bias or error that can affect internal validity. It refers to ‘systematic distortions when collecting information about exposures and disease’ (268).

Misclassification bias is one important source of information bias and refers to situations where there is systematic error in how the exposure and/or the outcome is classified. In our papers, there is possibility of exposure identification bias as all behaviours are self-reported. This may introduce recall bias where participants do not remember the behaviours they are asked to report. Most behaviours were, however, measured only for the previous 12 months, which should have facilitated recall.

Social desirability bias is perhaps a bigger problem in the studies included as part of this thesis and may lead to misclassification of the exposure or outcome. Exchange sex in particular may be a stigmatised behaviour and people may not volunteer this information. If some participants chose to not disclose having had exchange partners, this would likely have biased the association between exchange sex and HIV towards the null. However, the way the questions were asked in the NHBS questionnaire minimised this risk. The questions about exchange sex are nested among the questions detailing different behaviours with different partners, and simply ask how many partners the participants received money or drugs from in exchange for sex. In contrast, a stand-alone question about whether someone is a sex worker would probably have been subjected to much more social desirability bias. With regards to the number of partners in the previous 12 months, the reporting of this variable – explored as a mediator in Papers 1, 2 and 4 – could be subject to both recall and social desirability bias. This would only result in a biased finding if those who exchanged and those who did not misreported their behaviours to different extents.

Another aspect to consider that is related to misclassification is how we defined exchange sex. The introduction outlined that there exist no clear definition of exchange sex and that there is a great deal of variability in terms of client number and how large part of someone income comes from exchange sex. The definition of exchange sex used in this thesis was very sensitive in that it was enough for participants to have a single exchange partner in the past 12 months to be classified as someone who exchanged sex. This may limit the inferences we can make about some subpopulations of people who exchange sex who have more partners. Restricting the analyses in future to people with higher numbers of partners could provide more insights. However, people who reported a single exchange partner might have exchanged sex with them multiple times during the year in which case HIV risk might not be

that different from someone with more partners. Exploring this in more detail would require detailed partner level data on risk behaviours which was not available in the data.

Misclassification bias in terms of *outcome identification* could be an issue for Papers 1 and 2. In Papers 3 and 4 the outcome is HIV prevalence which is measured by a blood test and thus probably not subject to systematic bias. In Papers 1 and 2, however, one of the outcomes is HIV-positive-unaware which relies on the participant accurately reporting the results of their most recent HIV test. This possible bias was discussed in detail in section 6.1.1.3 above.

A further limitation related to information bias is that all analyses are cross-sectional and causality cannot be inferred, which is a limitation in terms of determining risk behaviours associated with acquisition of HIV infection. Furthermore, most behaviours were measured for the previous 12 months, and the analysis implicitly assumes that current risk behaviour is a marker of past risk behaviours. People may not, for example, have exchanged sex at the time of their HIV infection. In Paper 3, there is an indication that some women have been HIV-positive for a long period of time, estimates of the median time since diagnosis ranged from 6 years in Houston to 21 in Chicago. In particular, we are assuming in our mediation analysis that previous 12-month number of condomless partners is a proxy for past behaviour in mediation analysis in Papers 1, 2 and 4. This may not be correct, as people who are diagnosed with HIV might change their risk behaviours (89). However, for this bias to have an effect on our analysis, any such behaviour change would have to be different by exposure status (exchange sex or primary drug).

6.4.2.3 *Confounding bias*

Confounding is another important factor that can affect internal validity. Confounders are factors that are a cause of the outcome, or a surrogate measure of a cause, in unexposed people. Confounders must also be correlated with the exposure in the study population. Confounders must, however, not be affected by the exposure (269, 270).

In Papers 1 and 2 there were probably potential confounders that we were not able to measure and control for, such as different aspects of social disadvantage that may increase likelihood that people exchange sex and also influence HIV risk through separate pathways. We did attempt to account for this by including socioeconomic factors in multivariable models where appropriate, but there may be residual confounding from factors we were not able to measure. Other potential confounders could include personality traits around risk taking which could be associated both with exchange sex and, separately with HIV risk taking more broadly (271, 272).

In Paper 3 there could be unmeasured confounding in the comparisons between the sample of women who exchange sex and the two comparison samples. Such confounding may have biased our result in any direction. However, we minimised this risk of bias in sensitivity analysis by age-standardising the sample and by excluding women with a past history of injection drug use.

In Paper 4 on meth injection and HIV among MSM-IDU, it is possible that MSM who engage in sexual risk behaviours, and therefore would be at risk for HIV, are also more likely to use meth, rather than being at risk for HIV because they use meth (273). There is however evidence of a causal link between meth use and sexual risk behaviours from longitudinal studies and event-level analyses (274-276). A related consideration, although not an example of confounding, is that some men may start using meth after their HIV diagnosis perhaps in response to HIV-related stigma. They may also struggle with low energy levels and have challenges with feeling desirable (143, 277). However, by excluding men who started injecting after being diagnosed with HIV, we sought to limit this potential bias.

6.4.3 RDS assumptions

When discussing possible limitations to the analyses it is also relevant to consider whether the assumptions are met that are necessary for a sample obtained through RDS to approximate a population-based sample.

One assumption is that the population being recruited must know one another as members of the target population (i.e. PWIDs must know each other as PWIDs), in order to identify and recruit each other with coupons. In the RDS papers considered, this condition is likely to be met, although it may be a little more challenging for women who exchange sex, in particular for those who do not exchange sex very openly or who mainly recruit clients online and thus may not know a lot of other women who exchange sex.

Another assumption is that respondents must select randomly from their network when choosing people to whom they give coupons. This is potentially an issue in many RDS studies where methods research has suggested that people may primarily give coupons to people they know better. Simulations have shown that the RDS methodology is particularly sensitive to bias if participants select other participants on a factor related to the outcome (278). It is possible that that could have happened in the papers included here if people recruit others from the same sexual or drug use network, which could be related to the outcome of HIV prevalence. In the sampling of women who exchange sex, another issue may be that individual women may well know other women who exchange sex but might not meet them very often, or only know them online. We attempted to mitigate this in a couple of cities by

allowing people to photograph coupons and send them to others electronically, but this was only fully implemented towards end of data collection in one city.

The target population must also be adequately networked so that recruitment chains can progress and reach all subpopulations. This is probably not an issue for the samples used in Papers 1 and 4; however, as described above, women who exchange sex, particularly those who do not recruit clients on the street, may not be adequately networked with each other. This may be the reason why we recruited a smaller proportion of women who mainly find clients online.

A further assumption of RDS is that the sampling fraction is small, which means that the sample that will be recruited using RDS is small compared with the overall target population in the defined geographical area. This is to ensure that the ability for a participant to recruit remains constant over time. We recruited participants in large metropolitan areas so this assumption is likely to have been met.

Respondents must also be able to accurately report their network size. This is because during the survey, respondents are asked how large their peer networks are, and this information is later used during analysis. Respondents with smaller networks have a lower probability of being recruited, and their responses are given a higher weighting compared with someone with a large network if RDS weighted analysis is used (149, 152, 153, 157). We did not have reason to believe that this would be a problem in any of the samples.

Previous work on NHBS IDU data has shown that several of the RDS assumptions are met. The proportion of PWID who reported that they were recruited by a stranger was less than 5%, indicating that participants know each other as members of the target population. The population was also found to be adequately networked due to substantial cross recruitment between field sites, and finally the sampling fraction was found to be small (279).

6.4.3.1 RDS sampling and external validity

The extent to which the findings in the papers included in this thesis are externally valid depends to some extent on what we consider to be the ‘wider population’. We sampled high-risk populations in selected urban areas in the US. An RDS sample can, if the above assumptions are met, approximate a population-based sample. However, inferences can only be made about the source population from which the sample was drawn. This means that the ‘wider population’ in this context refers to members of the high-risk population in participating cities and this is the population relevant when discussing external validity. This is important to keep in mind as findings may not be representative of high-risk populations in

other cities or in less urban areas. However, Papers 1 and 2 contain data from more than 20 US cities which increases the likelihood that the results are generalisable to other cities. On the other hand, Paper 3 on women who exchange sex and Paper 4 on MSM–IDU who injected meth only used data from four and 10 cities, respectively, and findings may not be generalisable to other cities. Furthermore, the analyses only use data from the US, affecting the generalisability to populations in other countries. This is particularly the case for low- and middle-income countries but also in terms of the extent to which the findings apply to populations in other Western countries given some of the unique circumstances in the US with regards to socioeconomic inequality.

6.4.4 Venue based sampling

In Paper 2, data are not weighted to account for the complex venue-based sampling methodology used to recruit MSM. Some subgroups may be over- or under-represented leading to biased point estimates that are not representative of all MSM in the city. At the time Paper 2 was published, venue-based sampling weightings were under development for future NHBS data collection cycles.

7 CONCLUSIONS

This thesis uses data collected from multiple US cities to examine the intersection of risk for people belonging to more than one key population or vulnerable group. Much of the prior work examining HIV prevalence in these populations is limited to single cities and use convenience sampling. The data used for the papers here come from multiple US cities, sample size is large and data is collected rigorous methods.

7.1.1 Exchange sex

The studies included found that HIV prevalence was high among people who exchange sex and that sexual and drug-use risk behaviours are common.

Among women who exchange sex recruited from four US cities, the prevalence of HIV was almost three times as high as the prevalence among other women of low SES and almost nine times as high as among women in the general population in the same cities. These findings indicate that exchange sex may explain part of the high HIV prevalence, but that some may be related other factors related to risk of HIV that they share with women of low SES who do not exchange sex.

Among women who inject drugs and among MSM there was a significant difference in the prevalence of being HIV-infected but unaware of one's infection. More recent data indicate that MSM in particular might have misreported knowledge of their HIV status, but it is not clear whether this could have affected the validity of our findings with regards to the outcome of HIV infected but unaware. It is still of concern that overall prevalence of HIV is high among those who exchanged sex in light of the findings that sexual and drug-use risk behaviours were more commonly reported by people who exchanged sex compared to those who did not. This is an important argument for targeting services to people who exchange sex. In particular, testing, diagnosis and linkage to care and treatment are essential to minimise the risk for transmission.

Markers of low socioeconomic status were associated with exchanged sex and it is possible that these are indicators that people who exchange sex live and work in an environment that influence their overall HIV risk through different pathways.

7.1.2 MSM who inject meth

HIV prevalence was also found to be very high among MSM who primarily inject methamphetamine in comparison with MSM who primarily inject other drugs. This is remarkable given that the population of MSM who inject drugs is a population with particularly high HIV risk even compared to other key populations. The association between meth use and HIV infection was found to be mediated by sexual rather than drug-use risk behaviours. This is an important finding as services targeted at PWID often focus on injection-related risk rather than sexual risk and is an argument for ensuring targeted and tailored services toward this population to address both risk for HIV acquisition but also onward transmission given the high prevalence of risk behaviours.

8 POINTS OF PERSPECTIVE

8.1 TARGETING SERVICES

Services for people who belong to more than one key population or vulnerable group need to take into account the different sets of factors that could contribute to their risk for HIV acquisition or onward transmission. Services need to address both sexual and drug related risks, including addressing condom use as well as promote the use of PrEP. Harm-reduction services to reduce the risk associated with injection drug use is also important, including opioid substitution therapy and needle-syringe exchange services as well as drug treatment specifically for MSM who inject meth. To ensure that those infected receive the care that they need and to reduce the risk of onward transmission it is important to ensure frequent testing and linkage to care, treatment and retention in care for those infected.

Services should, where possible, be tailored to reach populations at risk in different ways beyond the traditional means: MSM who inject methamphetamine might not use low-threshold services targeted at PWID using opioids, and women who occasionally sell sex to people they find through friends and acquaintances will probably not use clinics targeted at sex workers. These populations need to be targeted in other ways such as through the club scene or through primary care and community organisations. There may also be innovative ways of reaching the populations at risk such as through online outreach (39-42). Services should be accessible and accommodating to the relevant populations who often face issues of intersecting stigma and discrimination.

Mental health services and services that address childhood violence are also needed to address some of the root causes of who people exchange sex or use drugs. Addressing the broader social and structural determinants of HIV risk is also essential including homelessness, lack of employment, stigma and the legal and policy context. Many of these structural determinants need to be addressed at a level far beyond the scope of public health and indeed of this thesis.

8.2 RECOMMENDATIONS FOR FUTURE RESEARCH

This findings in this thesis have given rise to several possible questions to address in futuer research.

With regards to the data sets used for the thesis – behavioural surveillance data from the US National HIV Behavioural Surveillance system – there are several analyses that could be done:

- To be able to determine whether exchange sex is associated with being HIV-positive–unaware among MSM it would be important to run the analyses again on more recent data where information about the presence of ARVs in the blood samples of participants is available. Future work on the population of PWID should also include testing for ARVs in the sample and adjustment of the analytic sample accordingly.
- The analysis of the association between methamphetamine use and HIV infection among MSM who inject meth could be repeated using data from one or more of the MSM cycles. In the current analysis, participants were recruited in the IDU cycles because they injected drugs and we looked at the subpopulation of those who also reported male-to-male sex. Using data from men who were recruited in the MSM cycle instead, restricted to those who reported injection drug use, would be interesting to do in order to see whether the association remained the same.
- Given the importance of treatment and viral suppression in order to prevent onward transmission, future analyses of NHBS data should characterise the continuum of care among the subpopulations with overlapping risks in order to determine the factors associated with testing, diagnosis, linkage to care, treatment and being virally suppressed. Qualitative research could complement these quantitative analyses to determine specific barriers to each part of the continuum of care.
- Data collection among women who exchange sex is being scaled up by the CDC and this will allow for a bigger sample to work with. Ideally, analyses should be stratified by how women find clients or by how frequently they exchange sex in order to gain a better understanding of different subpopulations of women who exchange sex.

Considering future research possibilities more broadly:

- Future work should consider innovative ways of recruiting people who exchange sex and find clients online as this subpopulation was under-represented in our sample.
- Given the limitations of cross-sectional data, it would be ideal, although practically challenging, to establish a cohort of people who exchange sex and document risk behaviours and HIV status over time in order to gain a better understanding of how social and behavioural risk influence the risk for HIV acquisition.
- As the relationships between socioeconomic factors, sexual and drug-use risk behaviours and HIV infection are highly complex, qualitative research could be a different avenue through which to explore how these factors interact for individuals and groups to increase vulnerability to HIV infection. Such in-depth insights could provide information that enables more nuanced and targeted interventions.
- A key to minimising risk for onward transmission is to understand the barriers to testing, linkage to care and treatment, as well as retention in care, for the populations studied where risks intersect. Here also, qualitative research could provide actionable insights to understand how to reach these populations and how to design services.

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11 ANNEX 1 – ADDITIONAL QUESTIONS USED IN PAPER 3

Check_HRW1. If R reported at least one exchange sex partner in the core survey (EXANY12M EQ 1), go to INTRO_HRW.
Else, go to HRW1.

Any exchange sex, 12m

HRW1.

In the past 12 months, did one or more men give you money or drugs to have vaginal, oral or anal sex with them?

ANYEXCH

Any exchange sex, 12m

No..... 0
Yes 1
Don't Know 9
Refuse to Answer 7

Check_INTRO_HRW. If R reported exchanging sex in the past 12 months, (ANYEXCH EQ 1), go to INTRO_HRW.
Else, go to INTRO_HRW2.

The following questions will be about experiences of women who exchange sex for money or drugs.

[Give Respondent Flashcard 1.]

Please keep in mind that when I talk about 'sex', I mean vaginal, oral or anal sex. When I talk about 'exchange sex', I mean a situation where a man gave you money or drugs to have sex with him. When I say 'client' or [local term], I mean a man who you exchange sex with.

INTRO_HRW.

We ask all women these questions, no matter how many men they have exchanged sex with. Some questions ask about private and sensitive things. If you are uncomfortable answering any particular question, we can skip it.

Sexual/physical violence, 12m

INTRO_HRW2. Earlier, I asked you about situations that may have happened with your sex partners during the past 12 months. The next questions are about situations that may have happened with ANYONE, [if R exchanged sex in the past 12 months, fill with "including clients, or [local term], other sex partners, or somebody else"; if R did NOT exchange sex in the past 12 months, fill with "including sex partners, or somebody else"].

HRW2.

SXVIOANY

In the past 12 months, that is, since [fill with interview month, formatted as text] of last year, did ANYONE force or pressure you to have vaginal, oral or anal sex when you did not want to? It could have been ANYONE.

Any sexual violence, p 12m

No..... 0
Yes 1
Don't Know 9
Refuse to Answer 7

Check_HRW3. If R did not report exchanging sex in the past 12 months (EXANY12M NE 1 AND ANYEXCH NE 1), or did not report any sexual violence (SXVIOANY NE 1), go to HRW5.
If R reported experiencing any sexual violence (SXVIOANY EQ 1), go to HRW3.

Who on this list forced or pressured you to have sex when you did not want to? You can choose more than one person.

HRW3.

[Give Respondent Flashcard 2.]

[READ Choices. CHECK ALL that apply.]

SXVIOL	Who caused sexual violence, p 12m	
SXVIOLA	Client or [local term]	
SXVIOLB	Pimp or manager or [local term]	
SXVIOLC	Police officer.....	
SXVIOLD	Boyfriend, spouse, or other sex partner.....	
SXVIOLE	Somebody else	
	Don't Know	9
	Refuse to Answer	7

Check_HRW4. If R reported experiencing sexual violence from 'somebody else', (SXVIOLE EQ 1), go to HRW4. Else, go to HRW5.

HRW4. Who was the other person who forced or pressured you to have sex when you did not want to?
SPECSXV Other person caused sexual violence

{text response; max length = 100 characters}

HRW5. In the past 12 months, did ANYONE slap, punch, shove, kick, shake or otherwise physically hurt you? It could have been ANYONE.
PHVIOANY Any physical violence, p 12m

No.....	0
Yes	1
Don't Know.....	9
Refuse to Answer	7

Check_HRW6. If R did not report exchanging sex in the past 12 months (EXANY12M NE 1 AND ANYEXCH NE 1), go to End of Local Questions.
If R reported experiencing any physical violence, (PHVIOANY EQ 1), go to HRW6.
If R did not report any physical violence (PHVIOANY NE 1), go to HRW8.

Who on this list slapped, punched, shoved kicked, shook or otherwise physically hurt you? You can choose more than one person.

[Give Respondent Flashcard 2.]

HRW6. [READ Choices. CHECK ALL that apply.]
PHVIOL Who caused physical violence, p 12m

PHVIOLA	Client or [local term]	
PHVIOLB	Pimp or manager or [local term]	
PHVIOLC	Police officer.....	
PHVIOLD	Boyfriend, spouse, or other sex partner.....	
PHVIOLE	Somebody else	
	Don't Know	9
	Refuse to Answer	7

Check_HRW7. If R reported experiencing physical violence from 'somebody else', (PHVIOLE EQ 1), go to HRW7. Else, go to HRW8.

HRW7. Who was the other person who slapped, punched, shoved kicked, shook or otherwise physically hurt you?

SPECPHV Other person caused physical violence

{text response; max length = 100 characters}

Methods of finding clients, 12m

In the past 12 months, what were **all the different ways** you found men to exchange sex with?

[Give Respondent Flashcard 3.]

[READ CHOICES. CHECK ALL that apply.]

HRW8.

INTERVIEWER: If clarification is needed, SAY: 'If there are some men that you have exchanged sex with more than once - think about how you first found them.'

CLNTLOC

Where found men to exchange sex with

CLNTLOCA

Walking on the street, or 'stroll' or [local term].....

CLNTLOCB

Picking up men in public places, such as bars, hotels, the mall, and other places.....

CLNTLOCC

Online, for example, websites or phone apps

CLNTLOCD

Working in a strip club

CLNTLOCE

Through a drug dealer or in a drug house or [local term]

CLNTLOCF

Working in a massage parlor or a brothel or [local term]

CLNTLOGG

Through an escort service

CLNTLOCH

Through a manager, pimp, or madam or [local term].....

CLNTLOCI

Through my boyfriend or husband.....

CLNTLOCL

Through friends, family or neighbors

CLNTLOCK

Some other way

Don't Know 9

Refuse to Answer 7

Check_HRW9. If R reported finding clients 'some other way', (CLNTLOCK EQ 1), go to HRW9.
Else, go to Check_HRW10.

HRW9.

How else did you find men to exchange sex with?

SPEEXCH

Other way found men to exchange sex

{text response; max length = 100 characters}

Check_HRW10. If R reported more than one way of finding clients, (more than one "Yes" response to CLNTLOCA to CLNTLOCK), go to HRW10.
Else, go to HRW12.

In the past 12 months, what was **the most common way** you found men to exchange sex with?

[Give Respondent Flashcard 3.]

[DO NOT READ CHOICES.]

HRW10.

INTERVIEWER: If clarification is needed, SAY: 'If there are some men that you have exchanged sex with more than once - think about how you first found them.'

CLNTCOMM

Most common way found men to exchange sex with

Walking on the street, or 'stroll' or [local term]..... 0

Picking up men in public places, such as bars, hotels, the mall, 1

and other places	
Online, for example websites or phone apps	2
Working in a strip club.....	3
Through a drug dealer or in a drug house or [local term]	4
Working in a massage parlor or a brothel or [local term]	5
Through an escort service	6
Through a manager, pimp, or madam or [local term]	7
Through my boyfriend or husband.....	8
Through friends, family or neighbors	9
Some other way	10
Don't Know	9
Refuse to Answer	7

Check_HRW11. If R reported most common way of finding clients was 'some other way', (CLNTCOMM EQ 10), go to HRW11. Else, go to HRW12.

HRW11. What was the most common way you found men to exchange sex with?
SPECCOMM Other most common way found men to exchange sex

 {text response; max length = 100 characters}

Exchange sex network

HRW12. How many women in [Insert name of MSA] do you know who exchange sex? Please include the woman who gave you the coupon if she exchanges sex.

EXCHMSA Number of women who exchange sex in the MSA

Range	0 - 7500
Don't Know.....	9999
Refuse to Answer	7777

Age when first exchanged sex

HRW13. How old were you the first time you exchanged sex? I mean the first time that a man gave you money or drugs to have vaginal, oral or anal sex with him.

EXCHANGE Age when first exchanged ex

Range	0 - 70
Don't Know.....	99
Refuse to Answer	77

Income from exchange sex

The next question is about money you make from exchanging sex. How much money do you typically make **per month** from exchanging sex?

HRW14.
INTERVIEWER: Please enter the dollar amount.
EXINCOME Avg. income per month from exchange sex

Range	0 - 100000
Don't Know.....	999999
Refuse to Answer	777777

Number of exchange sex partners, 12m

Earlier in the survey, we asked you how many of your casual male partners gave you money or drugs to have sex with them in the past 12 months. Now I will ask you about the total number of men you exchanged sex with in the past 12 months, that is, since [fill with interview month, formatted as text] of last year. This includes both casual partners and main partners.

[Give Respondent Flashcard 4.]

By "main partner", I mean a man you have sex with and who you feel committed to above anyone else. This is a partner you would call your boyfriend, husband, significant other, or life partner. And by "casual partner", I mean a man you have sex with but do not feel committed to or don't know very well."

INTRO_HRW15.

HRW15. In the past 12 months, in total, how many men gave you money or drugs in exchange for having vaginal, oral or anal sex with them?

EXNUM Total number of exchange partners, 12m

— — — —

Range	0 - 7000
Don't Know	9999
Refuse to Answer	7777

If R had 1 exchange sex partner (EXNUM EQ 1), go to HRW16.
 If R had more than 1 exchange sex partner (EXNUM GE 1), go to HRW17.
CHECK_HRW16. If R had 0 exchange partners or did not report the number of sex partners (EXNUM EQ 0, DK, or REF), go to HRW28.

HRW16. In the past 12 months, did you have vaginal sex with this man?

EXVS_O Vaginal sex exchange partner, 12m

No	0
Yes	1
Don't Know	9
Refuse to Answer	7

Check_HRW17. Go to Check_HRW18.

HRW17. In the past 12 months, with how many of these [fill with the total number of exchange sex partners] men did you have vaginal sex?

EXVS_M Number of vaginal sex exchange partners, 12m

— — — —

Range.....	0-7000
Don't Know	9999
Refuse to Answer	7777

HardEdit_HRW17. If # VS partners GT # exchange partners (EXVS_M GT EXNUM), DISPLAY: "**INTERVIEWER:** The response entered is inconsistent with a prior response (total number of exchange sex partners). Clarify and re-enter response to current or prior item as needed." Then go back to HRW17.
 Else, go to Check_HRW18.

Check_HRW18. If 1 exchange sex partner (EXVS_O EQ 1 or EXVS_M EQ 1), go to HRW18.
 If multiple exchange sex partners, (EXVS_M GT 1), go to HRW19.
 If no vaginal exchange sex partners, (EXVS_O EQ 0, DK, or REF) or (EXVS_M EQ 0, DK, or REF), go to Check_HRW20.

HRW18. In the past 12 months, did you have vaginal sex with this man without using a condom?

EXUVS_O Condomless vaginal sex exchange partner, 12m

No	0
Yes	1

Don't Know	9
Refuse to Answer	7

Check_HRW19. Go to Check_HRW20.

HRW19. In the past 12 months, with how many of these [fill with number of vaginal exchange sex partners] men did you have vaginal sex without using a condom?
EXUVS_M Number of condomless vaginal sex exchange partners, 12m

Range.....	0-7000
Don't Know	9999
Refuse to Answer	7777

HardEdit_HRW19. If # UVS exchange partners GT # VS exchange partners (EXUVS_M GT EXVS_M), DISPLAY: "**INTERVIEWER:** The response entered is inconsistent with a prior response (number of vaginal sex partners). Clarify and re-enter response to current or prior item as needed." Then, go back to HRW19.
 Else, go to Check_HRW20.

Check_HRW20. If 1 exchange sex partner (EXNUM EQ 1), go to HRW20.
 Else, go to HRW21.

HRW20. In the past 12 months, did you have anal sex with this man?
EXAS_O Anal sex exchange partner, 12m

No	0
Yes	1
Don't Know	9
Refuse to Answer	7

Check_HRW21. Go to Check_HRW22.

HRW21. In the past 12 months, with how many of these [fill with the total number of exchange sex partners] men did you have anal sex?
EXAS_M Number of anal sex exchange partners, 12m

Range.....	0-7000
Don't Know	9999
Refuse to Answer	7777

HardEdit_HRW21. If # AS partners GT # exchange partners (EXAS_M EXNUM), DISPLAY: "**INTERVIEWER:** The response entered is inconsistent with a prior response (total number of exchange sex partners). Clarify and re-enter response to current or prior item as needed." Then go back to HRW21.
 Else, go to Check_HRW22.

Check_HRW22. If 1 exchange sex partner (EXAS_O EQ 1 or EXAS_M EQ 1), go to HRW22.
 If multiple exchange sex partners, (EXAS_M GT 1), go to HRW23.
 If no anal exchange sex partners, (EXAS_O EQ 0, DK, or REF) or (EXAS_M EQ 0, DK, or REF), go to Check_HRW24.

HRW22. In the past 12 months, did you have anal sex with this man without using a condom?
EXUAS_O Condomless anal sex exchange partner, 12m

No	0
Yes	1
Don't Know	9
Refuse to Answer	7

Check_HRW23. Go to Check_HRW24.

HRW23. In the past 12 months, with how many of these [fill with number of anal exchange sex partners] men did you have anal sex without using a condom?
EXUAS_M Number of condomless anal sex exchange partners, 12m

Range..... 0-7000
Don't Know 9999
Refuse to Answer 7777

HardEdit_HRW23. If # UAS exchange partners GT # AS exchange partners (EXAS_M GT EXNUM), DISPLAY: "**INTERVIEWER:** The response entered is inconsistent with a prior response (number of anal sex partners). Clarify and re-enter response to current or prior item as needed." Then, go back to HRW23.
Else, go to Check_HRW24.

Check_HRW24. If 1 exchange sex partner (EXNUM EQ 1), go to EXOS_O.
Else, go to EXOS_M.

HRW24. In the past 12 months, did you have oral sex with this man?
EXOS_O Oral sex exchange partner, 12m
No 0
Yes 1
Don't Know 9
Refuse to Answer 7

Check_HRW25. Go to Check_HRW26.

HRW25. In the past 12 months, with how many of these [fill with the total number of exchange sex partners] men did you have oral sex?
EXOS_M Number of oral sex exchange partners, 12m

Range..... 0-7000
Don't Know 9999
Refuse to Answer 7777

HardEdit_HRW25. If # OS partners GT # exchange partners (EXOS_M GT EXNUM), DISPLAY: "**INTERVIEWER:** The response entered is inconsistent with a prior response (total number of exchange sex partners). Clarify and re-enter response to current or prior item as needed." Then go back to HRW25.
Else, go to Check_HRW26.

Check_HRW26. If 1 exchange sex partner (EXOS_O EQ 1 or EXOS_M EQ 1), go to HRW26.
If multiple exchange sex partners, (EXOS_M GT 1), go to HRW27.
If no oral exchange sex partners, (EXOS_O EQ 0, DK, or REF) or (EXOS_M EQ 0, DK, or REF), go to HRW28.

HRW26. In the past 12 months, did you have oral sex with this man without using a condom?
EXUOS_O Condomless oral sex exchange partner, 12m
No 0
Yes 1
Don't Know 9
Refuse to Answer 7

Check_HRW27. Go to HRW28.

HRW27. In the past 12 months, with how many of these [fill with number of oral exchange sex partners] men did you have oral sex without using a condom?
 EXUOS_M Number of condomless oral sex exchange partners, 12m

 Range..... 0-7000
 Don't Know 9999
 Refuse to Answer 7777

HardEdit_HRW27. If # UOS exchange partners GT # OS exchange partners (EXUOS_M GT EXOS_M), DISPLAY: "INTERVIEWER: The response entered is inconsistent with a prior response (number of oral sex partners). Clarify and re-enter response to current or prior item as needed." Then, go back to HRW27.
 Else, go to HRW28.

INTRO_HRW28. The next questions are about other experiences of women who exchange sex.

Arrest/police

HRW28. In the past 12 months, how many times have you been arrested because you exchange sex?
 ARRESTN Times arrested for exchanging sex, p 12m

 Range..... 0-7000
 Don't Know 9999
 Refuse to Answer 7777

HRW29. In the past 12 months, have police taken or destroyed your condoms?
 TAKECOND Condoms taken by police, p 12m

No..... 0
 Yes 1
 Don't Know 9
 Refuse to Answer 7

HRW30. In the past 12 months, have you avoided carrying condoms because you were afraid that the police would give you trouble?

AVDCOND Avoided carrying condoms, p 12m

No..... 0
 Yes 1
 Don't Know 9
 Refuse to Answer 7

Avoided health care

HRW31. Have you ever avoided going to health care services because you exchange sex?
 AVOIDHC Avoided health care services, ever

No..... 0
 Yes 1
 Don't Know 9
 Refuse to Answer 7

