Emerging practices and the potential to change HIV epidemiological trends: Pre-exposure prophylaxis as biomedical HIV prevention among gay and bisexual men who participate in chemsex

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Emerging practices and the potential to change HIV epidemiological trends: Pre-exposure prophylaxis as biomedical HIV prevention among gay and bisexual men who participate in chemsex

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A thesis in fulfilment of the requirements for the degree of

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Preliminary

Supporting Documentation

I   Thesis/Dissertation Sheet

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Abbreviation for degree as give in the University calendar	:	PhD
Faculty	:	Faculty of Medicine
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Abstract 350 words maximum: (PLEASE TYPE)

Within a population already at high risk of HIV, gay and bisexual men (GBM) who use drugs, particularly methamphetamine, to enhance sexual pleasure (chemsex) have previously been identified as being at higher risk of HIV compared to their non-drugs-for-sex peers. HIV pre-exposure prophylaxis (PrEP) has had a substantial impact on HIV prevention globally. This questions whether GBM who engage in chemsex remain at risk of HIV in the context of PrEP. This research explores ongoing HIV risk behaviours among men who engage in chemsex in the context of the availability of PrEP.

This thesis comprises six projects. The first project described the implementation of a cohort management system that I designed to automate data collection for this project. In 2014, baseline prevalence of methamphetamine use was high, as was concurrent use of erectile dysfunction medication (EDM) and gamma-hydroxybutyrate (GHB). The second and third projects examined EDM and GHB separately. Prior to the widespread availability of PrEP in Australia, use of these drugs was strongly associated with HIV risk behaviours. The fourth project was conducted in 2017 and measured incidence of PrEP initiation among GBM in the cohort, and identified factors associated with PrEP initiation. Many GBM who had reported high-risk behaviours subsequently initiated PrEP, but a large proportion of GBM at high-risk of HIV did not initiate PrEP. The fifth project demonstrated a change in HIV prevention among GBM who engage in chemsex. Prevalence of PrEP use among GBM who engage in chemsex increased dramatically between 2014 and 2017. With methamphetamine use consistently linked to HIV infection, the sixth project investigated the relationship between its use and HIV risk behaviours, specifically in the current context of HIV biomedical prevention. GBM who were previously considered at highest risk of infection are more likely to use PrEP to mitigate against the HIV risk in 2018.

PrEP as an HIV prevention strategy is changing the trajectory of the HIV epidemic among GBM in Australia. This thesis demonstrates a shift in epidemiology away from the previously highest risk practices due to the incorporation of PrEP into the regimens of GBM who engage in chemsex.

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2. Hammoud MA, Jin F, Lea T, Maher L, Grierson J, Prestage G. Off-label use of phosphodiesterase type 5 inhibitor erectile dysfunction medication to enhance sex among gay and bisexual men in Australia: results from the Flux Study. The Journal of Sexual Medicine 2017; 14(6): 774-84.

3. Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, Degenhardt L, Grierson J, Prestage G. Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men–results from the Flux Study. Sexual Health 2018; 15(2): 123-34.

4. Hammoud MA, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Prestage G. The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe. International Journal of Drug Policy 2018; 55: 197-204.

5. Hammoud MA, Vaccher S, Jin F, Bourne A, Maher L, Holt M, Bavinton BR, Haire B, Degenhardt L, Grulich A. Prestage G. HIV Pre-exposure Prophylaxis (PrEP) uptake among gay and bisexual men in Australia and factors associated with the nonuse of PrEP among eligible men: Results from a prospective cohort study. Journal of Acquired Immune Deficiency Syndromes 2019; 81(3): e73-e84.

6. Hammoud MA, Jin F, Maher L, Bourne A, Haire B, Saxton P, Vaccher S, Lea T, Degenhardt L, Prestage G. HIV biomedical protection among gay and bisexual men who use crystal methamphetamine. AIDS and Behavior 2019; Submitted 2019.

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Full title: Following Lives Undergoing Change (Flux) study: Implementation and baseline prevalence of drug use in an online cohort study of gay and bisexual men in Australia.
Authors: Mohamed A. Hammoud, Fengyi Jin, Louisa Degenhardt, Toby Lea, Lisa Maher, Jeffrey Grierson, Brent Mackie, Marcus Pastorelli, Colin Batrouney, Nicky Bath, Jack Bradley, Garrett Prestage
Journal: International Journal of Drug Policy
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Date accepted/ published: 20th November 2016

Status	Published	✓	Accepted and In press	In progress (submitted)	

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Full title: Off-Label use of phosphodiesterase type 5 Inhibitor erectile dysfunction medication to enhance sex among gay and bisexual Men in Australia: Results from the Flux Study

Authors: Mohamed A. Hammoud, Fengyi Jin, Toby Lea, Lisa Maher, Jeffrey Grierson, Garrett Prestage

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Details of publication #3:

Full title: Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men: Results from the Flux Study

Authors: Mohamed A. Hammoud, Adam Bourne, Lisa Maher, Fengyi Jin, Bridget Haire, Toby Lea, Louisa Degenhardt, Jeffrey Grierson, Garrett Prestage

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Details of publication #4:

Full title: HIV pre-exposure prophylaxis (PrEP) uptake among gay and bisexual men in Australia and factors associated with the non-use of PrEP among eligible men: Results from a prospective cohort study

Authors: Mohamed A. Hammoud, Stefanie Vaccher, Fengyi Jin, Adam Bourne, Lisa Maher, Martin Holt, Benjamin R. Banvinton, Bridget Haire, Louisa Degenhardt, Andrew Grulich, Garrett P. Prestage

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Details of publication #5:

Full title: The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe

Authors: Mohamed A. Hammoud, Stefanie Vaccher, Fengyi Jin, Adam Bourne, Bridget Haire, Lisa Maher, Toby Lea, Garrett Prestage

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- Data cleaning
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Garrett Prestage	[Signature removed]	09/09/19

Details of publication #6:					
Full title: HIV biomedical prevention as a harm reduction strategy among gay and bisexual men who use crystal methamphetamine					
Authors: Mohamed A. Hammoud, Fengyi Jin, Lisa Maher, Adam Bourne, Bridget Haire, Peter Saxton, Toby Lea, Louisa Degenhardt, Garrett Prestage					
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· Data collection	· Liaising with co-authors
· Data cleaning	· Journal submission and revisions

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Appendices

IX   Acknowledgements

Although my PhD research takes centre stage, behind the scenes of my doctoral thesis is the love, support, and investment of my family, friends, supervisors, and community. My collective network also shone a light in making my impossible, possible.

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X Glossary of terms

1,4-BD	1,4-butanediol
ACASI	Audio Computer-Assisted Self-Interview Software
AIDS	Acquired Immunodeficiency Syndrome
aORs	adjusted odds ratios
ART	Antiretroviral therapy
Australian PrEP Guidelines	PrEP prescribing guidelines for clinicians who will be initiating PrEP and monitoring people taking PrEP
Biomedically protected	Condomless anal intercourse while protected from HIV through the use of PrEP and ART
Biomedically unprotected	Condomless anal intercourse without the protected from HIV through the use of PrEP and ART
CAI	Condomless anal intercourse
Chemsex	The deliberate use of drugs to enhance sexual pleasure. Commonly used by gay and bisexual men in Western and Central Europe and some parts of Asia
CI	Confidence intervals
CLAI	Condomless anal intercourse
CLAIC	Condomless anal intercourse with casual partners
Conc.	Concurrent drug use
Concurrent drug use	Multiple drug use within a specified time period, but not necessarily on the same occasion
EDM	Erectile dysfunction medication
FAME	Follow-up Automated Management eSystem
Flux Study	Following Lives Undergoing Change Study
GAD7	Generalized Anxiety Disorder
Gay and bisexual men	Homosexually active men who identify as gay or bisexual
GBM	Gay and bisexual men

GHB	Gamma hydroxybutyrate
GBL	Gamma-butyrolactone
HAART	Highly active antiretroviral therapy
HIM Study	Health in Men Study
HIV	Human Immunodeficiency Virus
LSD	Lysergic acid diethylamid
MA	Methamphetamine
Men who have sex with men	All homosexually active men
MTV	Concurrent use of methamphetamine, PrEP ("Truvada"), and erectile dysfunction medications ("Viagra") in the previous six months
MV only	Concurrent use of methamphetamine and erectile dysfunction medications ("Viagra") without the use of PrEP ("Truvada") in the previous six months
Party-n-play	The deliberate use of drugs to enhance sexual pleasure. Commonly used by gay and bisexual men in North America and Australasia
PHQ9	Patient health questionnaire
Polydrug use	Simultaneous multiple drug use
PrEP	HIV pre-exposure prophylaxis
PrEP-eligible	Gay and bisexual men who report behaviours corresponding to the Australian PrEP Guidelines
PY	Person years
R-CAIC	Receptive condomless anal intercourse with a casual partner
Recent illicit drug use	Drug use in the previous six months
RSES	Rosenberg self-esteem scale
T only	Use of PrEP ("Truvada"), without the use of methamphetamine and erectile dysfunction medications ("Viagra") in the previous six months

| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| USID | Unique study identifier |

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XIII   Abstract

Within a population already at high risk of HIV, gay and bisexual men (GBM) who use drugs, particularly methamphetamine, to enhance sexual pleasure (chemsex) have previously been identified as being at higher risk of HIV compared to their non-drugs-for-sex peers. HIV pre-exposure prophylaxis (PrEP) has had a substantial impact on HIV prevention globally. This questions whether GBM who engage in chemsex remain at risk of HIV in the context of PrEP. This research explores ongoing HIV risk behaviours among men who engage in chemsex in the context of the availability of PrEP.

This thesis comprises six projects. The first project described the implementation of a cohort management system that I designed to automate data collection for this project. In 2014, baseline prevalence of methamphetamine use was high, as was concurrent use of erectile dysfunction medication (EDM) and gamma-hydroxybutyrate (GHB). The second and third projects examined EDM and GHB separately. Prior to the widespread availability of PrEP in Australia, use of these drugs was strongly associated with HIV risk behaviours. The fourth project was conducted in 2017 and measured incidence of PrEP initiation among GBM in the cohort, and identified factors associated with PrEP initiation. Many GBM who had reported high-risk behaviours subsequently initiated PrEP, but a large proportion of GBM at high-risk of HIV did not initiate PrEP. The fifth project demonstrated a change in HIV prevention among GBM who engage in chemsex. Prevalence of PrEP use among GBM who engage in chemsex increased dramatically between 2014 and 2017. With methamphetamine use consistently linked to HIV infection, the sixth project investigated the relationship between its use and HIV risk

behaviours, specifically in the current context of HIV biomedical prevention. GBM who were previously considered at highest risk of infection are more likely to use PrEP to mitigate against the HIV risk in 2018.

PrEP as an HIV prevention strategy is changing the trajectory of the HIV epidemic among GBM in Australia. This thesis demonstrates a shift in epidemiology away from the previously highest risk practices due to the incorporation of PrEP into the regimens of GBM who engage in chemsex.

Chapter One

Introduction

Emerging practices

1.1   Preamble

HIV remains a global health problem. With 36 million people currently living with HIV worldwide,[1] the epidemic does not discriminate against border crossings, population groups, or people of diverse genders, sexes, or sexualities. Yet, marginalised populations and their immediate partners are disproportionally affected and account for 47% of new HIV infections each year.[2] This is especially true among gay and bisexual men in many developed and developing countries.[3-5] Global HIV strategies highlight major inequities in the distribution of HIV, identifying gay and bisexual men as a key population.[6] In Australia, gay and bisexual men disproportionately carry the burden of HIV.[7]

Within a population already at high-risk for HIV, gay and bisexual men who use drugs are at higher risk of HIV compared to their non-drug-using peers. Drug use among gay and bisexual men has often been ascribed to the enhancement of sexual pleasure,[8-17] colloquially referred to as chemsex.[18] Chemsex has been strongly associated with HIV sexual risk behaviours and subsequent HIV infection.[8,9,14-16,19-31] Consequently, among gay and bisexual men, those who use drugs to enhance their sexual pleasure represent a subpopulation at a particularly high risk of HIV.

Different regions and populations are affected by the HIV epidemic in different ways.[32] Although new HIV infections declined globally by 16% between 2010 and 2017,[33] there were still over 1.8 million new infections each year since 2010.[34] This suggests that a nuanced, population and region-specific, tailored approach, adapting to evolving harm reduction technologies is likely to change current HIV epidemiological trends.

At the commencement of my PhD research in 2014, the global response to the HIV epidemic had seen significant advances in HIV prevention, namely through the use of antiretroviral drugs.[3] Among people living with HIV, use of antiretroviral drugs reduces the virus to undetectable levels, making it 'virtually impossible' to transmit HIV to others.[35-41] Similarly, use of antiretroviral drugs as an HIV pre-exposure prophylaxis (PrEP) among HIV-negative people is a highly effective HIV prevention strategy.[42-62]

PrEP as an HIV prevention strategy has started to change the trajectory of the HIV epidemic among gay and bisexual men.

Given gay and bisexual men are overrepresented in both prevalence of HIV and drug use, I explored the impact of biomedical prevention among gay and bisexual men who use drugs to engage in chemsex. Directed by a harm reduction approach,[63-65] I recognise the importance of acknowledging pleasure in drug use and sexual behaviours, as much as risk. This allowed me to address my PhD research objective; do gay and bisexual men who engage in chemsex remain at risk of HIV acquisition in the context of PrEP?

In this thesis, I demonstrate an emerging practice in HIV prevention. With the growing evidence in support of antiretroviral medications preventing onward transmission of HIV, and their prophylactic use in preventing HIV acquisition, these biomedical HIV harm reduction technologies have the potential to change the association between illicit

drug use and subsequent HIV infection. In this thesis, I highlight the need to shift from a paradigm of 'war on drugs' to one of evidence-based harm reduction which includes the use of biomedical HIV prevention strategies among gay and bisexual men, specifically among those who engage in chemsex.

1.2   Prelude to my PhD research

It became evident while formulating a research hypothesis that the introduction of PrEP could have the potential to change HIV epidemiological trends among gay and bisexual men, especially among those who engage in chemsex. To understand the contexts in which gay and bisexual men are at risk of HIV, I needed to explore HIV risk behaviours and drug use beyond an epidemiological perspective to understand the underlying factors that place these men at risks.

1.2.1   The *Health in Men* Study

The *Health in Men (HIM) Study* was an Australian prospective observational study conducted between 2001 and 2007. It investigated HIV risk among gay and bisexual men and identified factors associated with incident HIV infection from an epidemiological and behavioural perspective. Specifically, the *HIM Study* identified use of methamphetamine and erectile dysfunction medication as independent risk factors for HIV acquisition.[31] This became the focus of my PhD research.

My research grew out of the *HIM Study*, and the evidence it produced has been central to my research topic. Furthermore, data from the *HIM Study* formed the basis for the first *Australian PrEP Guidelines*.[66,67] These guidelines are based on behaviours

identified by the *HIM Study* that place gay and bisexual men at high risk of HIV, and therefore make them eligible to access PrEP.

1.3 The terminology used in this thesis

1.3.1 Chemsex, or party-n-play

There are several terms used to describe the subculture of gay and bisexual men who use drugs to enhance sexual pleasure. Chemsex and party-n-play both refer to the deliberate use of drugs to enhance sexual pleasure among gay and bisexual men.[18,68] However, these terms which have gained traction in different parts of the world are used interchangeably. Party-n-play is commonly used by gay and bisexual men in North America and Australasia, whereas chemsex is mostly used in Western and Central Europe and some parts of Asia.[69]

The author who coined the term chemsex suggested that gay and bisexual men who use illicit drugs to enhance sexual pleasure are motivated by psychological vulnerabilities.[70] As the term chemsex has gained more global recognition, it has become synonymous with gay men and problematic drug use. This was further exacerbated through the 2015 British documentary entitled 'Chemsex', which portrays drug use as a way for gay and bisexual men to cope with HIV, drug addiction, and acceptance.[71] It was also exacerbated by national and international media articles using sensationalist language, for example "the biggest crisis in the gay community in 30 years".[72-76] The stigma associated with the term chemsex could have unintentional consequences that may impact an already stigmatised population.

While the term party-n-play has historically been used in Australia, I have chosen to use the term chemsex throughout my thesis, with some caveats. Firstly, I do not wish to imply the tacit acceptance of a simplistic assumption that gay and bisexual men who use illicit drugs are solely motivated by psychological vulnerabilities. This thesis provides an evidence-based account of thousands of gay and bisexual men, with varying degrees of drug use, whether it be infrequent use, functional use, problematic use, or no use. Secondly, I have intentionally used the term chemsex to counter some of the sensationalism that accompanies this term and the misrepresentation that all gay men use drugs, and gay men who use drugs are motivated by psychological vulnerabilities.

Beyond the voyeuristic representation of a dangerous mix of gay and bisexual men, drugs, and sex, are the lives of thousands of gay men who party, have fun, and protect their health and wellbeing. Therefore, I offer a more nuanced alternative account that includes differing, and often divergent explanations.

1.3.2 Gay and bisexual men, or men who have sex with men

The terms 'gay and bisexual men' and 'men who have sex with men' have different meanings despite often referring to the same population group. To accurately address my research questions, the appropriate population and correct term should be used. Men who have sex with men has been used in literature since the 1990s,[77] and represents a broader population of all homosexually active men. From an epidemiological perspective, the term men who have sex with men was introduced to reflect risk behaviours of interest, not identity or contextual influences. Referring to the population as men who have sex with men did not purposefully intend to reduce individuals to their risk behaviours or imply a lack of importance into the meanings of social and political

aspects of identity, but simply focus on the actual risk behaviour to measure an outcome. However, the use of this term does not consider other factors that may influence risk, such as identity, community connectedness, and peer influence.

Using the term men who have sex with men in the context of this thesis would be problematic. Chemsex in itself is not a risk behaviour for HIV transmission, yet it is highly indicative of risk, such as engaging in condomless anal intercourse. Moreover, chemsex networks are mostly comprised of men who are gay community attached and gay-identified. How identities, community connectedness, and peer influence play a role in drug using and HIV sexual risk behaviours is central to investigating chemsex in relation to HIV transmission risk. This research project is based on a sample that is predominantly comprised of gay men, with some bisexual men. This includes transgender men who identify as gay or bisexual. Throughout this thesis, where the literature does not provide data on sexual identity, the term men who have sex with men will be used. Where sexual identity has been provided, including specifically the men in my PhD research, the population will be referred to as gay and bisexual men.

1.4 Outline of this chapter

The primary focus of my PhD research is to investigate HIV-related risk among gay and bisexual men who engage in chemsex. It does not focus on non-HIV related harms or problematic drug use. I acknowledge that non-HIV related harms and problematic drug use among gay and bisexual men may need to be addressed. However, this is beyond the scope of my PhD research. Following this preamble, I present this introduction chapter in sections. **Sections 2** and **3** review the epidemiological literature on HIV and drug use, respectively. In **section 4,** I review cofactors that exacerbate HIV risk through

sexual behaviours and describe drug use in the context of chemsex. **Section 5** explores subcultural affiliation to drug use, HIV risk behaviours, and its influence on harm reduction, and **section 6** reviews the current state of HIV harm reduction, focusing on antiretrovirals as HIV treatment and prevention. **Section 7** highlights the knowledge gaps and describes the objective of my PhD research. Lastly, **section 8** describes the new data collection and management methodology I have designed and used in this project.

Epidemiological trends in HIV

In this section I review the global state of HIV, highlighting that both global and Australian HIV strategies identify gay and bisexual men are among key populations vulnerable to HIV.

1.5 The global state of HIV

Since the start of the epidemic, it is estimated that 75 million people, globally, have acquired HIV.[78] According to the *Global Burden of Disease Study*, a comprehensive worldwide observational epidemiological study, the number of new HIV infections worldwide peaked at an estimated 3.2 million in 1999.[1] By 2017, this number had declined to 1.9 million. Between 1990 and 2017, the estimated number of people living with HIV increased from 8.7 million to 36.8 million.[1,78,79] Since the start of the epidemic, it is believed that about 32 million people have died from AIDS-related illnesses.[78] The annual number of AIDS-related deaths has declined from 1.9 million in 2006 during its peak, to 950,000 in 2017.[1]

In 2014, the *Joint United Nations Programme on HIV/AIDS (UNAIDS)* announced its ambitious 90-90-90 target.[80] This global strategy aims for 90% of people living with HIV to be diagnosed, 90% of people diagnosed with HIV to be accessing treatment, and 90% of people on HIV treatment to be virally suppressed, with fewer than 500,000 new infections worldwide by 2020. However, while the global incidence of HIV has

declined since 1996,[81] modelling estimates show the rate of decline is slower than what
is needed to reach the 2020 milestone.[82]

The HIV epidemic does not impact all regions uniformly, with some regions more
vulnerable than others. Globally, HIV incidence has been declining, with the reduction
of new infections strongest in regions most affected by HIV, such as Eastern and
Southern Africa.[82-84] However, over the past 20 years, HIV incidence has doubled in
eastern Europe and central Asia and risen by more than a quarter in the Middle East and
North Africa.[2]

1.6 HIV in Australia

The prevalence of HIV within the Australian population was estimated at 0.14% in
2017,[85] which is low in comparison with many other high-income countries.[79,81] In
2017, the HIV notification rate was 4.0 per 100,000,[7] and an estimated 27,545 people
were living with HIV. Of the estimated 27,545 people living with HIV, 89% were
diagnosed. Among those, 95% were retained in care (having had a viral load or CD4
cell count in the past year), and 87% were receiving antiretroviral therapy.
Antiretroviral therapy minimises disease progression for people living with HIV,[86] and
also reduces the risk of onward HIV transmission to HIV-negative sexual partners.[87] Of
those receiving treatment, 95% had a suppressed viral load (less than 200 RNA
copies/mL) (Figure 1.1).[7] This coverage corresponds to 74% of all people estimated to
be living with HIV in Australia having suppressed viral load in 2017 and exceeds the
UNAIDS 2020 target.[80] Australia is also on track to achieve the *UNAIDS 2030* targets of
95% of people living with HIV diagnosed, 95% retained in care, and 95% achieving a
suppressed viral load.[7] Between 2014 and 2018, there was a 23% decrease in the

number of newly diagnosed cases of HIV,[88-90] representing the lowest number of new
HIV notifications since 2001. Of the 835 newly diagnosed HIV cases in 2018, 61.6%
were attributed to male-to-male sex.[88] An additional 6.7% of infections were attributed
to male-to-male sex and injecting drug use.

Figure 1.1   Australian HIV diagnoses and care cascade, 2015–2017

	Living with HIV	Living with HIV and diagnosed	Retained in care	Receiving antiretroviral therapy	Supressed viral load
2015	25 543	22 583	21 454	19 164	17 505
2016	26 578	23 644	22 462	20 413	18 945
2017	27 545	24 646	23 414	21 560	20 412
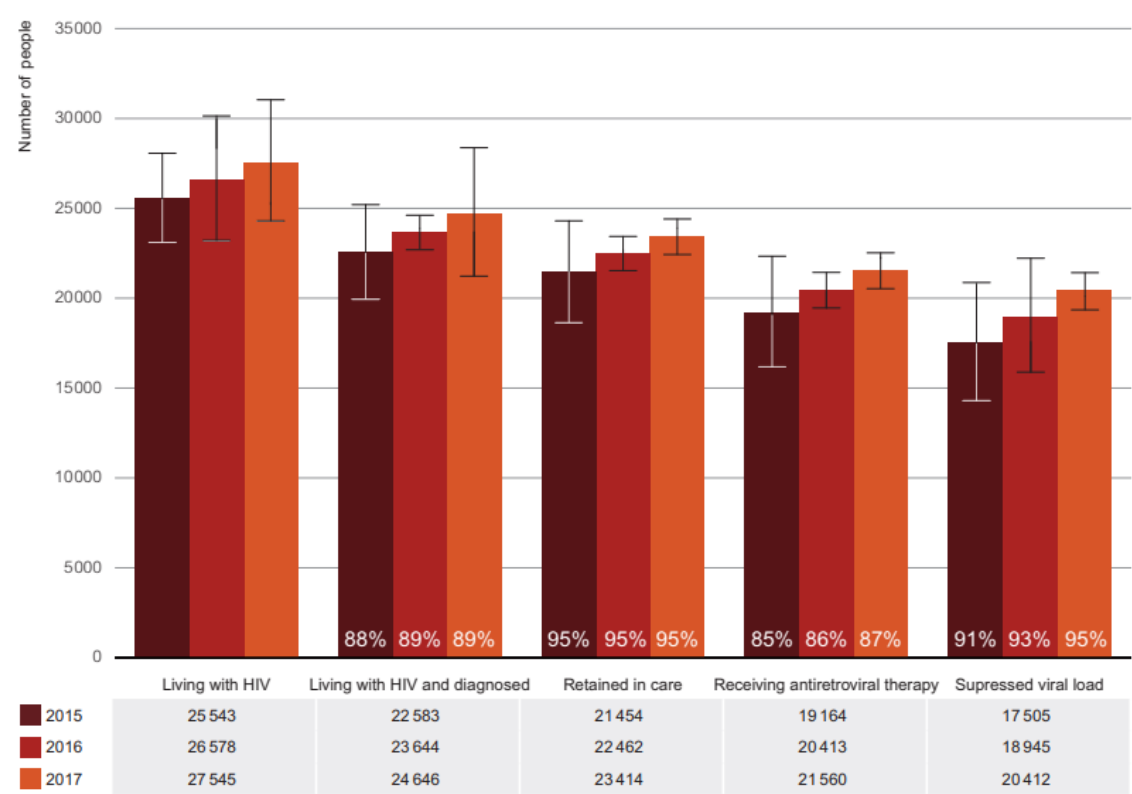
Error bars: range

Source: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia:
Annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney.[7]

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Australia's *National HIV Strategy* has been instrumental in response to the HIV
epidemic in Australia.[91] Currently in its eighth edition, the *National HIV Strategy* is
continually revised to respond to the changing epidemic, and has set the direction for
Australia's continuing response to HIV for 2018 to 2022.[91] Health departments in each

of the Australian jurisdictions are responsible for their own HIV treatment and prevention initiatives.[92-96]

1.7 Populations vulnerable to HIV

Just as HIV varies across geographic regions, it also varies across different population groups. Globally, almost half (47%) of new HIV infections are among adults who belong to five key vulnerable population groups and their sexual partners: men who have sex with men, people who inject drugs, sex workers, prisoners, and transgender people.[2] Risk of HIV is exacerbated when individuals belong to overlapping affected populations, such as men who have sex men, and who also inject drugs. These population groups make up a small proportion of the general population, yet they are disproportionally affected by HIV (Figure 1.2). In 2017, these population groups account for 95% of new infections in Eastern Europe, Central Asia, the Middle East, and North Africa, 90% in Western and Central Europe, and North America, 77% in Latin America, 84% in Asia, the Pacific, and Latin America, 40% in Western and Central Africa.[2]

Figure 1.2   Relative risk of HIV acquisition, by population group compared to the general global population, 2017
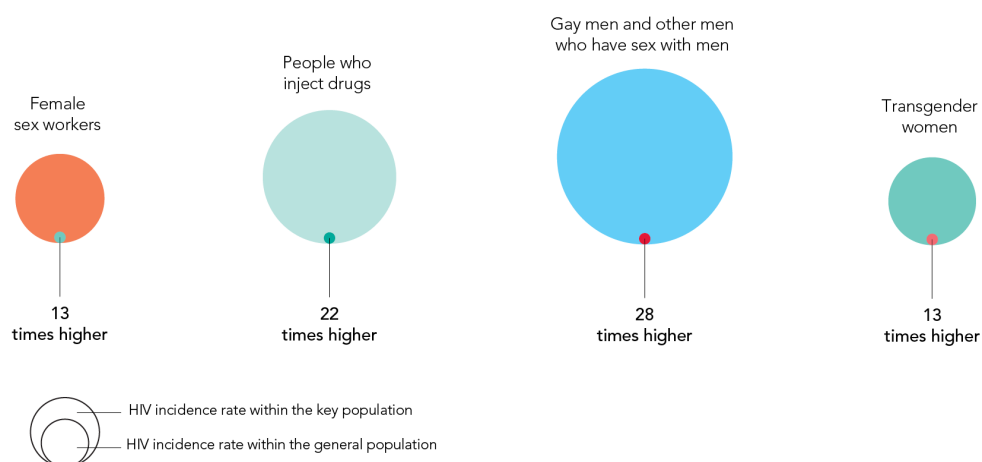
Source: Joint United Nations Programme on HIV/AIDS. Miles to go: closing gaps, breaking barriers, righting injustices. Geneva: UNAIDS 2018.[2]

1.7.1   Men who have sex with men

Globally, men who have sex with men are about 28 times more likely to acquire HIV than the general population.[2] The global rates of new HIV diagnoses have been decreasing since its peak in 1996.[1,82] However, at the time of initiating my PhD research in 2014, rates of diagnoses among men who have sex with men have not seen the same rates of decline.[4,97] In 2017, men who have sex with men accounted for 57% of new HIV cases in western and central Europe and North America, 41% in Latin America, 25% in Asia, the Pacific, and the Caribbean, 20% in eastern Europe, Central Asia, the Middle East, and North Africa, and 12% in western and central Africa.[2,82] Beyrer et al. (2013) published the aggregate HIV prevalence estimates for men who have sex with men. They demonstrate that the prevalence of HIV is dramatically higher among men who have sex with men than it is within the general population in every region (Figure 1.3). At the time of their publication in 2013, the overall HIV prevalence rates among

men who have sex with men show sustained epidemic patterns, with little evidence of declines. HIV prevalence among men who have sex with men appears disproportionately high in every region where data are available.

Figure 1.3   Comparison of HIV prevalence in men who have sex with men and the general adult population, by region
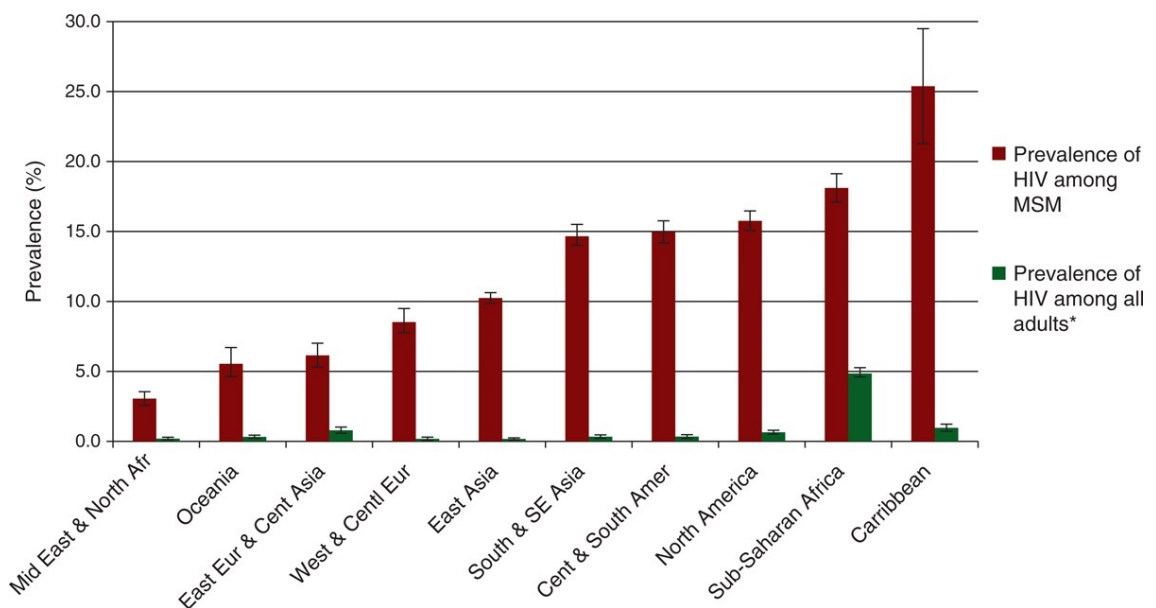
MSM: men who have sex with men; Mid: Middle; Afr: Africa; Eur: Europe; Cent: Central; SE: South East; Amer: America.

Pooled HIV prevalence among men who have sex with men, and among all men of reproductive age, by region, 2012.

Source: Beyrer C, Sullivan P, Sanchez J, Baral SD, Collins C, Wirtz AL, Altman D, Trapence G, Mayer K. The increase in global HIV epidemics in MSM. AIDS 2013; 27(17): 2665-78.[97]

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The HIV epidemic in Australia is concentrated among men who have sex with men. The HIV prevalence among the general Australian adult population is 0.14%,[85,98] while the HIV prevalence among men who have sex with men in Australia is estimated to be 7.9%.[7,85,99] Between 2008 and 2017, 84% of newly acquired HIV notifications were attributed to male-to-male sex, and 58% late diagnosis was attributed to male-to-male sex (Figure 1.4).[7] In 2018, of the 835 new HIV cases notified in Australia, 61.6% were

attributed to male-to-male sex, which continues to represent the main route of transmission.[88] In addition to these notifications, 6.7% of new HIV cases were attributed to men who reported both male-to-male sex and injecting drugs, totalling 68.3% for 2018.

Figure 1.4   HIV notifications classified as newly acquired or late diagnosed, by HIV exposure category, 2008-2017
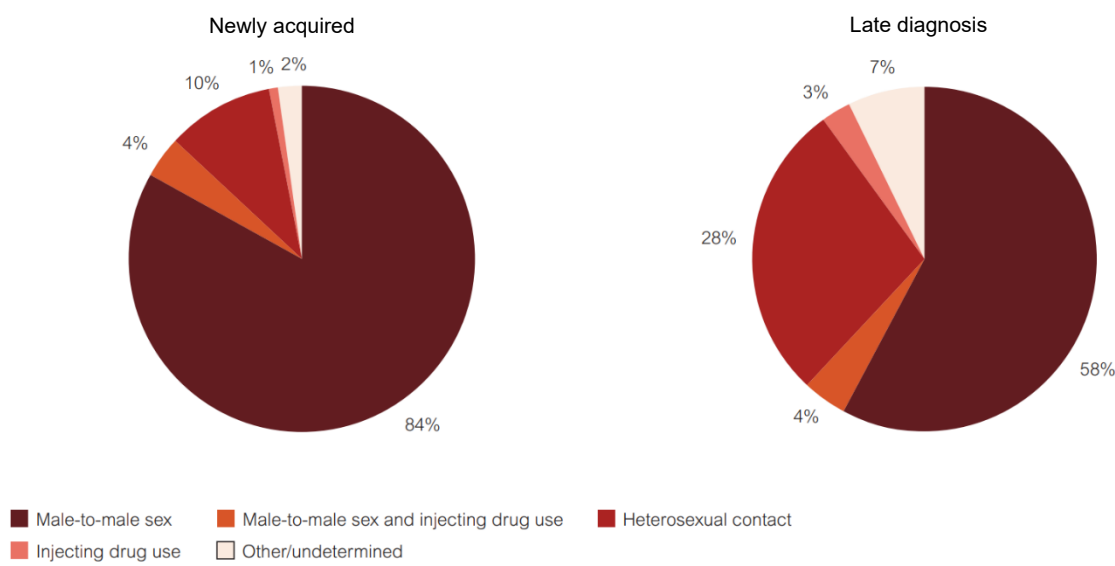
Newly acquired: Defined as newly diagnosed with HIV with a negative or indeterminate HIV antibody test or a diagnosis of primary HIV within one year before HIV diagnosis; Unspecified: All notifications that do not meet the definition of newly acquired HIV.

Source: Source: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney.[7]

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Epidemiological trends in licit and illicit drug use

In this section, I review the state of drug use among gay and bisexual men. As was the case regarding HIV, gay and bisexual men in Australia and similar countries are overrepresented in rates of drug use compared to other populations

1.8 The current state of drug use

The *World Drug Report 2018* estimates that approximately 275 million people aged between 15 and 64 used an illicit drug at least once in 2016.[100] Between 2006 and 2016, the number of people who used licit or illicit drugs increased from 208 million to 275 million, with an increase of 20 million people between 2015 and 2016 alone.[101] The World Health Organization estimated 450,000 deaths in 2015 were attributable to licit and illicit drug use,[100] with 167,750 a direct result from drug use disorders.[102]

1.8.1 Drug use in Australia

The latest report published by the *National Drug Strategy Household Survey*, a national survey collecting the prevalence of licit and illicit drug use across Australia, found that in 2016, among 23,722 respondents, 43% had ever used an illicit drug with 15.6% using an illicit drug in the previous twelve months.[103] The most commonly used illicit drugs

in the previous twelve months were cannabis (10.4%), recreational use of painkillers/opioids (3.6%), cocaine (2.5%) and ecstasy (2.2%). Prevalence of most illicit drug use remained stable between 2013 and 2016. However, use of hallucinogens, and synthetic cannabinoids have decreased. Cocaine use has been increasing since 2014, and as of 2016, it was at its highest rate in fifteen years. Use of gamma-hydroxybutyrate has fluctuated over time but has remained stable. In 2016, 1.6% of the Australian population reported injecting a drug in their lifetime, with 0.3% reporting injecting drugs in the previous year.[104]

Approximately 6.3% (1.3 million) of the Australian population had reported any use of methamphetamine in their lifetime. Among those who reported methamphetamine use in the previous twelve months, 20% reported at least weekly use, and 11.9% injected amphetamine-type drugs.[103] Between 2010 and 2016, weekly or more frequent use of methamphetamine more than doubled among people who reported use in the previous twelve months (9.3% in 2010 to 20.0% in 2016). In 2016, most methamphetamine users (57%) were using the derivative crystal methamphetamine.[103] Crystal methamphetamine use also doubled during this period, from 12.4% in 2010 to 32.0% in 2016.

The *2016 National Drug Strategy Household Survey* also investigated the frequency of drug use.[103] Cocaine (64%) and ecstasy (51%) were mostly used once or twice in the previous twelve months, with 2% and 3% respectively reporting weekly or more often use. At least weekly use was reported among 36% and 20% of recent use of cannabis and methamphetamine, respectively.

1.9 Drug use among gay and bisexual men

Gay and bisexual men have consistently been found to use most illicit drugs at higher rates compared to their heterosexual male counterparts.[14,19,105-112] Moreover, gay and bisexual men living with HIV have consistently been found to use illicit drugs at higher rates compared to HIV-negative gay and bisexual men.[19,113] These disproportionate rates of use have been shown across multiple countries and throughout time.[26,111,114-123]

The *National Drug Strategy Household Survey* is the only national data source by the Australian Institute of Health and Welfare that specifically disaggregates licit and illicit drug use data by sexual identity and provides comprehensive estimates.[103] However, reports on the survey do not consider the differences in drugs used, or drug using behaviours between these population groups.[107] The Australian Institute of Health and Welfare acknowledges there is a lack of publicly available and comprehensive data examining the use of drugs by people identifying as gender and sexually diverse, such as lesbian, gay, or bisexual people. They also note their data does not include estimates for transgender, intersex, or queer people.[104,124]

Since 2007, the *National Drug Strategy Household Survey* has reported higher levels of licit and illicit drug use in the previous twelve months among people who are gay, lesbian, or bisexual compared with their heterosexual counterparts.[103] These higher rates of drug use have remained stable.[103] However, their findings do not differentiate between gay, lesbian and bisexual people. In 2016, the *National Drug Strategy Household Survey* reported that 15.6% of the Australian population had used any drugs in the previous twelve months, 14.5% among heterosexual respondents, and 41.7% among lesbian, gay, and bisexual respondents.[103]

The *Gay Community Periodic Survey* has been collecting behavioural data on gay and bisexual men in major Australian cities since 1996. This ongoing surveillance project specifically targets gay and bisexual men who are socially and sexually connected to the gay community to monitor sexual and illicit drug using behaviours over time. In 2016, prevalence of illicit drug use reported in the previous six months among gay and bisexual men was substantially higher in the *Gay Community Periodic Survey* than the *National Drug Strategy Household Survey* (61.4% vs. 41.7%.[103,125]

1.10   Harms associated with drug use

Different patterns of drug use result in different types of harmful outcomes. Although the primary focus of my PhD research is HIV infection in the context of chemsex, I briefly describe harms commonly associated with drug use among gay and bisexual men. In **section 4** below, I describe in greater detail the context in which HIV occurs among gay and bisexual men.

Drug use disorders

Drug use disorders, formally known as drug dependence, refer to the impairment of people's lives due to use of illicit drugs. In 2017, it was estimated that globally, 176 million people had a drug use disorder.[126] The prevalence of drug use disorders varies between countries (0.4% – 3.5%).[127] Australia was estimated to have a 2.3% prevalence of drug use disorders in 2017.[127]

Death-related deaths

In 2017, it was estimated that globally there were 351,500 deaths directly due to drug use disorders.[83] This has increased from 284,000 in 2007. Deaths indirectly attributed to drug use, such as those relating to HIV and hepatitis C acquired through unsafe injecting practices, or from suicides, accounted for 63% of the deaths attributed to drug use in 2015.[100]

In Australia, there has been an increase in deaths that are directly attributable to drug use, with the number reaching the highest on record in 2017 at 1,808 deaths.[128] These drug-induced deaths were mainly associated with non-prescription use of benzodiazepines and oxycodone, which are prescription medications used to manage anxiety and pain, respectively.

Polydrug use exacerbate risk of overdose

Simultaneous use of multiple drugs, known as polydrug use, increases the likelihood of adverse events. As a central nervous system depressant, gamma-hydroxybutyrate has a high overdose liability,[129] particularly when used in combination with other depressants, such as alcohol.[130] Polydrug use of amyl nitrite and erectile dysfunction medication can result in a loss of consciousness due to a sudden and extreme drop in blood pressure.[131,132] Crystal methamphetamine used with speed or ecstasy can lead to a stroke, whereas use of crystal methamphetamine with alcohol, cannabis, or benzodiazepines increases the likelihood of overdose.[133]

Injecting drugs exacerbate risk of overdose

Injecting delivers the drug directly into the bloodstream. It bypasses the liver metabolism which would usually decrease the amount of drug that ends up in the bloodstream.[134] This makes it harder to gauge how much of the drug to use, as opposed to smoking or snorting where the dose can be increased incrementally until the desired effect is achieved. In addition, because of the rapid onset of the effects from injecting drugs, an overdose can occur very quickly, requiring immediate action.[135]

Needle and syringe sharing

Receptive needle and syringe sharing, which involves the reuse of injecting equipment, needles, and syringes, that have been used by others is a major risk factor for HIV and hepatitis C infection. HIV, specifically, can remain viable for several weeks within contaminated injecting equipment.[136-138] In a systematic review, Patel et al. (2014) estimated the per-act HIV transmission though sharing needles was 63 per 10,000 exposures (95% confidence interval [CI]: 41 – 92). Data from the *Australian Needle and Syringe Program Survey*, an annual behavioural surveillance survey providing serial point prevalence estimates of HIV and hepatitis C and monitors injecting behaviours, reported an increase in receptive needle and syringe sharing, from 16% in 2014 to 18% in 2018.[140] In Australia, gay and bisexual men living with HIV are more likely to report injecting drug use in the previous six months than HIV-negative men.[123,140]

Blood borne viruses

Drug use among gay and bisexual men, particularly when used to enhance sexual pleasures, has been associated with receptive condomless anal intercourse and incident HIV infection (discussed in greater detail in **section 4**).[8,9,15,16,19,22,23,25,27,29] Use of drugs to enhance sexual pleasure has also been implicated with hepatitis C infection.[141] The prevalence of hepatitis C infection has increased in the previous ten years among gay and bisexual men living with HIV in Australia,[142] and internationally.[143-145] Among the general population, compared to HIV-negative people, people living with HIV are 1.6 times more likely to have hepatitis C infection.[146,147] This increased to 6 times among people living with HIV who inject drugs and 7.5 times more likely among gay and bisexual men living with HIV.[146,147]

A converging intersection between HIV risk and pleasure

Sections 2 and **3** explored the epidemiological trends of HIV and licit or illicit drug use, showing that gay and bisexual men are overrepresented in both global health concerns in Australia and internationally. In this section, I review HIV risk factors by exploring sociobehavioural factors that perpetuate the risk of HIV transmission specific to gay and bisexual men. I start this section by reviewing the cofactors that exacerbate HIV risk through sexual behaviours, partners, and networks. I then review the literature on licit and illicit drug use in relation to HIV risk, followed by reviewing motivations for its use. I close this section by highlighting inherent limitations in in HIV harm reduction strategies among gay and bisexual men who use drugs.

1.11 Cofactors perpetuating HIV transmission

Multiple biological, psychological, and social factors place gay and bisexual men at higher risk of HIV, including barriers to testing,[148] lack of knowledge of their own and their partners' HIV status,[3] homophobia, discrimination, and stigma,[149] and institutional barriers and policy gaps.[150-152] Moreover, gay and bisexual men who are sexually adventurous are more likely to engage in HIV sexual risk behaviours and to experience subsequent HIV infection.[15,153-155] Understanding the complex interconnections of these

factors is key to HIV prevention and altering unchanging epidemiological trends in this population.

1.12 Hierarchy of HIV risk through sexual behaviours

Per-act estimates of HIV transmission vary considerably due to differences in biological and behavioural cofactors.[156] However, all studies that estimate per-act probabilities in the context of male-to-male sex show considerable consistency, with the collated results suggesting a hierarchy of HIV risk through sexual behaviours. Sexual transmission of HIV can be estimated as per-act transmission (the risk per sexual contact), or per-partner transmission (the risk per sexual partner). In the following section, I review per-act estimates of HIV transmission for various sexual behaviours in the context of men who have sex with men. These comparisons for per-act estimates were made between the pre-highly active antiretroviral therapy (pre-HAART) era (between 1981 and 1996), and the early-HAART era (between 1996 and 2002), and so describe the per-act estimates between different stages in the HIV epidemic prior to the current HIV biomedical era. The likelihood of risk in the more recent context of widespread availability of antiretrovirals used as treatment or its prophylactic use is discussed in **chapters 5** through **8**.

Perceived risk of HIV through sexual behaviours has changed over time.[157-159] These perceptions can influence HIV risk and harm reduction practices. I compare mean scores of perceived HIV risk through sexual behaviours from 1,222 HIV-negative gay and bisexual men in Australia to per-act probability of HIV risk through sexual transmission. In Australia, HIV risk perception on sexual practices also suggest a

hierarchy, which broadly reflects the per-act probability of HIV risk through sexual transmission.[160]

1.12.1   Receptive and insertive oral intercourse

Quantifying HIV transmission through oral sex among gay and bisexual men is difficult, as oral intercourse is frequently combined with other HIV sexual risk behaviours, such as anal intercourse. Nonetheless, the risk of HIV transmission through oral intercourse is estimated to be lower than for anal intercourse (Table 1.1).[161] This is due to the oral cavity being relatively resistant for HIV, with a thick layer of epithelial cells, a lower number of CD4 target cells, and a higher concentration of antiviral antibodies.[162] The likelihood of HIV transmission through oral intercourse is exacerbated when the receptive partner has cuts or ulcers in the mouth, or if sexually transmitted infections are present.[162] However, even under these circumstances, the risk of HIV transmission is still considered low.[162-165]

1.12.2   Receptive and insertive condom-protected anal intercourse

Consistent and correct use of condoms is a highly effective HIV prevention strategy. Available estimates of per-act HIV transmission through condom-protected anal intercourse were similar for receptive or insertive sexual behaviours, regardless of the sexual partner's HIV status, or the HAART era (Table 1.1).[161,163,166,167] Among HIV-negative gay and bisexual men in Australia, the perceived risk of HIV transmission through condom-protected anal intercourse had lower mean scores compared to any condomless anal intercourse behaviours.[160]

Condom failure (slippage or breakage), or inconsistent or infrequent condom use increases the likelihood of HIV acquisition.[168] In a sample of 207 men who have sex with men from three United States cities, the likelihood of condom failure is 4.1 times higher during sexual intercourse with a non-regular partner (95% CI: 1.5 – 11.7), 2.0 times more likely when intoxicated or using drugs (95% CI: 1.1 – 3.8), and 3.7 times more likely with inconsistent condom use (95% CI: 2.0 – 6.6).[168] Inconsistent condom use has also been ascribed to decreased sexual sensitivity, [169,170] and erectile dysfunction.[171]

1.12.3   Insertive condomless anal intercourse

Insertive condomless anal intercourse has a higher per-act HIV transmission rate than to insertive or receptive condom-protected anal or oral intercourse (Table 1.1).[161,163,172] Gay and bisexual men in Australia correctly perceive insertive condomless anal intercourse to have a higher transmission risk than condom protected anal intercourse.[160]

Some studies have found circumcision to be protective against HIV infection during condomless anal intercourse,[173] particularly in low and middle income countries.[174] In uncircumcised men, the inner surface of the foreskin is much thinner, and there is a higher concentration of Langerhans cells near the surface of the foreskin,[175] which are target cells for HIV.[173,176] However, circumcision has not been consistently demonstrated as an effective HIV prevention strategy in gay and bisexual men.[177-179] Circumcision may offer some protection among gay and bisexual men who exclusively take the insertive position during condomless anal intercourse.[178]

1.12.4 Receptive condomless anal intercourse

Compared to other sexual behaviours, receptive condomless anal intercourse has the highest per-act estimates for HIV transmission (Table 1.1). [139,161,163,172] The lining of the rectum is thin which increases the likelihood of HIV entering the bloodstream, and is also more susceptible to microscopic tears during anal intercourse.[180] The rectum also has a higher density of C-C chemokine receptor type 5, which HIV requires to enter the host cell.[181,182]

Per-act estimates were initially calculated for receptive condomless anal intercourse where the insertive partner was known to be HIV positive and untreated. Per-act estimates were slightly lower in the early-HAART era compared to the pre-HAART era. Jin et al. (2010) demonstrated that withdrawing or inserting ejaculation could modify per-act transmission rates. Ejaculation within the rectum has the highest per-act estimate compared to any other sexual behaviours. Among gay and bisexual men in Australia, the perceived HIV-related risk reflects these per-act estimates. Receptive condomless anal intercourse with an HIV positive sexual partner had the highest mean scores.[160] In Australia, HIV risk perception on sexual practices also suggest a hierarchy, which broadly reflect the per-act probability of HIV risk through sexual transmission.[160]

Table 1.1   Per-act estimates of HIV transmission risk through sexual behaviours

Study	Type of study (n)	Condition	Per-act probability
Receptive and insertive oral intercourse			
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.04 (95% CI 0.01 – 0.17)
Insertive condom-protected anal intercourse			
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.04 (95% CI 0.01 – 0.11)
Receptive condom-protected anal intercourse			
Buchbinder et al. (1996) [163]	Cohort study (n=1,975)	HIV positive partner	0.04 (95% CI 0.00 – 0.15)
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.18 (95% CI 0.01 – 0.11)
Insertive condomless anal intercourse			
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.06 (95% CI 0.02 – 0.19)
Jin et al. (2010) [172]	Cohort study (n=1,427)	Circumcised †	0.11 (95% CI 0.02 – 0.24)
Buchbinder et al. (1996) [163]	Cohort study (n=1,975)	HIV positive partner	0.14 (95% CI 0.04 – 0.29)
Jin et al. (2010) [172]	Cohort study (n=1,427)	Uncircumcised †	0.62 (95% CI 0.07 – 1.68)
Receptive condomless anal intercourse			
Buchbinder et al. (1996) [163]	Cohort study (n=1,975)	HIV negative partner	0.03 (95% CI: 0.00 – 0.11)
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.27 (95% CI 0.04 – 0.49)
Buchbinder et al. (1996) [163]	Cohort study (n=1,975)	Unknown serostatus partner	0.40 (95% CI: 0.26 – 0.59)
Buchbinder et al. (1996) [163]	Cohort study (n=1,975)	HIV positive partner	0.60 (95% CI: 0.34 – 1.09)
Jin et al. (2010) [172]	Cohort study (n=1,427)	With withdrawal †	0.65 (95% CI 0.15 – 1.53)
Vitinghoff et al. (1999) [161]	Cohort study (n=2,189)	HIV positive or unknown serostatus partner	0.82 (95% CI 0.24 – 2.76)
Jin et al. (2010) [172]	Cohort study (n=1,427)	With ejaculation †	1.43 (95% CI 0.48 – 2.85)

† Based on the assumptions that the actual HIV prevalence in HIV status unknown partners and in HIV negative partners was 10% and 0.5%, respectively.

1.13   HIV risk by sexual partners type

Partnership types also affect the impact of HIV prevention strategies.[157,183] However, there have been limitations in the literature on sexual partner types, namely the inconsistencies in differentiating sexual partnership categories. For example, some data made no distinction between sexual partner types, most use two categories (regular or steady partner and casual partners; or alternatively steady and anonymous), whereas others use three categories (regular partner, casual partners, and fuckbuddies; or alternatively regular, casual, and anonymous). This is further limited by the inconsistent labels used to categorise these sexual partnership types and definitions.[183] Nonetheless distinguishing between partner types allows us to identify the different degrees of risk associated with different sexual partners.[4,184,185] Casual partners have been identified as the key driver of the HIV epidemic among gay and bisexual men.[186,187] In a 2017 Australian study among gay and bisexual men's experience of HIV seroconversion, the *Seroconversion Study*, 10.6% attributed the source person of their infection as being their regular partners, and 23.3% attributed it to a fuckbuddy.[188] However, most (66.1%) attributed their infection to a casual partner, in either new or short-term partnerships. These findings have been replicated by other studies in Australia.[189-191]

1.14   HIV risk though a higher number of sexual partners

Gay and bisexual men report more sexual partners than their heterosexual male counterparts.[192-195] In a large national household survey in Australia, the *Second Australian Study of Health and Relationship,* 40% of gay and bisexual men reported more than 50 lifetime same-sex partners,[196] compared to 8% of heterosexual men.[197]

This higher number of sexual partners could exacerbate the likelihood of HIV transmission, especially given the higher proportion of gay and bisexual that are living with HIV compared to the general population. This increases the chances of having sexual encounters with people living with HIV, particularly those who remain undiagnosed.

Varghese et al. (2002) provide per-act relative risk estimates based on knowledge of sexual partners HIV status. They found that men who engaged in sexual intercourse with men of an unknown HIV status had a 43-fold higher relative risk of HIV acquisition, and a 430-fold higher relative risk of HIV acquisition with partners known to be HIV positive, compared to men who had known HIV-negative sexual partners.

1.15   HIV risk in the context of licit and illicit drug use

Research on drug use among gay and bisexual men has primarily focused on the type of drug used, and the associated risk behaviours. In two cohort studies of Australian gay and bisexual men, despite a general association between drug use and condomless anal intercourse with casual partners in the preceding six months, no such association at the event-level was found.[28,199] Event-level data suggest that among men who had engaged in condomless anal intercourse with casual partners in the preceding six months, drug use may have been as common on occasions when they used condoms as it was on occasions when they did not use condoms.[199,200] Conversely, although men who took risks sexually were more likely to use drugs, condomless anal intercourse with casual partners was also a strong predictor of subsequent use of amphetamine-type substances among men who had not initially been using such substances.[199,200] These findings supported the contention that the use of drugs was often specifically for the purpose of

enhancing and extending sexual experiences,[201] and suggests a subcultural association rather than a direct causal relationship.

While most drug use has been associated with sexual risk behaviour among gay and bisexual men,[14,19-21,105-112] the particular use of methamphetamine and erectile dysfunction medication, separately and concurrently (using both drugs within a specified time period, but not necessarily on the same occasion), has been independently associated with HIV seroconversion.[31] From the *HIM Study*, Prestage et al. (2009) found that gay and bisexual men who use methamphetamine were 1.8 time more likely to acquire HIV compared to gay and bisexual men who did not use drugs (Table 1.2). The recreational use of erectile dysfunction medication was associated with a 4.1 times higher likelihood to acquire HIV. Furthermore, with the concurrent use of methamphetamine and the recreational use of erectile dysfunction medication the likelihood to acquire HIV increased 8.1 times. These findings suggest that the association between use of drugs and subsequent HIV infection was strongest for drugs used specifically to enhance sexual pleasure.

Table 1.2   Stratified analysis of the association between methamphetamine and erectile dysfunction medication and HIV seroconversion

	Person years	HIV infections		Hazard Ratio	95% CI	p trend
		n	Incidence per 100 PY			
No drug use	1,105.3	4	0.36	1	–	<0.001
MA only	580.8	4	0.69	1.82	0.46 – 7.30	
EDM only	743.9	11	1.48	4.08	1.30 – 12.81	
Con. MA and EDM	637.6	19	2.98	8.06	2.74 – 23.71	

CI: confidence interval; MA: methamphetamine; EDM: erectile dysfunction medication; Conc.: Concurrent drug use.

Source: Prestage G, Jin F, Kippax S, Zablotska I, Imrie J, Grulich A. Use of Illicit Drugs and Erectile Dysfunction Medications and Subsequent HIV Infection among Gay Men in Sydney, Australia. The Journal of Sexual Medicine 2009; 6(8): 2311-20.[31]

1.15.1   Reasons ascribed for drug use

In the *National Drug Strategy Household Survey*, the most common reasons ascribed for the use of illicit drugs were curiosity (65%), and friends or family offered it or were using it (50%).[103] These published results did not differentiate reasons for use between heterosexual and lesbian, gay, or bisexual people. Most research for drug use among gay and bisexual men has tended to focus on individual psychological factors including the effects of homophobia,[202] sexual abuse,[203] and social isolation.[204] Descriptions of the motivations for drug use among gay and bisexual men have often been based on an assumed causative link between drug use, experiences of stigma,[205] and poor mental health,[70,115] as well as an assumption that drug taking leads to sexual risk taking.[70,115,202,203,205-207] Commonly, the higher prevalence of illicit drug use among gay and bisexual men is attributed to what is described as minority stress.[207] Minority stress theory states that gay and bisexual men experience elevated social stress due to the perceived and enacted stigma towards sexual minorities. This could have an additive effect on general psychosocial stressors, thereby increasing the susceptibility for poor mental health and problematic drug use. Nonetheless, the pursuit of pleasures from drug use is a key motivation for gay and bisexual men as it for other populations who use illicit drugs.[208]

Gay and bisexual men also have higher rates of anxiety and depression.[209-213] Peer support in general, and greater social engagement with other gay men have been shown to counter the negative mental health effects of homophobic stigma.[21,153,214-218]

1.15.2   Drugs used to enhance sexual pleasure

The types of drugs used during chemsex differ across time, space, and population groups.[15,16,22,24,26,111,114,115,117-120,123,219] Mephedrone, for example, is a popular drug among gay and bisexual men in the United Kingdom,[20] but its use in Australia remains rare. The *HIM Study* showed that individual gay and bisexual men's use of particular drugs changed over time, but overall rates remained very high.[220] In Australia, crystal methamphetamine is commonly used during chemsex, but use of gamma-hydroxybutyrate is also not uncommon (Figure 1.5).[125,186,221-226]

Drugs used for chemsex are often chosen specifically to increase the levels of sexual excitement and reduce inhibitions.[16,30,227] In this context, gay and bisexual men often also use erectile dysfunction medication, usually recreationally, to enhance and extend their sexual functioning or to overcome the erectile dysfunction that often accompanies methamphetamine use.[31,227-233]

Figure 1.5   Prevalence and trends of recreational drug use in the previous six months among men who have sex with men in Australia, 2009-2018
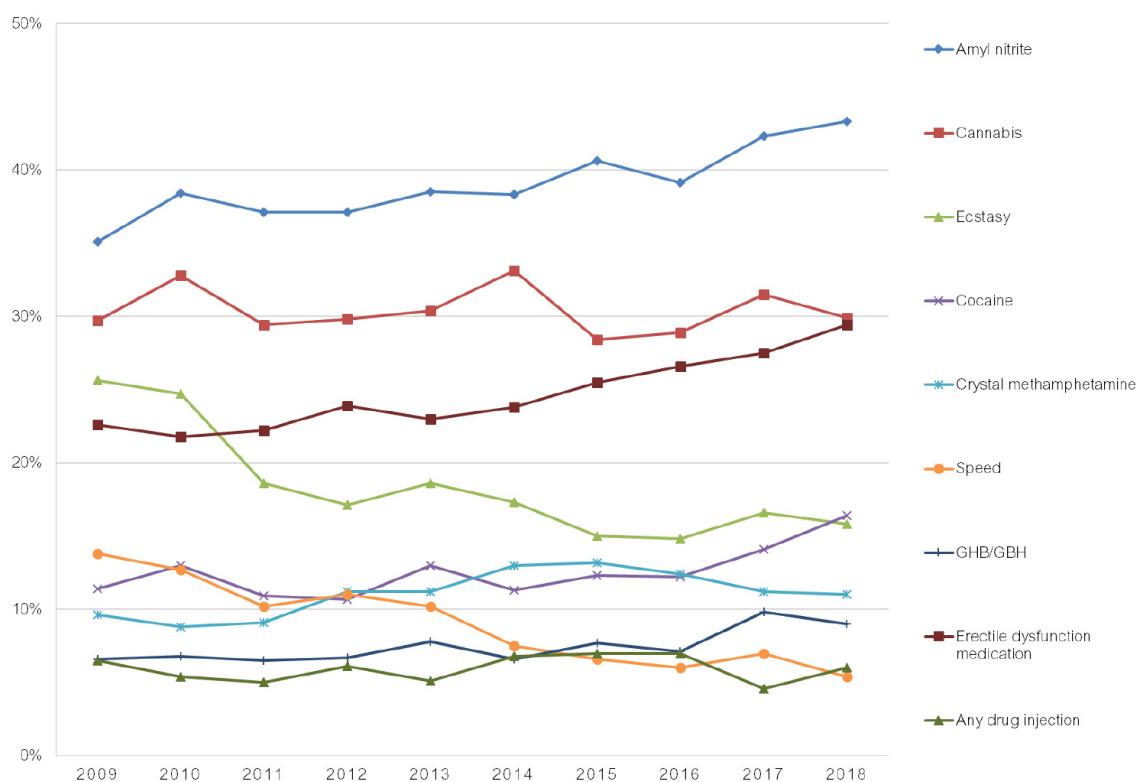
GHB/GBL: gamma-hydroxybutyrate/gamma-butyrolactone.

Source: Bryant J, Rance J, Treloar C. Annual Report of Trends in Behaviour 2019: Viral Hepatitis in Australia. Sydney: Centre for Social Research in Health, UNSW Sydney. 2019.[236]

Amyl nitrite

Although not a focus in this PhD research, use of amyl nitrite has been historically cited as a risk factor for HIV among gay and bisexual men.[166,234] Known as poppers, liquid gold, rush, purple haze, and buzz, amyl nitrite is classified as an inhalant, it belongs to a class of drugs known as alkyl nitrates, which also includes butyl nitrite, isobutyl nitrate and nitroglycerine.[235] Amyl nitrite is a vasodilator, which are medicines that cause the blood vessels in the body to dilate and the involuntary smooth muscles to relax.[235]

In Australia, use of inhalant including amyl nitrites increased from 0.4% in 2001 to 1.0% in 2016 among individuals aged 14 years or above.[103] Prevalence of amyl nitrite among gay and bisexual men has increased from 35.1% in 2009, to 43.3% in 2018.[236] Reasons for amyl nitrites use among gay and bisexual men are ascribed to its muscle relaxing properties which enable easier penetration during receptive anal intercourse.[237,238] Due to its specific use to facilitate and enhance sexual pleasure, use of amyl nitrites has been associated with HIV sexual risk behaviours.[237,238]

Crystal methamphetamine

Crystal methamphetamine is colloquially known as ice, crystal meth, shabu, crystal, glass, shard, and P, and it usually comes as small chunky clear crystals that look like ice.[210] Methamphetamine in Australia come in three forms: speed, base, and crystal methamphetamine, often distinguished by their appearance and perceived purity. Crystal methamphetamine, specifically, is stronger and more addictive than the powder form speed.[235] Crystal methamphetamine is generally smoked for immediate effect, or injected with a 15 to 30 second delayed onset of effects..

In 2016, 6.3% of Australians aged fourteen years and over had ever used amphetamine-type drugs, including 1.4% who had used amphetamine-type drugs in the previous twelve months.[103] Prevalence of crystal methamphetamine use among Australian gay and bisexual men increased from 9.6% in 2009 to 11.0% in 2018.[236] Although prevalence of crystal methamphetamine use has increased nationally among gay and bisexual men, in Australia's three most populous cities, prevalence of crystal methamphetamine has decreased between 2014 and 2018 (14.6% to 10.0% in Sydney; 10.5% to 9.2% in Melbourne, and 10.1% to 8.3% in Queensland).[125,223,224]

Gamma-hydroxybutyrate

Gamma-hydroxybutyrate is also known as G, fantasy, grievous bodily harm, juice, liquid ecstasy, liquid E, liquid X, Georgia Home Boy, soap, scoop, cherry meth, blue nitro, and fishies. Gamma-butyrolactone and 1,4-butanediol (1,4-BD) are chemicals that are closely related to gamma-hydroxybutyrate.[239] Once gamma-butyrolactone or 1,4-BD enter the body, they convert to gamma-hydroxybutyrate almost immediately. Gamma-hydroxybutyrate is usually swallowed, but sometimes it is injected or inserted anally (shafted).[235]

In 2016, recent use of gamma-hydroxybutyrate in Australia by people aged 14 or older was very low (0.1%).[103] However, prevalence of gamma-hydroxybutyrate use had been steadily increasing over time among gay and bisexual men in Australia, from 6.6% in 2009 to 9.0% in 2018 (Figure 1.5).[236] This increase in gamma-hydroxybutyrate use coincides with the decrease in crystal methamphetamine use.[236] Its increasing use was accompanied by growing concerns about overdose and other negative health outcomes.[130] Among gay and bisexual men, reasons for gamma-hydroxybutyrate use was commonly ascribed to enhancing sexual pleasure, which represents a key motivation for its use.[10,11,17,240] Its use, therefore, also likely applies to chemsex networks, but there has been little specific evidence concerning the role of gamma-hydroxybutyrate or of its association with sexual risk behaviours, which is the focus of **chapter 4**.

Recreational use of erectile dysfunction medication

Although illicit drugs are commonly used to engage in chemsex, non-psychoactive licit drugs are also often used to enhance the sexual experience. In particular, the

recreational use of erectile dysfunction medication is specifically for the purposes of prolonging erections,[232] enabling more intense sexual function during sex partying,[231] or countering erectile dysfunction commonly associated with use of crystal methamphetamine.[230,241] Prestage et al. (2009) have previously highlighted the key role of the recreational use of erectile dysfunction medication for sex partying among gay and bisexual men.

Among Australian gay and bisexual men, prevalence of erectile dysfunction medication use increased from 22.6% in 2009 to 29.4% in 2018 (Figure 1.5).[236] Recreational use of erectile dysfunction medication has been associated with sexual risk behaviours,[31,242] such as increased numbers of sex partners,[243] and condomless anal intercourse.[233] Despite its association with HIV risk behaviours, few studies have previously described the characteristics and contexts of gay and bisexual men who use erectile dysfunction medication, which I address in **chapter 3**. Use of erectile dysfunction medication has also been concurrently reported with other illicit drugs commonly used to enhance sexual pleasure, such as gamma-hydroxybutyrate,[244] crystal methamphetamine,[31] and amyl nitrites.[229]

Polydrug use

Several motives have been ascribed to polydrug use among gay and bisexual men, including an attempt to increase sexual arousal, confidence, inhibitions, and stamina,[30] or to facilitate the type of sex they want to engage in.[107] Among gay and bisexual men, a common polydrug combination is the use of erectile dysfunction medication to offset the erectile dysfunction that often accompanied use of crystal methamphetamine.[245,246] Polydrug use with erectile dysfunction medication, particularly when combined with crystal methamphetamine has been implicated in HIV infection and the transmission of

other sexually transmitted infections, due to the combined higher levels of sexual risk behaviours associated with their use.[120,233,243]

1.16 An inherent limitation in HIV prevention strategies

Prior to PrEP becoming more widely available, the HIV risk associated with chemsex among gay and bisexual men was not new knowledge. Yet, there was little change in HIV epidemiological trends among gay and bisexual men in the decade prior to beginning my PhD research in 2014. This may suggest that previous HIV prevention strategies were inherently limited as they applied to gay and bisexual men who engage in chemsex.

The effects of drugs commonly used in chemsex include euphoria, enhanced feelings of intimacy, increased sexual arousal, increased energy, and lowered inhibitions.[11,17,19,20] These effects may disinhibit impulse control and impair risk judgement,[247,248] which may, to some degree, explain the higher rates of HIV infection among gay and bisexual men who use drugs. For some gay men to engage in the sex they want, HIV prevention strategies usually required correct condom use, and in some cases, they had to forgo pleasure due to decreased sensitivity or erectile dysfunction that may accompany drug or condom use. Some strategies required knowledge of the sexual partner's HIV status and negotiation of sexual positioning in a sexual-social setting, often while disinhibited due to their drug use.

Subcultural affiliation influence on behaviour

The associations between drug use and high-risk HIV risk behaviours have long been reported. However, there has been little change in drug using behaviours and HIV risks over time. This raises questions as to whether the focus of HIV risk among gay and bisexual men may not be specific to the types of drugs used, but rather the networks in which drugs are used.

1.17   A shared understanding of risk and pleasure

Social behaviours are heavily influenced by the cultural and societal norms that prevail at a given time and place.[249,250] Gay community norms regarding understandings of pleasure and HIV risk are strong influences on sexual behaviours and HIV risk reduction practices among gay and bisexual men.[216,217,251-256] Combined, this suggests that gay and bisexual men may adjust their sexual practices according to shared understandings of HIV risk and gay community norms, particularly those regarding "safe sex".[216-218] Drug use among gay and bisexual men, including harm reduction practices, can similarly reflect normative values within specific gay community subcultures.[218]

1.18   Chemsex

Drug use is strongly associated with social engagement with other gay men.[15,28,123,257] Relationships between sexual risk behaviour, HIV acquisition, and drug use among gay and bisexual men are mediated by subcultural affiliations.[252,258] The links between drug use, gay community engagement, and HIV risk have drawn attention to the phenomenon of chemsex and calls for new harm reduction approaches to prevent increases in HIV transmissions or drug use effects.[20,21]

Isaiah-Green et al. (2006) argue that social connectivity is inevitably linked to chemsex behaviours. Gay and bisexual men who engage in chemsex are consequently at greater risk of HIV infection.[201,260] The sex practices commonly associated with chemsex include condomless anal intercourse, a higher number of sexual partners, and group sex.[15,19,22,25,27,153,261,262]

Use of drugs among gay and bisexual men often play an important role in sex. Specifically, drugs used to enhance sexual pleasure are commonly used in gay party subcultures and sexually adventurous networks.[12,13] Chemsex behaviours have been associated with condomless anal intercourse with casual partners and with incident HIV infection among gay and bisexual men.[22,263-265] Discussions about chemsex, therefore, often frame chemsex drugs as the drivers of 'risky' sex.[12,154,266] However, although the association between chemsex and sexual risk is a foreseeable consequence, the risk itself does not necessarily figure in the motivation for these behaviours.[30,153]

1.19 Knowledge gaps in drug use among gay and bisexual men

To determine the extent to which gay and bisexual men who engage in chemsex remain at risk of HIV, two questions will need to be answered:

1. What are the characteristics of gay and bisexual men who engage in chemsex networks, and what drugs do they use?

2. To what extent do these men engage in behaviours that may represent potential risk for HIV infection?

As such, these two questions form two aims of this research project. To determine the potential risk for HIV transmission among gay and bisexual men who engage in chemsex, the next section reviews the literature on HIV harm reduction among people who use drugs, and harm reduction specific to sexual behaviours among gay and bisexual men.

HIV Harm Reduction

Harm reduction refers to behaviours and policies designed to reduce the negative consequences associated with risk behaviours. All Australian jurisdictions have health promotion policies to reduce the harms associated with drug use.[267-270] Programs include those for demand reduction, and those that seek to reduce harm among those who use drugs. There are also programs that seek to reduce the risk of HIV transmission in the context of drug use. HIV prevention campaigns targeting gay and bisexual men often also address drug use, yet, the prevalence of drug use and HIV infection remain high within gay and bisexual communities.

1.20 Cofactors modifying per-act transmission

The links between drug use and HIV risk have generated considerable research in relation to the phenomenon of chemsex, including concerns about its role in gay communities.[20,21,69] This calls for new harm reduction approaches to prevent increases in HIV transmissions or drug use effects. In this thesis, I seek to identify the characteristics of chemsex networks that represent potential HIV risk particularly in the context of developments in biomedical prevention. For the purpose of this thesis, I refer to the use of antiretroviral medicines to prevent HIV transmission as biomedical prevention, while behavioural prevention includes sex practices that are less risky (i.e.

are lower on the perceived and risk hierarchies described above), such as condom use, negotiated safety, serosorting, and seropositioning.

1.21 Behavioural HIV risk reduction

Throughout the HIV epidemic, gay and bisexual men have developed new harm reduction strategies to protect themselves and their sexual partners from HIV. This section describes behavioural HIV prevention strategies among gay and bisexual men.

1.21.1 Condom use

Described in **section 1.12.2**, condom-protected anal intercourse is a highly effective HIV prevention strategy. However, rates of condom use began to decline before PrEP became more widely available but the decline in condom use has accelerated as PrEP use has increased in recent years.[271] Reasons for non-use of condoms among gay and bisexual men have been ascribed to lack of availability, and the reduction of pleasure.[264,272,273] Condoms have rarely been found to be viewed, or experienced, favourably, other than with regard to the fact that they can reduce the risk of transmission (or pregnancy for heterosexual encounters).[274-276]

1.21.2 Seroadaptive behaviours

Seroadaptive behaviours, including serosorting and seropositioning, are HIV risk reduction strategies used by gay and bisexual men, based on knowledge of oneself and partner HIV status,[277] and offer an alternative to the use of condoms.[278] Serosorting refers to engaging in condomless anal intercourse with a sexual partner based on

concordant HIV status.[278,279] Two variations of serosorting have emerged. In Australia, serosorting usually refers to restricting condomless anal intercourse to partners with concordant HIV status while continuing to engage in other sexual behaviours with discordant HIV partners.[217] However, an alternate variation of serosorting restricts any sexual contact to concordant HIV partners,[280] which may perpetuate stigma towards people living with HIV.

Serosorting

The *HIM Study* investigated the effectiveness of serosorting among casual partners as an HIV harm reduction strategy. Compared to men who did not engage in condomless anal intercourse, men who used serosorting as an HIV harm reduction practice were 3.11 times (95% CI 1.09 – 8.88) more likely to seroconvert, thus serosorting with casual partners might not be effective in HIV prevention.[264] However, men who engaged in serosorting were at lower risk of infection than were men who engaged in condomless anal intercourse without the perceived benefit of serosorting.

Strategic positioning

Strategic positioning, or seropositioning, refers to a harm reduction practice whereby HIV-positive men take the receptive role during condomless anal intercourse, and HIV-negative partners take the insertive role.[281] Men in serodiscordant relationships have commonly adopted this strategy.[4] Results from the *HIM Study* found that strategic positioning did not significantly increase the risk of HIV infection (hazard ratio [HR]: 1.54; 95% CI: 0.45 – 5.26).[264]

Negotiated safety refers to HIV-negative seroconcordant couples agreeing to engage in condomless anal intercourse with each other, while continuing to use condoms or avoid anal intercourse with other sexual partners.[216] From the *HIM Study*, men who used negotiated safety as a harm reduction strategy were not significantly more likely to HIV seroconvert compared with men who did not engage in condomless anal intercourse (HR: 1.67; 95% CI: 0.59 – 4.76; p value: 0.338).[264]

1.22   Biomedical HIV prevention strategies

This section reviews the use of antiretrovirals as an HIV harm reduction strategy among gay and bisexual men. I will review the use of antiretrovirals as treatment among people living with HIV and their application as treatment as prevention (known as TasP), as well as the prophylactic use of antiretrovirals among HIV-negative people (known as PrEP).

1.23   HIV Treatment as Prevention

Among people living with HIV, correct and consistent use of antiretrovirals has been demonstrated to prevent onwards transmission by suppressing viral replication thereby reducing the viral load to undetectable levels.[282] This is referred to as Treatment as Prevention, or Undetectable=Untransmissible (U=U).[283]

Several randomised controlled trials have demonstrated the efficacy of treatment as prevention. Launching recruitment in 2005, the *HIV Prevention Trials Network (HPTN)*

052 study planned to follow-up serodiscordant couples until 2014.[35] However, after 1,763 couples had accrued a combined follow-up of 3,152 couple-years, an interim analysis showed a 96% reduction in HIV transmission among HIV-negative people when the HIV-positive partner immediately started antiretroviral therapy regardless of their CD4 count, compared to delayed treatment. The trial ended with all people living with HIV on the study offered immediate treatment. Cohen et al. (2015) final results report that compared to delayed antiretroviral therapy, early antiretroviral therapy was 93% effective in preventing HIV transmission with no linked seroconversions after a combined 18,540 person-years of follow-up.[36,37]

Homosexual couples comprised only 2% of *HPTN 052* trial participants.[37] Consequently, *HPTN 052* could not provide sufficient evidence for the applicability of these findings to gay and bisexual men. Two observational studies involving gay and bisexual men were conducted to respond to this knowledge gap. Both the European-based study, *Partners of people on ART – a New Evaluation of the Risks (PARTNER),* [38-40] and the Australia, Brazil and Thailand-based *Opposites Attract Study,*[41] reported no phylogenetically-linked HIV infections between gay serodiscordant couples after a combined total of 2,059 couple-years of follow-up. Both studies report that condomless anal intercourse with serodiscordant partners is more likely to occur when the sexual partner living with HIV reports an undetectable viral load.

The studies mentioned above focused on gay and bisexual serodiscordant couples. However, some studies have reported on the application of treatment as prevention as a strategy among casual sexual partners, specifically in the context of relying on undetectable viral loads,[284,285] and viral load sorting.[286,287]

1.24 Prophylactic use of antiretrovirals

Prophylactic use of antiretroviral drugs is beneficial in two circumstances: Following an unanticipated exposure to HIV; or in preparation against anticipated exposure.

1.24.1 Post-exposure prophylaxis (PEP)

Prophylactic use of antiretroviral drugs following an HIV exposure to prevent HIV infection commenced in the mid-1990s, and was the first strategy to use antiretrovirals to prevent HIV infection.[288] Pathogenesis studies suggested there was a 72-hour period after HIV exposure and before the systemic spread of HIV.[289] This suggested an opportunity to prevent infection.[290] Between 2013 and 2017, the prevalence of PEP use among gay and bisexual men has been increasing in Australia, from 4% to 8%,[125,223-226] PEP use has also increased overseas.[291,292] This increase may be attributed to improved knowledge and awareness of PEP among gay and bisexual men. This may also highlight the need for new HIV prevention strategies to capture at risk gay and bisexual men. Despite the availability of other HIV prevention strategies, increases in the prevalence of PEP use indicates the need for new novel harm reduction technologies to ensure suitable strategies are available for different people.

1.24.2 Pre-exposure prophylaxis

The co-formulation of emtricitabine and tenofovir, and its generic formulations when used as PrEP, is highly effective in preventing HIV infection.[42,43] Prophylactic use of antiretrovirals as PrEP among humans has been established in six randomised

controlled trials. While PrEP has also been shown to be effective in preventing HIV in other populations including injecting drug users and heterosexual people,[54-62] I will focus on research regarding gay and bisexual men.

The *Iniciativa Profilaxis Pre-Exposición (iPrEx)* was the first randomised control trial to publish primary results for the use of daily PrEP.[44] Among 2,470 men who have sex with men and 29 transgender women in six countries followed for 3,324 person-years, Grant et al. (2010) reported a 44% (95% CI: 15 – 35) risk reduction of HIV infection among participants in the active drug arm compared to the placebo control arm. Participants self-reported high levels of adherence to daily use of PrEP, but tests of drug concentration in the blood indicated low levels of adherence.[45] In a prespecified case-control analysis, they compared drug concentrations in blood samples among participants who remained HIV-negative and participants who seroconverted. Restricting the analysis to participants with a detectable study drug concentration in the treatment group, the estimated risk reduction increased to 92% (95% CI: 40 – 99) compared to those who had no detectable drug concentration.[44] In a sub-study, Anderson et al. (2012) found that participants with drug concentration that were consistent with taking four or more pills per week was associated with a 96% (95% CI: 90 – 99) risk reduction, and that efficacy increased to 99% (95% CI: 96 – 99) risk reduction with use of seven pills per week.[46] This positive correlation was confirmed by their open-label extension (OLE) of the study, *iPrEX-OLE*, which followed 1225 HIV-negative men who have sex with men and transgender women for an additional 72 weeks.[47]

The *Pre-exposure Option for reducing HIV in the UK: immediate or Deferred (PROUD)* study was an open-label, randomised immediate-deferred control trail for

PrEP among 544 gay and bisexual men at high risk of HIV conducted in the United Kingdom.[48] An interim analysis after 504 patient-years of follow-up had been accrued found an 86% (95% CI: 64 – 96) reduction in risk of HIV in the modified intention-to-treat analysis. This analysis resulted in the deferred arm of *PROUD* being stopped, with all participants in this arm offered PrEP. These results strengthened the evidence for PrEP use and effective HIV prevention among gay and bisexual men.

The *Intervention Prophylactique pour Et avec les Gays (IPERGAY)* was a randomised controlled trial comparing PrEP to a placebo conducted in France and Canada. It trialled a peri-coital dosing regimen (taking two pills 2-24 hours before sexual contact, and one pill every 24 hours until 48 hours had passed after the last sexual contact).[49,50] This strategy is often referred to as on-demand PrEP. Molina et al. (2015) reported an 86% (95% CI: 40 – 98) risk reduction in 431 person-years of follow-up.[49] However, interpretation of these findings should be done with caution. *IPERGAY* recruited a small number of men who reported infrequent sex. Due to the frequency of exposure, the median number of pills taken per month during the study was 15 pills, which is equivalent to four pills per week. This approximately equates to a daily pill schedule with similar coverage to four pills per week. Nonetheless, on-demand PrEP has been shown to be equally as effective as daily dosing in men who have sex with men, with their open label extensions and subsequent analyses reporting a revised risk reduction estimate closer to 97% (95% CI: 81 – 100).[51]

The *Bangkok Tenofovir* study was a randomised controlled trial investigating the efficacy of PrEP among people who inject drugs.[52] Choopanya et al. (2013) reported a 49% (95% CI: 10 – 72) risk reduction of HIV in their modified intention-to-treat analysis in 9,665 person-years of follow-up. In a separate analysis, they reported an

84% (95% CI: 40 – 98) HIV risk reduction when restricting the analysis to participants who self-reported adherence at greater than or equal to 97.5%[53]

1.25   Treatment as Prevention in Australia

The *Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine* recommend newly diagnosed people living with HIV initiate antiretroviral therapy, irrespective of CD4 count.[293] This recommendation is consistent with the *United States Department of Health and Human Services*, who changed their own recommendations following the reporting of studies showing the benefits for initiating treatment early.[294]

Treatment coverage among people living with HIV is high and has been increasing over time.[7] As demonstrated in **section 2**, of the estimated 27,545 people living with HIV in Australia in 2017, 89% were diagnosed, 95% of whom were retained in care. Most (87%) of those in care were receiving antiretroviral therapy, of whom 95% had a suppressed viral load (Figure 1.1). The *Gay Community Periodic Survey* shows that most (91.8%) HIV-positive gay men are on treatment or have an undetectable viral load in 2017.[271] In Australia, there has been a rapid and dramatic reduction in the time to treatment post-diagnosis with 33% of diagnosed individuals initiating antiretroviral therapy within two weeks post diagnoses, and 64% within four weeks (Figure 1.6).[295]

Figure 1.6   Time to antiretroviral therapy for New South Wales, Australia residents newly diagnosed with HIV in January 2013 to June 2018
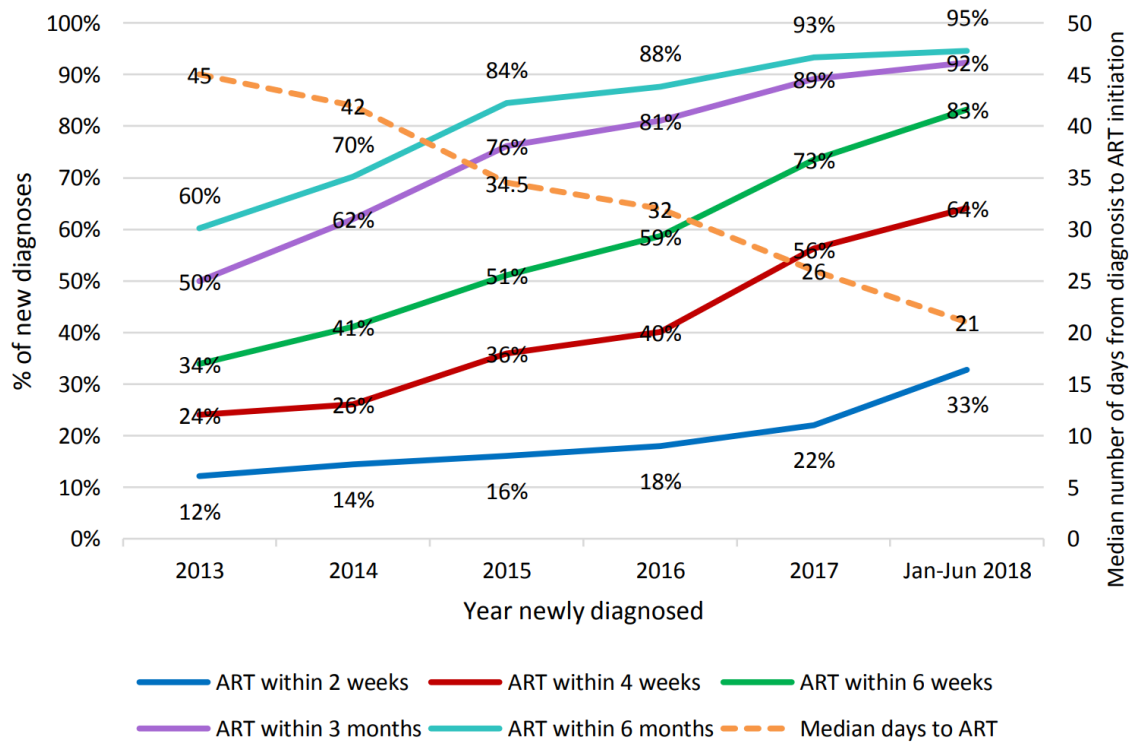
ART: antiretroviral therapy.

Source: NSW Health. NSW HIV Strategy 2016-2020. Quarter 4 & Annual Report 2018. Data report. New South Wales, Australia 2018.[295]

Permission obtained from the Kirby Institute, UNSW Sydney ©

1.26   PrEP in Australia

The first *Australian PrEP Guidelines* were first published in 2017.[66,67] The *HIM Study* provided the basis for formulating the criteria for identifying gay and bisexual men at high risk of HIV, and therefore identifying those eligible to access PrEP.[264] For gay and bisexual men to be considered at high risk of HIV infection, and therefore eligible to access PrEP, they would need to report at least one episode of any criteria listed in Table 1.3. Gay and bisexual men who meet any of these criteria, herein described as "PrEP-eligible," are considered at high risk of HIV seroconversion.[66,67,264] The

guidelines were based on data that were collected between 2001 and 2007, so not all

relevant or commonly used drugs had been considered for analysis.

Table 1.3 Practices and conditions associated with high HIV incidence among men who have sex with men

Findings from the HIM Study Risk factor (Previous six months)	Associated HIV incidence	Australian PrEP Guidelines Recommend prescribing daily PrEP (Previous three months)
Regular sexual partner of a man with HIV infection with whom condoms were not consistently used (HIV-positive partner is not on treatment and/or has detectable viral load)	5.36 per 100 PY 95% CI (2.78-10.25)	A regular sexual partner of an HIV-infected men (not on treatment and/or detectable viral load) with whom condoms were not consistently used
At least one episode of condomless anal intercourse with any casual male partner with HIV infection or a male partner of unknown HIV status	2.31 per 100 PY 95% CI (1.48-3.63)	At least one episode of receptive condomless anal intercourse with any casual HIV-infected male partner or a male partner of unknown HIV status
Rectal gonorrhoea diagnosis	7.01 per 100 PY 95% CI (2.26-21.74)	Rectal gonorrhoea, rectal chlamydia or infectious syphilis diagnosis
Rectal chlamydia diagnosis	3.57 per 100 PY 95% CI (1.34-9.52)	
Methamphetamine use	1.89 per 100 PY 95% CI (1.25-2.84)	Methamphetamine use, which may increase the risk of HIV acquisition

PY: person years; CI: confidence interval.

Source: Wright E, Grulich A, Roy K, Boyd M, Cornelisse V, Russell D, O'Donnell D, Whittaker B, Crooks L, Zablotska I. Australasian society for HIV, viral hepatitis and sexual health medicine HIV pre-exposure prophylaxis: clinical guidelines. Update April 2018. Journal of virus eradication 2018; 4(2): 143.[67]

A recent analysis estimated the number of potential PrEP users among men who have sex with men in Australia.[296] Using conservative estimates by including men who reported more than 10 sexual partners in the previous six months, the proportion of gay and bisexual men in Australia who meet the criteria to access PrEP was 9.7% (95% CI: 9.0% – 10.4%). Receptive condomless anal intercourse with casual partners was the most commonly met criterion estimated at 6.1% (95% CI: 5.6% - 6.7%). Monthly methamphetamine use was estimated at 1.4% (95% CI: 1.1% - 1.7%). These estimates, however, substantially increase when the frequency of behaviours is considered.[296] Using a less conservative estimate by including men who reported any sexual intercourse with a man in the previous 12 months, the estimate for eligibility to access PrEP increases to 28.4% (95% CI: 27.4% – 29.5%). The proportion for receptive condomless anal intercourse increases to 15.5% (95% CI: 14.6% – 16.4%). For any methamphetamine use in the previous six months, the estimates increase to 9.4% (95% CI: 8.7% – 10.1%).

Differences in these estimates questions the sensitivity of the *Australian PrEP Guidelines*. Specifically, individual's perception of their own level of risk in relation to the frequency of engaging in high-risk behaviours during a prespecified timeframe, and how that is conveyed to prescribing clinicians. Although engaging in HIV risk behaviours less frequently decreases the probability of infection, a single HIV risk episode also has the potential for HIV infection.

1.26.1　Access to PrEP in Australia

Australia's *National HIV Strategy* prioritises gay and bisexual men for HIV prevention.[91] However, Australian regulatory requirements meant that the Australian government would not subsidise PrEP until the appropriate approval processes were completed.[297,298] As an interim measure, and to provide supporting evidence for the approval processes, most state governments funded large-scale PrEP implementation trials. Since 2014, state-funded programs have provided PrEP to gay and bisexual men at high risk of HIV, as determined by the *Australian PrEP Guidelines*.[66,67] By the end of 2017, almost 16,000 HIV negative people were accessing PrEP through state-funded PrEP trials and implementation studies.[7]

HIV prevention strategies have not always been consistent across Australian jurisdictions. These inconsistencies can be seen through HIV-negative men's access to PrEP. The first PrEP implementation trial in Australia was in the state of Victoria. *VicPrEP* commenced in June 2014 and enrolled 115 participants.[299,300] This was followed by a demonstration project in November 2014 in New South Wales, *PrELUDE*, which had 327 participants.[301] In Queensland, *QPrEP* enrolled 50 participants starting September 2015.[302] In December 2015, the New South Wales state government funded a large-scale implementation trial for high-risk individuals. The *Expanded PrEP Implementation in Communities in New South Wales PrEP Implementation in Communities in New South Wales (EPIC-NSW)*, enrolled over 4,000 participants in the first nine months.[92] By mid-2018, EPIC-NSW had recruited nearly 10,000 participants.[303] In July 2016, Victoria ran an implementation trial, *PrEPX*,[297] with 2,300 participants, and in September 2016, Queensland expanded *QPrEP* to 2,000 participants (Figure 1.7).[302]

Figure 1.7   Cumulative number of gay men enrolled in Australian PrEP
implementation programs 2016 – 2017, by month
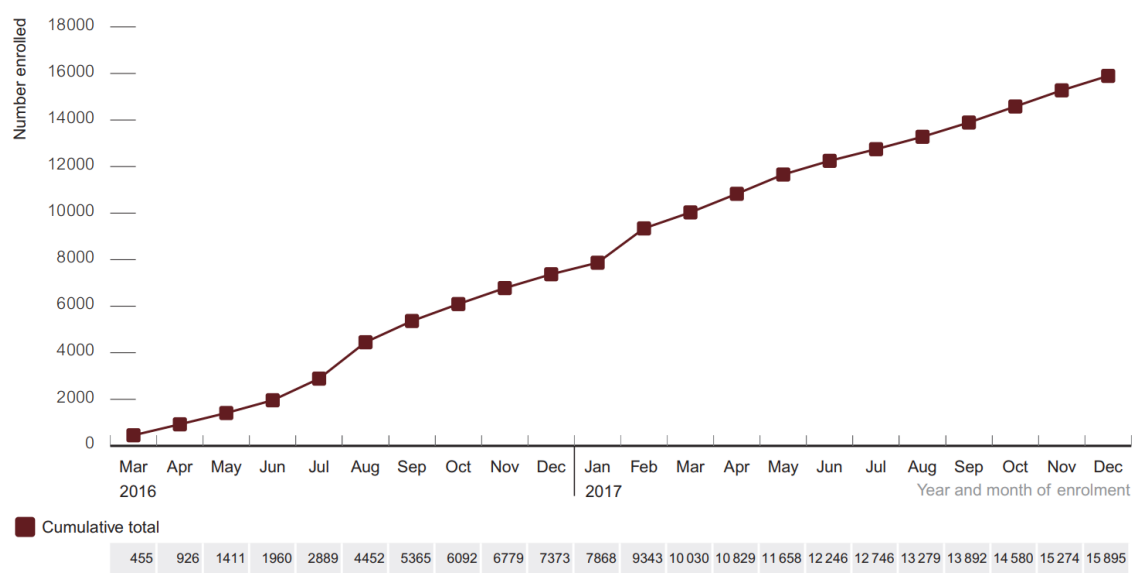
Source: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney 2018.[7]

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By December 2017, there was an estimated 31,502 gay and bisexual men eligible for PrEP.[304] Among those, 15,895 were accessing it through demonstration projects, and some through personal importation.[7] To access PrEP through these trials, gay and bisexual men had to meet the *Australian PrEP Guidelines* and so may have been motivated to report such behaviours.[66,67] With that, it cannot be certain to what extent their responses for entry to the trials were accurate.

PrEP was approved for its preventative use in Australia by the *Australian Therapeutic Goods Administration* in May 2016.[305] PrEP was subsequently approved for public subsidy by the *Pharmaceutical Benefits Scheme* in Australia in 2018, ensuring that individuals at high risk of HIV now have affordable access.[306,307] Australian behavioural surveillance found that PrEP use increased from 2% to 24% among HIV-negative gay

and bisexual men between 2013 and 2017.[271] During the same period, among men who were HIV negative or untested and not on PrEP, the proportion who reported having engaged in receptive condomless anal intercourse with casual partners remained steady at 19.6%. Alongside other population level HIV prevention strategies,[39,41] there was a 23% rapid decline in HIV infections in Australia.[88-90]

1.27 Changes in HIV prevention strategies in response to available technologies

Surveys of sexual behaviour among gay and bisexual men in Australia suggest that they have adjusted their HIV prevention strategies throughout the epidemic. Using available data, I describe changes in behavioural harm reduction strategies over time among gay and bisexual men in Australia.

Condoms were first promoted for HIV prevention among gay and bisexual men in Australia and elsewhere during the mid-1980s,[308,309] and were rapidly adopted by gay and bisexual men during the 1980s, particularly with casual partners.[216,310] Following the widespread recommendations for condom use among gay and bisexual men, there was a decrease in the prevalence of condomless anal intercourse with casual partners between 1986 to 1990 with prevalence remaining fairly stable through the 1990s.[308] Use of condoms halted the upward trend in new infections in Australia. Although HIV infections in Australia stopped increasing in the mid-1980s, there was no further decline. However, rates of new infections remained stable despite campaigns for consistent condom use. Feachem (1995) report to the Commonwealth Government of Australia suggested that increases in condom-protected anal intercourse, and decreases

in condomless anal intercourse may partly explain the decline in incidence of HIV among gay and bisexual men at that time.[308]

A systematic review looking at prevalence of condom use between 1990 and 2013 found that condom use among gay and bisexual men who engage anal intercourse with regular or casual partners had decreased in high income countries.[311] Australian data do not show the same trends across the same time period: Rates of condom use among gay and bisexual men in Australia remained stable until the late 1990s, but during the late 1990s, the prevalence of condomless anal intercourse with casual partners increased. This increase was subsequently followed by increases in new infections.[312] The rates of condomless anal intercourse remained stable, suggesting there was no further decline in condom use.[313-315]

The differences observed in Australian data may not be solely due to differences in the HIV epidemic across regions but may also reflect differences in how regular partners have been distinguished from casual partners. Australian data showed more condomless anal intercourse with regular partners than casual partners due to negotiated safety and was quite stable over time for regular partners.[316,317] Rates of condom use began to decline before PrEP became more widely available but the decline in condom use has accelerated as PrEP use has increased in recent years.[271]

The response to HIV prevention in the context of antiretrovirals as treatment or prevention may reflect similar patterns. Data collected from the *Gay Community Periodic Survey* between 2000 and 2015 was used to project the anticipated effects of PrEP on sexual practices with casual male partners among gay and bisexual men in Australia.[186] Estimating a 15% increase in the prevalence of PrEP use by 2020, two scenarios were depicted (Figure 1.8). The first scenario represents the ideal situation,

with the increase in PrEP use reducing the proportion of gay and bisexual men engaging in condomless anal intercourse with causal partners. The second scenario depicts an opposite trend, with the increase in PrEP use reducing the proportion of gay and bisexual men who report consistent condom use with casual partners. To achieve the ideal scenario of PrEP use reducing the proportion of gay and bisexual men who engage in condomless anal intercourse with causal partners, interventions targeting these high-risk men are needed.

Figure 1.8   Projected scenarios depicting effects of PrEP use on sexual practices with casual male partners, 2000 - 2020
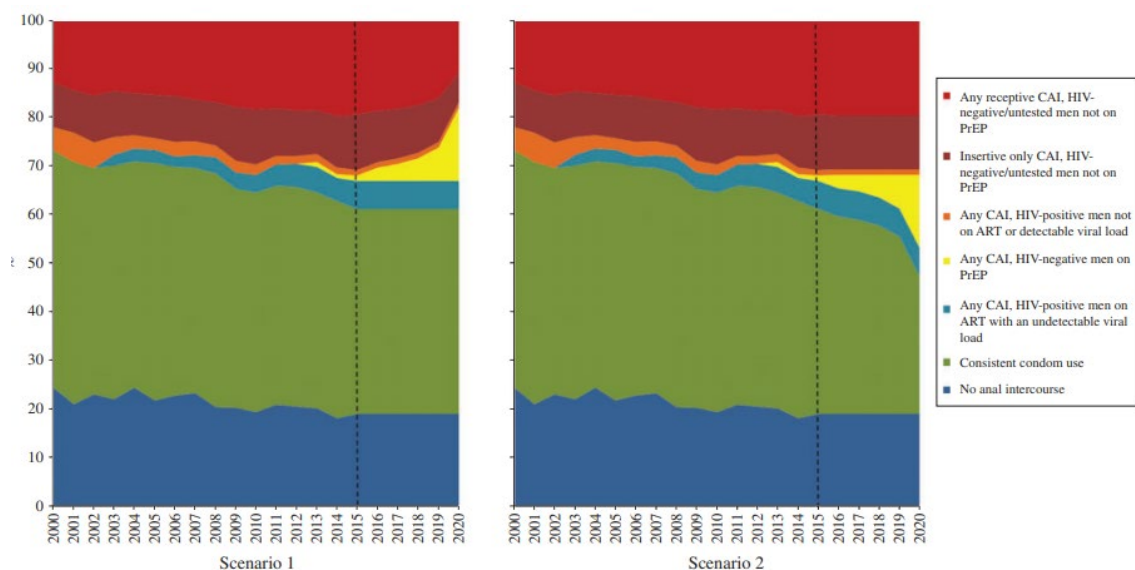
CAI: condomless anal intercourse; ART: Antiretroviral therapy; PrEP: Pre-exposure prophylaxis

Source: Holt M, Lea T, Mao L, Zablotska I, Lee E, de Wit JBF, Prestage G. Adapting behavioural surveillance to antiretroviral-based HIV prevention: reviewing and anticipating trends in the Australian Gay Community Periodic Surveys. Sexual Health 2017; 14(1): 72-9.[186]

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1.28   HIV harm reduction among people who use drugs

Harm reduction has been a principle of Australian governments' approach to drug use for several decades. Since 1985, the Australian *National Drug Strategy* has provided an overarching framework for a consistent and coordinated approach to dealing with licit and illicit drug use in Australia. The *National Drug Strategy* aims for a balanced approach across three pillars of harm minimisation.[318] These are: *Demand Reduction*, preventing or delaying the initiation, reducing the misuse, and supporting recovery; *Supply Reduction*, preventing or reducing the production of illicit drugs and controlling and regulating the availability of licit drugs; and *Harm Reduction*, reducing adverse health. Gay and bisexual men are identified as a priority population.[318]

1.28.1   Needle and syringe programs

Needle and syringe programs can substantially reduce the risk of HIV infection by providing people who inject drugs free access to sterile needs and syringes, and facilities for safe disposal of used equipment.[319] Needle and syringe programs were introduced in Australia in 1987.[320] Receptive syringe sharing decreased from 31% in 1995 to 16% in 2014.[321] Low rates of HIV transmission among people who inject drugs in Australia are testament to the success of this strategy. In 2017, 2.1% of people who inject drugs and attend needle and syringe programs were living with HIV; just 1% if gay and bisexual men are excluded.[7] The effectiveness of these programs was evaluated in Australia. Between 2000 and 2009, approximately 32,050 new HIV infections had been prevented as a direct result of the Needle and Syringe Programs.[322] The program resulted in health care cost savings of over $4.00 AUD for every dollar spent.[322]

1.29 Knowledge gaps in HIV harm reduction among gay and bisexual men who engage in chemsex

The relationship between drug use and HIV sexual risk behaviours in the context of PrEP has not yet been explored. To determine the extent to which men who engage in chemsex remain at risk of HIV in the context of PrEP, two further questions will need to be addressed:

1. What is the incidence of PrEP uptake among gay and bisexual men, particularly those who engage in chemsex?

2. What factors are associated with the use or non-use of PrEP as a HIV harm reduction strategy, particularly in the context of chemsex?

These questions form two further aims of this research project and will be discussed in **chapters 2** through **7**.

The potential for change

PrEP as a harm reduction strategy has the potential to change the trajectory of the HIV epidemic among gay and bisexual men. In this section, I summarise the current knowledge gaps regarding PrEP use among gay and bisexual men who engage in chemsex and present the objectives and aims for my PhD research that has been designed to address these knowledge gaps.

1.30   Normative values

Aspects of drug using behaviours among gay and bisexual men, including in relation to minimising harm, have similarly been found to reflect normative values within specific gay community subcultures.[114,218,323] Gay and bisexual men have a shared understanding of risk and pleasure in relation to drug use and sexual behaviour that is likely to underpin their own drug using behaviour. In relation to HIV harm reduction practices, including condom use, social engagement with other gay men has been indicative of greater knowledge of and access to those prevention methods.[216,217] Normative values within specific gay community subcultures affect sexual behaviour and drug use practices among gay and bisexual men, particularly in relation to harm reduction practices.[218] This may also be true within chemsex networks who tend to be highly socially engaged with gay community and so are possibly also aware of their risks.[324,325]

Normative values may therefore also be central to the adoption of new HIV prevention strategies, such as PrEP among gay and bisexual men.[250,252-256]

The influence of social, community, and interpersonal factors on the initiation of PrEP remains unclear. How engagement in particular sexual and social networks might influence the commencement or changes over time in harm reduction strategies, with the advent of PrEP, needs further investigation.

1.31   The specific role of drug use in HIV infection

The *HIM Study* showed that individual gay and bisexual men's use of drugs has changed over time, but overall rates remained very high.[220] As PrEP changes what sexual behaviours are considered a risk for HIV transmission,[287] patterns of drug use and their associations with HIV risk may also have changed. When considering the role of drugs, particularly among gay and bisexual men, HIV research has tended to focus on the interconnections between drug use, sexual risk behaviour, and subsequent HIV infection. The specific role of drug use in HIV sexual risk behaviour within chemsex networks in the context of PrEP availability remains unclear. In my PhD research, I explore the associations between drug use and HIV infection in the context of PrEP.

1.32   Drug use and condomless anal intercourse

Current behavioural HIV prevention strategies have not specifically addressed gay and bisexual men who engage in chemsex. Previous associations between use of illicit drugs and condomless anal intercourse with casual partners have not been tested in the context of PrEP. Thus, it is unclear whether the protection of PrEP has any impact on

condomless anal intercourse with casual partners among gay and bisexual men who engage in chemsex.

1.33   Knowledge gaps

No recent national or international data on licit or illicit drug use and associated harms in the context of PrEP among gay and bisexual men exist outside clinical settings. At the time of the inception of this research project, there were few quantitative data to indicate the prevalence of PrEP use among chemsex networks, or whether those who participate in chemsex are utilising biomedical HIV prevention strategies.[326,327] Additionally, no community-based cohort studies had examined PrEP uptake in individual gay and bisexual men in Australia, or assessed uptake against *Australian PrEP Guidelines*. Patterns of sexual behaviour have changed with increasing use of PrEP,[271] but less is known about their impact on drug use and the practice of chemsex.

1.34   Research objective and aims

Gay and bisexual men who engage in chemsex have traditionally been considered one of the highest risk groups for HIV infection. The introduction of PrEP has the potential to disrupt the associations between illicit drug use and subsequent HIV infection within chemsex networks. This research project focuses on the contexts in which gay and bisexual men use licit and illicit drugs, the motivators for their use, and the role of new biomedical HIV harm reduction strategies.

The objective of this thesis is to determine the extent to which gay and bisexual men who engage in chemsex remain at risk in the context of biomedical prevention, and

what factors are associated with ongoing risk behaviours. This objective will be achieved by doing the following:

1. Set up a national prospective observational study of licit and illicit drug use among gay and bisexual men.

2. Describe the characteristics of Australian gay and bisexual men who engage in chemsex and the types of drugs used.

3. Describe the extent to which men who engage in chemsex also engage in behaviours that may represent potential HIV risk.

4. Measure the incidence of PrEP uptake among gay and bisexual men and describe uptake and non-uptake of PrEP among men who engage in chemsex.

5. Identify factors associated with use of PrEP as a harm reduction strategy.

1.35   Thesis outline

This thesis is presented as a series of publications. Following this chapter, six results chapters were used to address the thesis aims. **Chapters 2** through **7** have been published in international peer-reviewed journals. Before each chapter, I provide a brief summary to provide a context for the chapter. Following each chapter, I provide a brief summary of the key findings as they relate to the aims of this thesis. **Chapter 8** concludes the thesis by highlighting the implications of this research.

Published papers are presented in the formats in which they appear in each journal. Spelling, specific terms, referencing style, and acronyms used reflect the preference of the journal. Permission for these works to be included in this thesis was granted by the co-authors for each manuscript.

Modernising Data Collection

Details on the methodology and recruitment used to address my research aims are described in detail in **chapter 2**. In this section, I describe my role in the formation and management of the study which provided the data to address my thesis aims. I also discuss the formation of a unique automated cohort management system that I designed specifically for this research project and I describe its expansion as a new research tool that is now available for other research projects.

1.36   Collecting the right data

In 2014, I started my PhD research at the Kirby Institute, UNSW Sydney under the supervision of Associate Professor Garrett Prestage, and Dr Fengyi (Jeff) Jin. The project was funded by the Australian Research Council to investigate drug using behaviours and beliefs, and associated harms, among gay and bisexual men, known as the *Following Lives Undergoing Change (Flux) Study*. I was responsible for establishing and maintaining the *Flux Study*, which in turn, would provide the data to address my own research aims. *Flux* would collect sensitive data about illicit drug use, so participants' identity and confidentiality would need to be strictly maintained. With limited resources for staff support, time needed to maintain the study while working on my thesis needed to be considered.

1.36.1   Considering study designs

Online platforms are increasingly being used for research methodologies.[328] Benefits of online data collection include user-friendliness and high-quality data integrity. Specific to my PhD research objectives, online platforms would facilitate expanded geographic coverage in a geographically dispersed country, rather than obtaining a sample restricted to major cities where drug using behaviours are often clustered.[271]

Cross-sectional and repeated cross-sectional designs can be reasonably cost-effective, allow anonymous participation, and measure changes in prevalence of drug use, or other relevant behaviours, over time.[329] However, a cross-sectional design cannot measure incidence or track changes in individual behaviours. Cohort studies can provide the necessary data to address both research questions. However, cohort studies usually involve high costs to maintain and require a substantial commitment of research staff time. Retrospective cohort studies were considered, but there are no large databases that have routinely collected illicit drug use data, nor do they usually record sexuality.

The appropriate design to address the research objectives was a prospective observational study. However, feasibility of such a design was problematic due to limited funds and time required to maintain such studies. Adapting innovative modern technologies to cohort studies could overcome the resource limitations by allowing for automated data management.

Original power calculations for the *Flux Study* determined a minimum of 1440 gay and bisexual men with an average follow-up of 1.5 years were needed to provide sufficient power to measure the incidence of illicit drug use (discussed in detail in **chapter 2**).

Moreover, to capture the contexts in which these changes in behaviours occurred, the questionnaire could not be a simple, brief survey that collected limited information. Rather, it would need to capture detailed behaviours concerning multiple facets of gay and bisexual men's lives. Building from the *HIM Study*, a 300-item questionnaire was developed, with questions about HIV and STI testing behaviours, sexual behaviours, mental health, subcultural affiliation, licit and illicit drug use, and attitudes and opinions. On average, it would take one hour to complete each survey.

To address the project aims, the study needed to systematically follow-up individual participant involvement over 1.5 years, at six-monthly intervals. More specifically, I needed to track each participant's changes in behaviours and ensure the follow-ups were conterminous. This would allow estimates of prevalence and incidence of licit and illicit drug use, understand the context in which drugs were used, determine the patterns and predictors for changes in behaviours, and observe the differences in HIV harm reduction strategies in the context of licit and illicit drug use.

1.37 Modernising research methodologies

With no automated system available for cohort management, and drawing on my background in software engineering, I developed an automated cohort management system specifically designed to maintain large scale prospective observational studies of the kind that was envisaged. This system has been named the *Follow-up Automated Management eSystem* (*FAME*). Originally named the *Flux Automated Management eSystem*, the system was renamed as this methodology has since been adapted for use in other research projects, nationally and internationally.

I specifically designed *FAME* to automatically maintain large-scale prospective observational studies.[330] *FAME* enables cost effective management of research studies and ensures a simple, straightforward experience for participants, while protecting participant confidentiality and data integrity, and encrypting participant data.

1.37.1   Automated cohort maintenance

FAME automatically allowed participants to enrol into the study, sends copies of participants' consent forms, and managed cohort retention. All communications with participants are automatically generated through the *FAME* system based on their deidentified unique study identifier, containing a unique link to the participants' individually tailored questionnaire. These communications can be triggered by specific individualised factors, such as failure to complete a survey, or by the structured system that applies to the entire cohort. For example, *FAME* can automatically send notifications every six months to invite participants a new survey, or by some other pre-determined intervals depending on the specific condition established by the user.

Participants click on the link contained in their email, redirecting them to their own questionnaire and automatically recording their unique study identifier, thereby removing the possibility of human error in linking data via their unique study identifier, and further protecting confidentiality (Figure 2.2).

1.37.2   Generating unique data

My PhD research aims were to track individual changes in behaviours over time, and report on the incidence of licit and illicit drug use. *FAME* provides the opportunity to

track and identify the behaviours that have changed in the participants' life, as well as collecting data that may be related to these changes. As such, each follow-up questionnaire was executed based on each participant's personal history, rather than a generic form, ensuring that each questionnaire was individually tailored to reflect each participants' own circumstances.

The process was designed to enable maximum automation and digital management of the study to ensure a simple, accurate, and straightforward experience for recruiting participants. The development of *FAME* allowed me to successfully implement my PhD project, building Australia's first online prospective observational study of licit and illicit drug use among gay and bisexual men. At the time of writing, and to the best of my knowledge, it is also the only extant study of this type anywhere in the world.

1.38 Expansion into other studies

FAME was originally designed to assist me in collecting data and maintaining a large prospective observational study while concurrently undertaking my PhD research. I had no intention to expand this system beyond this use. After the demonstrated success in automatically maintaining the *Flux Study*, *FAME* began to receive recognition within the research program in which I was based. In January 2016, I was seconded to adapt *FAME* for use in the establishment of a large PrEP implementation study, the *Expanded HIV pre-exposure prophylaxis (PrEP) implementation in communities in New South Wales, Australia* (*EPIC-NSW*) *Study*.[298] Some months later, I was also asked to use the *FAME* system for the development of another PrEP implementation trial, the *Pre-exposure prophylaxis for HIV Implementation Trial in Western Australia, Australia* (*PrEPIT-WA*).[331]

FAME is adaptable to a large variety of research questions. To cater for the large-scale rapid rollout of these PrEP implementation studies across multiple clinical sites, I designed and implemented a study specific adaption of *FAME*. This included the addition of an automated behavioural risk assessment which corresponded to the *Australian PrEP Guidelines*,[66,67] a clinician's database portal which automatically assessed biological eligibility based on test results, and automatically consolidated data collection between risk assessment, biological eligibility, and behavioural surveillance. *FAME* successfully and seamlessly enrolled over 10,000 between *EPIC-NSW* and *PrEPIT-WA* (Figure 1.9).[295]

Figure 1.9   Enrolment of participants in EPIC-NSW, by study week, from 1 March 2016 to 30 April 2018
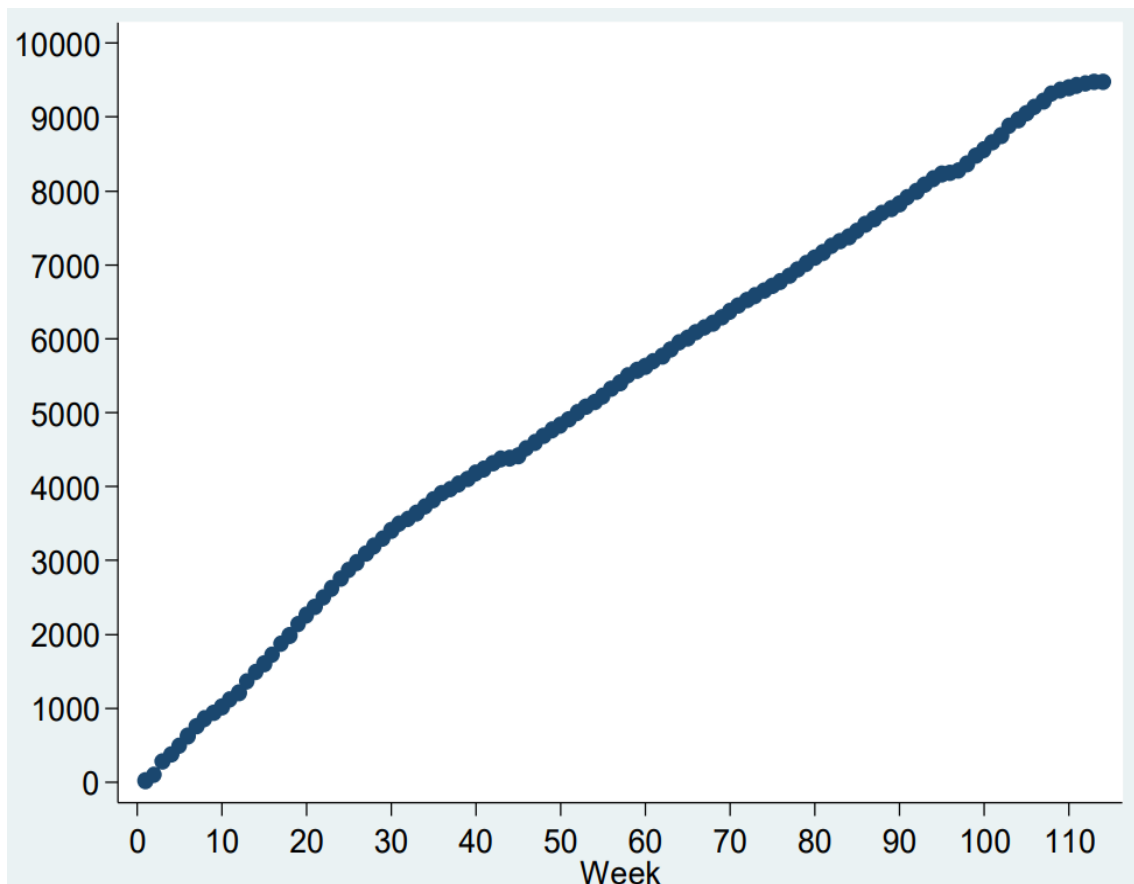
Source: NSW Health. NSW HIV Strategy 2016-2020. Quarter 4 & Annual Report 2018. Data report. New South Wales, Australia 2016.[295]

1.39   Facilitating cross-institution international collaboration

This sophisticated and novel methodology was used as the tool to collect data to answer a series of complementary research questions proposed in this thesis, and for the *Flux Study* more broadly. Originally designed to be study specific, *FAME* relieves administration burden, thereby enhancing researcher capacity to focus on other work, making it highly attractive to potential research collaborators, who have since adapted its use, both nationally and internationally. To date, *FAME* has been used by three Australian cohort studies, two PrEP implementation trials, and one clinical demonstration project looking at the use of doxycycline as STI PrEP (known as the *Syphilaxis Study*).

The demonstrable success of the *Flux Study* by use of *FAME* resulted in researchers at the Department of Social and Community Health, School of Population Health, University of Auckland, New Zealand, replicating the *Flux Study* for the New Zealand population (known as *Flux NZ*). *FAME* currently maintains the *Flux NZ* cohort automatically and remotely. Moreover, researchers at the *National Drug and Alcohol Research Centre*, (*NDARC*), *UNSW Sydney* are currently preparing to replicate the *Flux Study* and use *FAME* to investigate licit and illicit drug use among lesbian, bisexual, and queer women in Australia. Finally, *FAME* has is currently being used to set up a national cohort study investigating the mental health of gender and sexuality diverse youth. Plans are underway by *ACON* (the largest gender and sexuality diverse health organisation in Australia) to use the *FAME* system to evaluate the long-term impact of peer-led education and support programs among gay and bisexual men who engage in

chemsex, linking these data to the *Flux Study*. *FAME* permits cross-institutional, interdisciplinary, multi-site collaboration, and data sharing.

Section Nine

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Chapter Two

The current state of drug use

2.1 Measuring baseline prevalence of licit and illicit drug use among gay and bisexual men in Australia

2.1.1 Publication details

Hammoud MA, Jin F, Degenhardt L, Lea T, Maher L, Grierson J, Mackie B, Pastorelli M, Batrouney C, Bath N, Bradley J, Prestage G. Following Lives Undergoing Change (Flux) Study: Implementation and baseline prevalence of drug use in an online cohort study of gay and bisexual men in Australia. International Journal of Drug Policy 2017; 41: 41-50.

2.1.2 Thesis aims related to this chapter

Thesis aim 1: Set up a national prospective observational study of licit and illicit drug use among gay and bisexual men.

2.1.3   Chapter two in context

Addressing **thesis aim 1**, this chapter describes how I established the *Flux Study*, a prospective observational study of licit and illicit drug use among gay and bisexual men in Australia. This study aimed to identify individual and contextual factors associated with drug use, including changes in patterns of drug use over time. In turn, this study provided the data for my research project. To run a large-scale cohort study with limited funds, I personally designed, developed, and implemented *FAME*, a fully automated cohort management system. I describe the design and implementation of *FAME* to capture sensitive data in a geographically disperse country, and how I used it to establish a national prospective observation study of licit and illicit drug use among gay and bisexual men.

I intended to capture data among gay and bisexual men with varying degrees of drug use. This included men who use and men who do not use drugs, to provide a more detailed understanding of licit and illicit drug use among gay and bisexual men in Australia. **Chapter 2** describes the prevalence of licit and illicit drug use at baseline. Guided by the results from the *HIM Study*,[1] I paid particular attention to the concurrent use of crystal methamphetamine and the recreational use of erectile dysfunction medications as they were strong predictors of HIV infection, independent of sexual risk behaviour.[†]

[†] List of references for citations provided in chapter contexts and summaries are provided on page 237
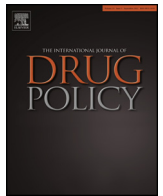
Research paper

Following Lives Undergoing Change (Flux) study: Implementation and baseline prevalence of drug use in an online cohort study of gay and bisexual men in Australia

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ARTICLE INFO

ABSTRACT

Background: Drug use among gay and bisexual men (GBM) is higher than most populations. The use of crystal methamphetamine, erectile dysfunction medication (EDM), and amyl nitrite have been associated with sexual risk behaviour and HIV infection among gay and bisexual men (GBM).

Objective: This paper describes an online prospective observational study of licit and illicit drug use among GBM and explores baseline prevalence of drug use in this sample. Capturing these data poses challenges as participants are required to disclose potentially illegal behaviours in a geographically dispersed country. To address this issue, an entirely online and study specific methodology was chosen.

Methods: Men living in Australia, aged 16.5 years of age or older, who identified as homosexual or bisexual or had sex with at least one man in the preceding 12 months were eligible to enrol.

Results: Between September 2014 and July 2015, a total of 2250 participants completed the baseline questionnaire, of whom, 1710 (76.0%) consented to six-monthly follow-up. The majority (65.7%) were recruited through Facebook targeted advertising. At baseline, over half (50.5%) the men reported the use of any illicit drug in the previous six months, and 28.0% had used party drugs. In the six months prior to enrolment, 12.0% had used crystal methamphetamine, 21.8% had used EDM, and 32.1% had used amyl nitrite. Among the 1710 men enrolled into the cohort, 790 men had used none of these drugs.

Conclusion: Ease of entry and minimal research burden on participants helped ensure successful recruitment into this online cohort study. Study outcomes will include the initiation and cessation of drug use, associated risk behaviours, and health consequences, over time. Results will provide insights into the role gay community plays in patterns of drug use among GBM.

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Background

The prevalence of licit and illicit drug use among gay and bisexual men (GBM) is higher than in other population groups (Bolding, Hart, Sherr, & Elford, 2006; Cochran, Ackerman, Mays, & Ross, 2004; Hickson, Bonell, Weatherburn, & Reid, 2010; Lea et al., 2013b; Newcomb, Ryan, Greene, Garofalo, & Mustanski, 2014; Roxburgh, Lea, De Wit, & Degenhardt, 2015). In Australia, more than half of GBM reported recent (previous six months) illicit drug use (Lea et al., 2013b). One in twenty (5.6%) reported recent injection drug use (Lea et al., 2013a). Few studies have reported on incidence or risk factors for, initiation and cessation of, or changes in, drug use over time, or on the harmful outcomes of such use, among Australian GBM.

Associations between drug use and sexual risk behaviour among GBM

Condomless anal intercourse (CAI) with casual male partners is the primary risk factor for HIV infection among GBM (Elford, 2006; Jin et al., 2009; Zablotska, Prestage, Middleton, Wilson, & Grulich, 2010). Drug use, particularly when used to enhance sexual pleasures has been associated with CAI with casual partners and with incident HIV infection among GBM (Bolding et al., 2006; Buchacz et al., 2005; DiFrancesico, Ostrow, & Chmiel, 1996; Koblin et al., 2003; McCabe, Hughes, Bostwick, West, & Boyd, 2009; Prestage, 2009; Prestage, Grierson, Bradley, Hurley, & Hudson, 2009a; Rusch, Lampinen, Schilder, & Hogg, 2004; Solomon, Kiang, Halkitis, Moeller, & Pappas, 2010). Specifically, crystal methamphetamine, erectile dysfunction medication (EDM), and amyl nitrite, either used separately or in combination, have been most strongly implicated in sexual risk behaviours and HIV infection (Fisher, Reynolds, & Napper, 2010; Prestage, Jin, Kippaz, Zablotska, Imrie, & Grulich, 2009b). Previous research suggests that the use of these drugs increases the possibility of sexual risk behaviours and HIV infection (Fisher et al., 2010; Prestage et al., 2009b).

Most studies to date have focused on drug use and HIV risk behaviours among GBM as a simple one-way association, often implying direct causality but lacking clear evidence. Far less is known about the role of social, community, and interpersonal factors in predicting uptake, cessation, and harmful drug use.

Research into motivations for drug use among GBM has typically focused on individual psychological factors including the effects of homophobia, social isolation, and sexual abuse (Hatzenbuehler, 2009; Stall et al., 2001). Participation in aspects of gay community has been associated with increased levels of drug use (Lea, Reynolds, & De Wit, 2013c). Specifically, sexually adventurous GBM participating in intensive sex partying is a key factor in sexual risk behaviour and HIV infection (Halkitis & Palamar, 2008; Halkitis, Palamar, & Mukherjee, 2007; Hurley & Prestage, 2009; Mansergh et al., 2001; Prestage et al., 2009a; Prestage et al., 2009b; Semple, Zians, Strathdee, & Patterson, 2009; Solomon et al., 2010). This suggests that relationships between sexual risk behaviour, HIV acquisition, and drug use among GBM are mediated by subcultural affiliations.

Other drug-related harms and consequences

Although less often explored, the prevalence of drug-related harms such as dependence and overdose is high (Bolding et al., 2006; Prestage et al., 2009b; Semple et al., 2009; Stall et al., 2001; Zablotska et al., 2010). Social support provided through aspects of gay community can mediate individuals' drug use to prevent associated harms (Bauermeister, 2008). Further insights into specific behavioural practices and social norms within different segments of the gay community may identify barriers to the adoption of harm reduction messages and inform better targeting of harm reduction programmes.

Attitudes and beliefs about drug use in gay communities

Sexual practices among GBM are influenced by shared understandings of HIV risk and gay community norms, particularly those regarding 'safe sex' (Kippax, 1993). This may also be true of drug-using behaviours and attitudes toward harm reduction. Further research is required about the role of participation in aspects of gay community sexual and social life, and how engagement in these influences the initiation and cessation of drug use and other changes in drug use over time.

The shared understandings of risk and pleasure in relation to drug use and sex among GBM are likely to be key factors in their drug using behaviour. Broad attitudes toward drug use among GBM

have been explored elsewhere (Halkitis, Fischgrund, & Parsons, 2005; Jerome, Halkitis, & Siconolfi, 2009; Palamar & Halkitis, 2006) but normative beliefs about drug use within Australian gay community networks have not been previously investigated.

Study aims

In this paper, we describe the methodology and report baseline prevalence of licit and illicit drug use among men enrolled in the Following Lives Undergoing Change (Flux) study.

Flux was established to:

1. Identify individual and contextual factors associated with initiation and cessation of drug use and changes over time in patterns of sexual and drug use behaviours among GBM men.
2. Describe the relationship between social and community norms and drug use behaviours and beliefs among GBM.
3. To describe the role of particular aspects of gay community sexual and social life, and participation in these, in relation to attitudes and beliefs about drug use and drug-use behaviours.

We developed sophisticated and automated procedures specific to this study. This paper will demonstrate the novel application of this methodology to address the study aims and provide details of the characteristics of the cohort and their drug user profile.

Methods

The Flux study is being conducted nationally in Australia using online survey techniques. We systematically enrol and follow-up individual GBM to collect information about drug use, risk behaviour and associated harms, and gay community engagement. We obtained additional optional consent at enrolment for linkage to hospitalisation datasets to identify drug-related presentations and to the national HIV registry to confirm prevalent and incident HIV infections. The Flux protocol and all supporting documentation have been approved by Human Research Ethics Committee of the University of New South Wales.

Study design

We enrolled a broad sample of GBM including both current users and non-users of illicit drugs at baseline. The study will monitor changes in drug use and associated harms, beliefs and attitudes, and engagement with gay community networks over time through self-completion of online questionnaires at six-monthly intervals.

A unique integrated system of digitally linking individually tailored questionnaires, study databases, and communications with participants, was developed for this study and was named the Flux Automatic Management eSystem (FAME). It was designed to be specific to this study but can be adapted to other research projects.

Power calculation and sample size

The event-driven approach was used for sample size calculations in order to compare the incidence of drug initiation between men who reported CAI with casual partners in the last 6 months and those who did not. To enable an 80% statistical power to detect a two-fold increase in the incidence of drug initiation of crystal methamphetamine, EDM, and amyl nitrite, or a minimum of 67 cases of initiation use of these drugs are required over a total of 540 person-years of follow-up. Based on our previous studies, we assumed an incidence of 10 per 100 person-years of initiation of these drugs (Prestage et al., 2009b) and a prevalence of 25% in men reporting CAI with casual partners in the Gay Community Periodic

Surveys (ongoing behavioural surveillance survey of GBM in Australia). Therefore, we proposed to recruit 360 men who did not have a history of using these drugs at baseline with an average follow-up of 1.5 years. From the Health in Men study, around 75% of men reported a history of using any of the three drugs (Prestage et al., 2009a), hence the total sample size of 1440 men.

Eligibility and participation

Eligibility criteria for the study were being male, currently living in Australia and aged 16.5 years or older, and identifying as a gay/homosexual or bisexual man or had sex with at least one man in the preceding twelve months.

No incentives were provided to promote enrolment. Recruitment into the Flux study was achieved entirely online. Advertising through a wide range of social media was used to reach a diverse sample of GBM across Australia, with varying degrees of gay community engagement. These included: Popular gay and bisexual 'dating' sites and apps; and Facebook. The study was also promoted through gay community events and organisations, with potential participants being provided a direct link to the study website. Advertising aimed to reach a broad sample of GBM [Appendix I] but some advertising was more targeted to specifically attract GBM who were not using drugs [Appendix II]. Enrolment commenced in September 2014 and was completed in July 2015.

Measures

Questionnaire items included: Demographic characteristics; social and community engagement with gay men; HIV and viral hepatitis status; lifetime and recent (previous six months) licit and illicit drug use; negative consequences and the perceived benefits of drug use; sexual behaviours; stigma and mental health; attitudes to gay community and drug use; and access to harm reduction resources and treatment services.

Previously used measures of drug use (Degenhardt, Day, Gilmour, & Hall, 2005), and additional items devised specifically for GBM were used, as well as our previously validated measures of sexual risk behaviour and engagement in gay community (Jin et al., 2009; Zablotska, Kippax, Grulich, Holt, & Prestage, 2011). Measures of gay community engagement included two different kinds of measures: Scales measuring the extent of community engagement, and indicator variables for types of engagement (Kippax et al., 1998). The generalised anxiety disorder assessment (GAD7; Spitzer, Kroenke, Williams, & Löwe, 2006), the measure of sexual sensation seeking (Kalichman, Heckman, & Kelly, 1996), and the patient health questionnaire (PHQ9; Kroenke, Spitzer, & Williams, 2001) were also included (Fig. 1).

Implementation

Procedures for streamlined digital processing and data protection—FAME

The FAME process was designed to enable maximum digital management of the study and to ensure a simple, straightforward experience for participants. Each participant was digitally assigned a unique study identifier (USID) through the survey platform upon entry to the consent form. The USID was used to link to their unique records on all study data sources. It will remain the participants' unique identifier throughout the study and is central to the implementation of FAME. All communications with participants were automatically generated using their USID to automatically link to their own records. Individual participants' records from the consent form, baseline questionnaire, and all

follow-up rounds were, and will continue to be matched through the USID. Access to any data or identifying information has been protected by secure barriers at each level of access (see Fig. 2).

The Flux web page

All recruitment advertisements and recruitment email invites were directed to the Flux web page (http://www.flux.org.au), which provided a detailed description of the study aims, requirements for participation, the time required for survey completion, information about ethical approval, and study contact information. Once the participant clicked on the "Enrol Now" button on the Flux website, they were redirected to the online consent form.

Online platform

All study forms are hosted by SurveyGizmo™, an online survey creator with many features that permitted us to design customised questionnaires tailored and automated to the specific needs of the project. Specifically, this allowed us to confidentially link data using the FAME process between study websites, external databases, and study questionnaires.

Online consent form

Participant confidentiality was strictly maintained at all times. For added protection, the consent form and subsequent survey forms were designed as separate online self-complete forms. They needed to be digitally linked automatically to minimise processing of individual forms and potential errors. The consent and survey forms were digitally linked via the FAME process using the digitally generated USID. At this point, participants could decide whether to join the Flux cohort and agree to six-monthly follow-up surveys, or simply complete the baseline survey anonymously.

Those participants who chose to complete the baseline questionnaire anonymously were re-directed into the baseline survey form (by-passing the cohort-specific consent requirements). Their USID and consent type were the only items automatically inserted into the baseline survey form. A total of 108 participants (20.0%) who initially chose to anonymously complete the baseline questionnaire changed their mind at the end of the baseline entry to subsequently join the Flux cohort.

Participants who chose to join the cohort study moved on to the next page of the consent form, which listed additional, optional consents for data linkage. Participants were required to create a Flux user account to enable ongoing contact with them during the life of the study. They were asked to enter their full name, email address, and phone numbers, and their preferred method of contact. To further protect the participants' identity, they were also required to create a Flux profile name. The Flux profile name is comprised of the name of participants' first pet and the name of the first street on which they lived. This name was used in all communications with the participants.

Baseline assessment

Once their Flux account was created, participants could either commence the baseline questionnaire immediately or defer until a later time. Participants who deferred their entry were automatically emailed a PDF copy of their consent form via the FAME process which was addressed to their Flux profile name, and a unique link to their baseline survey form [Appendix III]. There was no identifying information attached to this link. This link simply provided participants with access to the survey, thereby circumventing the need for individual passwords. This further protects the participants' confidentiality. The link contained the USID which
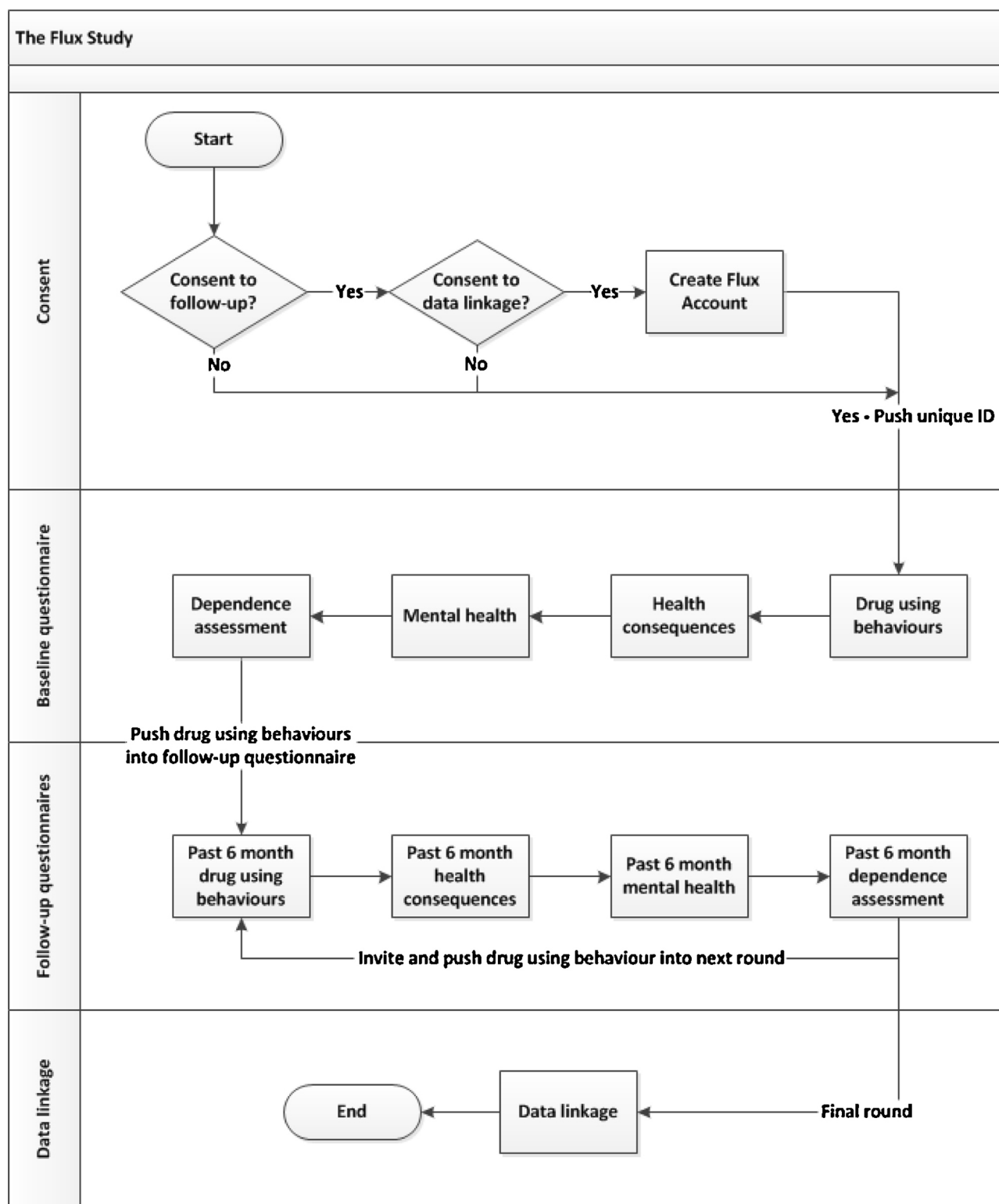
Fig. 1. Flux study pathway.

was pushed into the baseline survey form when the link was triggered. These deferring participants were sent an email reminder to complete their questionnaire the following week, also containing their USID and unique link to the survey form. This process was automatically executed by the FAME process.

Participants who chose to immediately proceed to the questionnaire were automatically moved to the baseline survey form and FAME automatically sent an email to the participants

with their consent forms and their unique links back into the survey form. By clicking this link, participants automatically returned to the point where they left off should they close their session, either intentionally or unintentionally. Providing each participant with their own unique link prevented duplicated and lost entries.

Upon entry into the baseline survey form, the participants' USID and Flux profile name were automatically inserted from the
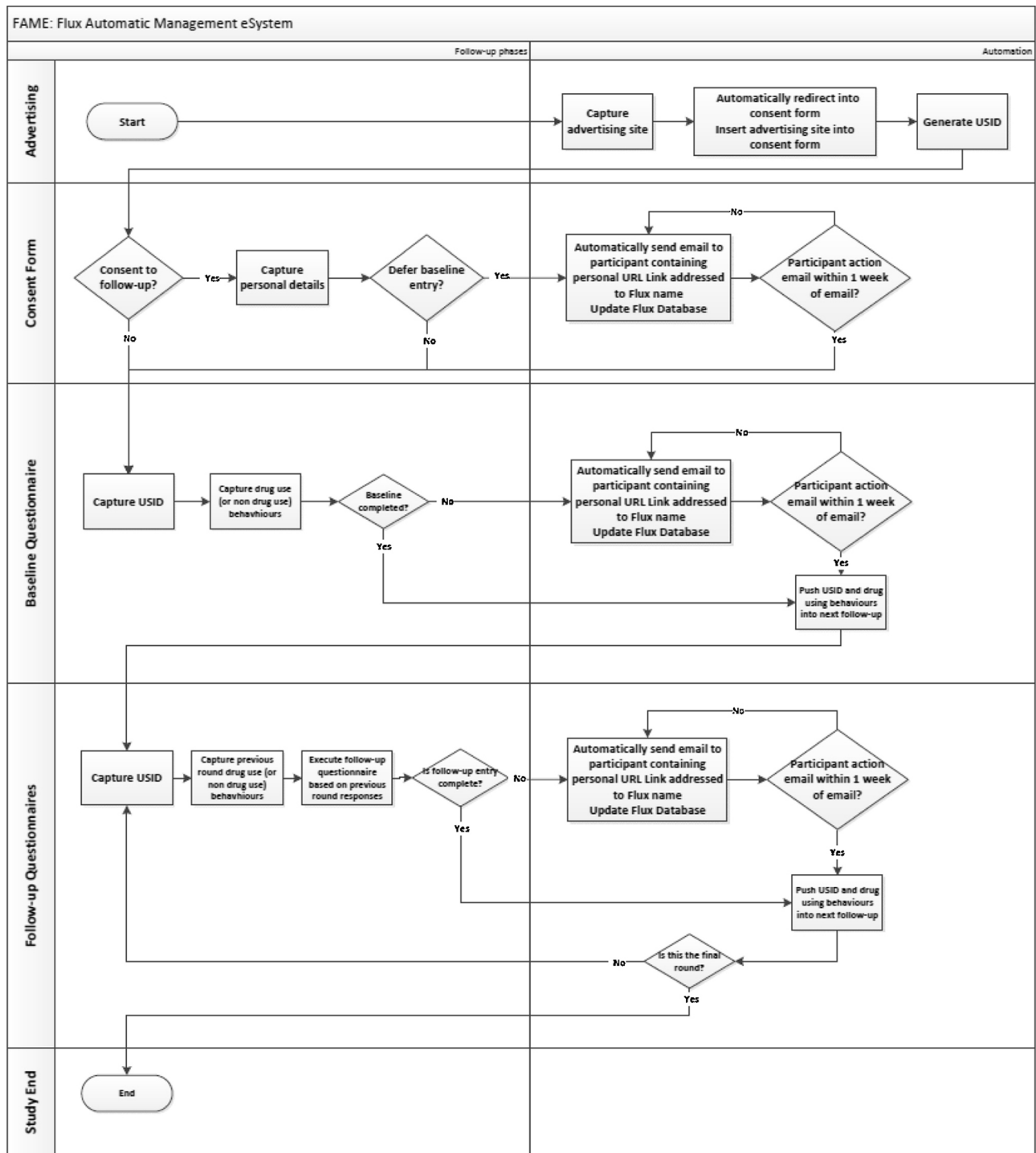
Fig. 2. The FAME Process.

consent form into the baseline survey form. No identifying details were included in survey forms. Upon submitting their final responses, participants received an automatically generated email via FAME confirming their completion of the baseline questionnaire.

Follow-up questionnaires

Six months after completing the baseline questionnaire, participants were invited to complete their first follow-up questionnaire. Invitations were sent by email and an accompanying SMS addressed to their Flux profile name. Every participant received an email containing a unique link to their personally tailored survey form. Clicking this link redirected them to a welcome page. Here, they verify that their USID was correct. Once confirmed, key responses from their baseline questionnaire were automatically loaded into the follow-up survey form. Using their baseline responses, the follow-up survey form was executed in a unique pattern, skipping redundant questions to ensure they were only asked relevant questions. For example, if a participant was not

using drugs at baseline and reported using drugs at follow-up, specific questions about those changes in drug using behaviours were displayed. So, relevant questions were only asked of those who meet the specific criteria.

Study database

A separate encrypted and protected study tracking database was specifically designed to track participants' progression throughout the study and store the Flux mailing list. Other than participants' own chosen email addresses, no identifying information was included in the tracking database, and the USID was used to link with participants' own records.

To identify which participants were due to be invited or reminded, and on what dates, a query was created within the study database, automatically generating a list of only those being invited into the next round, or those being reminded about survey completion. Upon generation, these lists were uploaded into SurveyGizmo™, from where each participant received an email uniquely addressed to their Flux profile name, with the link to their survey form containing their USID. Upon clicking this link, they were returned to their current position in the questionnaire.

Cohort maintenance

To maintain a large volunteer online cohort, it is essential to closely monitor participation to ensure the accuracy of participants' contact information, and completion of data. The emails sent to participants upon enrolment also provided an opportunity to determine if they had provided valid email addresses. A customised email verification was embedded into the consent form requiring participants to enter their email address twice; they were unable to proceed unless the two email addresses matched. Only two emails bounced using this verification system.

To prevent duplicate entries, the USID was appended to the end of each survey link, disabling that number from being re-used as an entry (no IP addresses or system identifying information were captured). If the link was previously activated, the participant would be sent to the last page they had completed. This also provided a user-friendly way for participants to save and continue their participation.

The automated weekly query within the study database identified participants who had not completed their responses to each survey round. This process was repeated for ten weeks or until each individual participant completed his questionnaire. Of those who joined the study (1710), 1576 (92.1%) completed the baseline questionnaire without needing an email or SMS reminder. Sixty-three participants completed their response after the first reminder, and 54 completed after the second reminder; only 18 required subsequent reminders.

A key aspect of cohort maintenance is to ensure ongoing engagement with, and feedback to, study participants. A Flux Facebook page (www.facebook.com/fluxstudy) maintained an online public presence for participants. While there is always the potential to influence responses, the Facebook page has articles for information and communication to participants, but opinions are not expressed by the study team. In addition, a quarterly eNewsletter is sent to the participants with study developments and findings, milestones, and events.

Data linkage

The optional consents were to link participants' responses with external databases. Identification and verification of self-reported baseline and incident HIV infections within the cohort will be achieved by linkage to the HIV registry. Linkage with hospital separations will identify drug-related incidents within the cohort. These data linkages will be completed at the end of the study period.

Results

In total, 21,014 clicks were received on the studys website, and 6810 clicked through to the consent form. Of these, 4306 clicks were received past the first page of the consent form where they indicated their level of consent (six-monthly follow-up or baseline only). A total of 2943 people completed the consent form (six-monthly follow-up or baseline only), and 2705 men commenced survey responses, of whom 2250 (83.2%) provided sufficiently complete baseline data for tracking trends in drug use over time. Of the 2250 participants who completed the baseline questionnaire, 1710 (76.0%) gave consent to follow-up at six-monthly intervals. Of those who consented to follow-up, 1478 commenced the baseline questionnaire immediately, and 233 deferred their baseline entry and completed it at a later time. Of the 1710 participants who provided consent to follow-up, 1015 (59.3%) also provided any consent to data linkage (match participant responses to state and national health registries).

The majority of participants (either enrolled or anonymous) were recruited through Facebook targeted advertising (Table 1). About one in six were recruited through popular gay dating sites and one in twenty through smartphone or tablet dating apps. Small proportions were recruited through participants' own personal networks and gay community organisations or events. There were some differences in types of drugs used based on where participants were recruited, but these differences were not consistent across the different recruitment sources, nor in the types of drugs used.

Most participants identified as cisgender men (99.2%) and there were 17 transgender or intersex men (0.8%). The mean age of the sample was 33.0 years (SD 12.6; range 16.6–81.0) however, 35.9% were aged less than 25. Most identified as gay or homosexual, but about one in twelve identified as bisexual. Only seven identified as heterosexual, and a small proportion reported other identities such as uncategorised, queer, pansexual, bi-curious, asexual, and fluid. Men who did not consent to follow-up, and were not enrolled in the cohort were younger (p = 0.001), and significantly less likely to identify as gay (p < 0.001) compared to men who consented to follow-up (Table 1).

Over half (50.5%) the men reported that they had used any illicit drug in the previous six months. Over a quarter (28.0%) had used party drugs (ecstasy, speed, cocaine, crystal methamphetamine, gamma hydroxybutyrate [GHB], ketamine, lysergic acid diethylamide [LSD]) in the previous six months. The most common drugs used were marijuana, amyl nitrite, and ecstasy (Table 2). About one in eight men (12.0%) had used crystal methamphetamine in the previous six months. Men who were enrolled in the cohort were more likely to have used illicit drugs in the previous six months.

A key aim of this study was to identify men who initiated crystal methamphetamine, EDM, and amyl nitrite, over time. Therefore, we needed to identify men who did not use these drugs at baseline. Among the 1710 men enrolled into the cohort, 1487 (86.9%) had not used crystal methamphetamine in the six months prior to enrolment, 1315 (76.9%) had not used EDM, and 1133 (66.2%) had not used amyl nitrite. In total, 790 men (46.2%) had used none of these drugs (Table 3). Among the 540 men who participated anonymously, 495 (91.7%) had not used crystal methamphetamine in the six month prior to completing the baseline questionnaire, 445 (82.4%) had not used EDM, and 395 (73.1%) had not used amyl nitrite. In total, 316 men (58.5%) who participated anonymously had used none of these drugs (Table 3).

Table 1
Characteristics of the sample.

	Enrolled full cohort participants n = 1710 (76.0) n (%)	Anonymous baseline only participants n = 540 (24.0) n (%)	Total N = 2250 N (%)
Mean age in years (SD)**	33.7 (12.5)	30.9 (12.6)	33.0 (12.6)
Sexual orientation***			
Gay	1544 (90.2)	446 (82.6)	1990 (88.4)
Bisexual	122 (7.1)	77 (14.3)	199 (8.8)
Heterosexual	2 (0.1)	5 (0.9)	7 (0.3)
Other	43 (2.5)	12 (2.2)	55 (2.4)
Recruitment source**			
Social media (Facebook)	1137 (66.5)	341 (63.1)	1478 (65.7)
Dating site (Manhunt/Squirt)	293 (17.1)	100 (18.5)	393 (17.5)
Phone apps (Grindr/Jack'd)	69 (4.0)	43 (8.0)	112 (5.0)
Personal networks	81 (4.7)	24 (4.4)	105 (4.6)
Gay community organisations	43 (2.5)	6 (1.1)	49 (2.2)
Community events (Fair day)	20 (1.2)	7 (1.3)	27 (1.2)
Other	68 (4.1)	19 (3.6)	87 (3.9)
Geographical location*			
New South Wales	697 (40.7)	198 (36.7)	985 (39.8)
Victoria	428 (25.0)	135 (25.0)	563 (25.0)
Queensland	265 (15.5)	91 (16.9)	356 (15.8)
Northern Territory	12 (0.7)	5 (0.9)	17 (0.8)
Western Australia	118 (3.9)	34 (6.3)	152 (6.8)
South Australia	99 (5.8)	42 (7.8)	141 (6.3)
Australian Capital Territory	67 (3.9)	12 (2.2)	79 (3.5)
Tasmania	18 (1.1)	15 (2.8)	33 (1.5)
Overseas	5 (0.3)	4 (0.7)	9 (0.4)
Did not answer	2 (0.1)	4 (0.7)	6 (0.3)

* p < 0.05.
** p < 0.01.
*** p < 0.001.

Discussion

We have established an entirely online cohort study of incidence and risk factors for initiation, cessation, and changes in drug use over time among Australian GBM. The characteristics of both the enrolled and the anonymous participants in the Flux sample, while somewhat younger, are otherwise comparable to those of other samples of Australian GBM (Lea et al., 2013b; Prestage et al., 2009a; Zablotska, Holt, & Prestage, 2012). We have demonstrated the ability to collect sensitive information while protecting participants' confidentiality. Flux has further demonstrated that it is possible to achieve these outcomes with minimal direct labour costs by developing the FAME to digitally link study databases, online data collection tools, and communications with study participants. Investing in this technical infrastructure facilitates flexible and individually tailored study participation.

The greater efficiency, ease of participation, and protection of data integrity against human error is an advantage compared to non-online cohorts. It also allows participants to decide their level of engagement, participation, and flexibility.

The initial recruitment target, which was based on our sample size calculations, was surpassed. This was achieved due to large enrolments obtained through targeted advertising, particularly of younger men.

As has been found in other samples of GBM (Roxburgh et al., 2015; Zablotska et al., 2012), men in this study reported rates of substance use that were substantially higher than in the adult male population as a whole. Whereas general population studies have found that about one in six (17.3%) adult men report recently using any illicit drugs, with 2.5% recently using crystal methamphetamine (Roxburgh et al., 2015), half (50.5%) of men in the Flux study were found to recently use illicit drugs with 12.0% recently using

Table 2
Use of illicit drugs in previous six months.

	Enrolled full cohort participants n = 1710 (76.0) n (%)	Anonymous baseline only participants n = 540 (24.0) n (%)	Total N = 2250 N (%)
Cannabis*	522 (30.5)	140 (25.9)	662 (29.4)
Amyl nitrite**	578 (33.8)	145 (26.9)	723 (32.1)
Ecstasy**	329 (19.2)	69 (12.8)	398 (17.7)
Meth/amphetamine (speed)	109 (6.4)	26 (4.8)	135 (6.0)
Cocaine*	229 (13.4)	52 (9.6)	281 (12.5)
Lysergic acid diethylamide (LSD)**	72 (4.2)	9 (1.7)	81 (3.6)
Crystal methamphetamine**	224 (13.1)	45 (8.3)	269 (12.0)
Ketamine*	74 (4.3)	11 (2.0)	85 (3.8)
Gamma hydroxybutyrate (GHB)**	132 (7.7)	24 (4.4)	156 (6.9)
Heroin	3 (0.2)	0 (0.0)	3 (0.1)

* p < 0.05.
** p < 0.01.
*** p < 0.001.

Table 3
Combined use of crystal methamphetamine, EDM, and amyl nitrite.

	Enrolled full cohort participants n = 1710 (76.0) n (%)	Anonymous baseline only participants n = 540 (24.0) n (%)	Total N = 2250 N (%)
Used crystal methamphetamine only	26 (1.5)	4 (0.7)	30 (1.3)
Used erectile dysfunction medication only	289 (16.9)	65 (12.0)	354 (15.7)
Used amyl nitrite only	252 (14.7)	75 (13.9)	327 (14.5)
Used crystal methamphetamine + erectile dysfunction medication	28 (1.6)	10 (1.9)	38 (1.7)
Used crystal methamphetamine + amyl nitrite	30 (1.8)	9 (1.7)	39 (1.7)
Used erectile dysfunction medication + amyl nitrite	156 (9.1)	39 (7.2)	195 (8.7)
Used all three	140 (8.2)	22 (4.1)	162 (7.2)
Used none	790 (46.2)	316 (58.5)	1106 (49.1)

crystal methamphetamine (use in the past six months). However, in comparison to other convenience samples of Australian GBM (Lea et al., 2013b; Prestage et al., 2009a), participants in the Flux study were no more likely to report the use of drugs, and in some cases could be described as being somewhat less likely.

In addition to its high efficiency and minimal staff requirements, the design and execution of an online methodology provided many advantages. We were able to conduct a large national study in a geographically dispersed country and to attract both men that are engaged and not engaged with gay community life (Table 2). Online self-completion protects participant confidentiality by minimising direct involvement with study staff. Similar to Audio Computer-Assisted Self-Interview Software (ACASI), the online methodology potentially reduces social desirability bias in reporting illegal or stigmatised behaviours (Davis, Couper, Janz, Caldwell, & Resnicow, 2010; De Vaus, 2013; Engel & Schutt, 2016). The online methodology also provides a streamlined experience for the participants. Questions and sections of each survey were tailored to match participants' previous responses; not just within the current round, but also from previous rounds. Whether the cohort includes few or many participants or is a national or international study, the cost and time management essentially remains the same when using the FAME system. This has contributed to a high completion rate once survey responses were commenced.

After accounting for set-up costs, we will achieve these outcomes at a significantly reduced cost compared to traditional cohort studies while maintaining high levels of participant engagement and confidentiality at all stages. Nonetheless, an entirely online cohort removes direct human interaction with participants. The absence of an interviewer also removes the ability for interviewers to clarify and probe participant responses (Davis et al., 2010; De Vaus, 2013; Engel & Schutt, 2016). However, as this study sought detailed information about sensitive and potentially illegal behaviours, self-completion in the privacy of their own homes, at their own time and pace, may reduce social desirability bias (White, Day, & Maher, 2007).

Our study design did not permit clinical data collection to verify self-reported medical conditions. We will, however, collect information such as drug-related hospital admissions, HIV status, and deaths for those who gave consent to data linkage. As with most social and behavioural populations engaged in illicit or stigmatized behaviours, whether online or face-to-face, we could not guarantee individuals' identity. Nonetheless, for those consenting to follow-up, we were able to verify a valid email address. Regardless of any differences in drug use patterns according to recruitment source, drug use within this sample was similar to drug use in other samples of GBM in Australia (Lea et al., 2013b). We achieved this diverse sample by recruiting participants through a variety of sources.

Conclusions

Having successfully implemented FAME to establish the first entirely online cohort study of drug use among Australian GBM, the Flux study will be able to provide data on incidence and factors associated with initiation and cessation, and changes in patterns of drug use and related harms over time. The high rates of illicit drug use in this sample indicate the need for longitudinal enquiry and follow up to assess continuing and changing patterns of drug use over time within this population.

Funding source declaration

Author agreement/declaration

All authors certify that they have seen and approved the final version of the manuscript being submitted. All authors warrant that the article is the authors' original work, has not received prior publication and is not under consideration for publication elsewhere.

Appendix I.

Flux is about caring for your friends and community

Appendix II.

Appendix III.
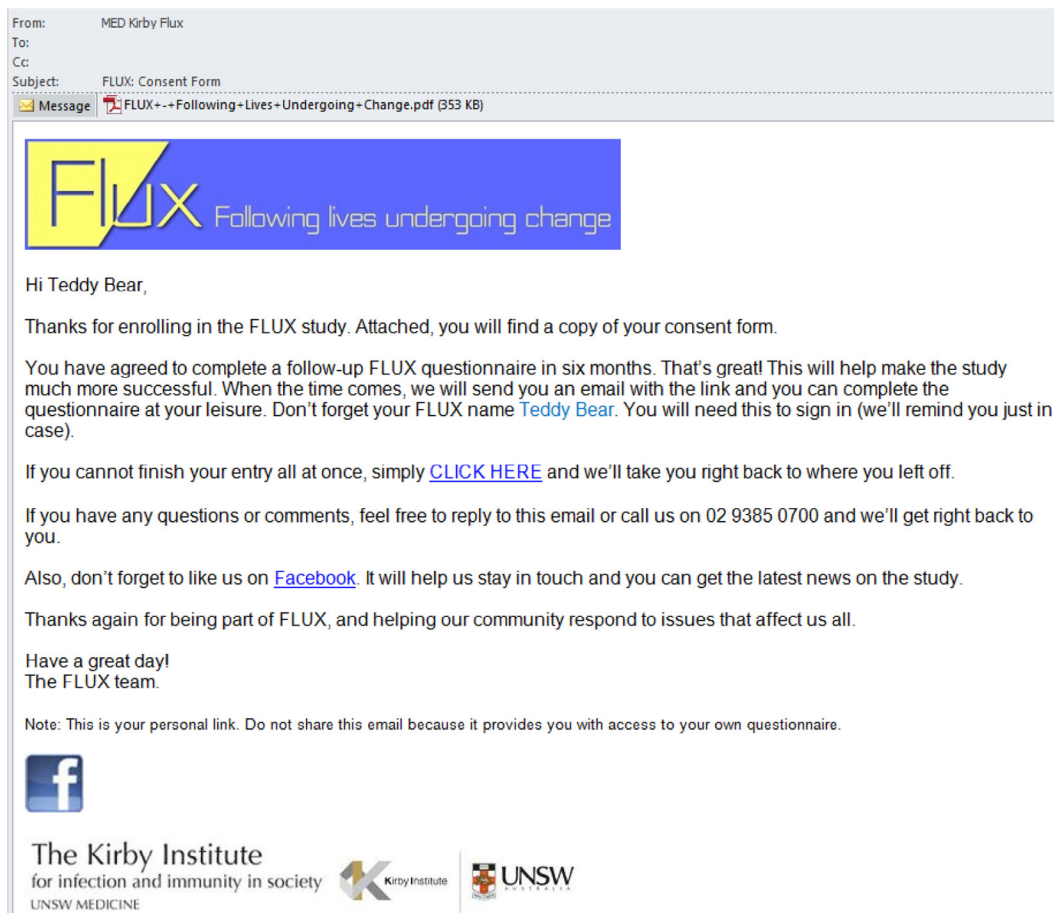
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2.1.4   Chapter two summary

I created *FAME* as the essential infrastructure to underpin prospective observational studies and made it available to other researchers, thereby reducing the resource and cost burdens while improving data integration and participant experience. Using *FAME*, I developed one of the largest prospective observational studies of licit and illicit drug use among gay and bisexual men, making it the pre-eminent cohort study of drug use among gay and bisexual men internationally.

The successful establishment of the *Flux Study* enabled data collection of baseline drug use prevalence data for a large sample of gay and bisexual men in a geographically dispersed country. Prevalence of illicit drug use within this sample was similar to that of other studies of Australian gay and bisexual men,[2-6] and internationally.[7-12] The prevalence of concurrent use of key chemsex drugs, such as crystal methamphetamine and gamma-hydroxybutyrate, were also reported at high rates of use in this sample. This suggests that gay and bisexual men who use these drugs in this sample were doing so to engage in chemsex. However, further investigation was warranted.

Chapter Three

Chasing trends

3.1 Recreational use of erectile dysfunction medication to engage in chemsex and its associations with HIV risk behaviours

3.1.1 Publication details

3.1.2 Thesis aims related to this chapter

Thesis aim 2: Describe the characteristics of Australian gay and bisexual men who engage in chemsex and the types of drugs used.

Thesis aim 3: Describe the extent to which men who engage in chemsex also engage in behaviours that may represent potential HIV risk.

3.1.3   Chapter three in context

Prestage et al. (2009) had previously identified that the recreational use of erectile dysfunction medications substantially increased the likelihood of HIV infection among gay and bisexual men (Table 1.2). **Chapter 2** showed that there was a high proportion of men in the *Flux Study* who used erectile dysfunction medications. Did men in this sample use erectile dysfunction medications based on medical indication, or were they using it recreationally to enhance sex, particularly in the context of chemsex?

Addressing **thesis aims 2** and **3**, in **chapter 3** I use baseline survey data to investigate the characteristics of gay and bisexual men who use erectile dysfunction medications to engage in chemsex. I also describe the extent to which use of erectile dysfunction medications to engage in chemsex is associated with HIV risk behaviours before the widespread availability of PrEP in Australia.

ERECTILE FUNCTION

Off-Label Use of Phosphodiesterase Type 5 Inhibitor Erectile Dysfunction Medication to Enhance Sex Among Gay and Bisexual Men in Australia: Results From the FLUX Study

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ABSTRACT

Background: Gay and bisexual men (GBM) use oral erectile dysfunction medications (EDMs) often with little evidence of medical indication necessitating their use.

Aim: To investigate the prevalence, contexts, and motivations for oral EDM use and its relation to sexual risk behavior.

Methods: A total of 2,250 Australian GBM completed an online survey of licit and illicit drug use and their associated behaviors. Multivariate logistic regression analysis identified factors associated with use of EDMs in the previous 6 months and, for those who had used EDMs, factors associated with use on a weekly basis.

Outcomes: Any EDM use and at least weekly use in the previous 6 months.

Results: The median age of the sample was 33.0 years (range = 16–81). Two thirds (67.7%) reported no lifetime history of EDM use. Approximately 1 in 10 participants (11.1%) had last used an EDM more than 6 months previously. In the previous 6 months, 11.5% reported using EDMs less than monthly, 5.3% reported using EDMs approximately monthly, and 4.5% reported using EDMs at least weekly. Of men who had used EDMs in the previous 6 months, common reasons cited for its use were to maintain an erection for longer (73.3%), to make it easier to "get hard" (67.3%), and difficulty in attaining or maintain an erection (53.5%). Use of EDMs in the previous 6 months was associated with illicit drug use and higher rates of sexual risk behavior. Weekly users were more likely to have severe anxiety than less frequent users.

Clinical Translation: The use of EDMs in the context of intensive sex partying, with the associated potential for increased risk of HIV transmission and illicit drug use, indicates a need to consider the use of EDMs among GBM in HIV prevention and minimizing harm.

Strengths and Limitations: This large-scale study of drug use among GBMs includes comprehensive detailed data on their history of use and rationales for use. Our online methodology potentially decreases social desirability bias in reporting illegal or stigmatized behaviors. This volunteer online convenience sample might not be representative of all GBMs in Australia.

Conclusion: GBMs who used an oral EDM in the previous 6 months often used it for recreational purposes, but many of those who used it on a weekly basis also might have used it for therapeutic reasons. GBMs often use EDMs to enhance their sexual experiences often in the context of intensive sex partying (which can include risky sexual behavior). Hammoud MA, Jin F, Lea T, et al. Off-Label Use of Phosphodiesterase Type 5 Inhibitor Erectile Dysfunction Medication to Enhance Sex Among Gay and Bisexual Men in Australia: Results From the FLUX Study. J Sex Med 2017;14:774–784.

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Key Words: Viagra; Cialis; Levitra; Oral Erectile Dysfunction Medication; Off-Label Use; Gay and Bisexual Men; Intensive Sex Partying; HIV Risk Behaviors and Transmission; Phosphodiesterase Type 5 Inhibitor

INTRODUCTION

Gay and bisexual men (GBMs) use erectile dysfunction medications (EDMs) such as Viagra (sildenafil citrate; Pfizer, Mission, KS, USA), Cialis (tadalafil; Eli Lilly and Company, Indianapolis, IN, USA), and Levitra (vardenafil HCl; GSK, Brentford, UK) often with little evidence of medical indication that might necessitate their use.[1−5] EDMs were developed to treat medically diagnosed erectile dysfunction,[6] which currently affects more than 150 million men worldwide.[7] EDMs currently remain the first-line treatment for erectile dysfunction because of their efficacy and safety.[8] Nevertheless, EDMs also have been used recreationally particularly among GBM.[4,5,9] Off-label use of EDMs is sometimes used to counter the effects of other illicit recreational drugs[10] and/or to enhance sexual experiences among GBM. EDM use, particularly combined with illicit drug use (such as amyl nitrite, γ-hydroxybutyrate, and crystal methamphetamine) have been implicated in the transmission of sexually transmissible infections, including HIV, because of higher levels of sexual risk behaviors.[2,11−15]

Intensive sex partying has been described as a combination of several factors associated with the risk of HIV infection.[16] These include being very sexually active; being closely involved in gay community social and sexual networks; engaging in group sex; engaging in condom-less anal intercourse (CLAI); and using party drugs.[16] EDM use for intensive sex partying has been associated with sexual risk behaviors,[3,4] such as increased numbers of sex partners[2] and CLAI.[15]

Sexual sensation seeking has been found to be a strong indicator of men at risk of HIV and of GBM who engage in sexual risk behaviors and of the association between drug use and risky sex.[17] It also has been associated with many indicators of intensive sex partying.[16,18]

Sexual practices among GBM are influenced by shared understandings of HIV risk and gay community norms, particularly those regarding "safe sex."[19,20] Aspects of drug using behaviors among GBM, particularly in relation to minimizing harm, have similarly been found to reflect normative values within specific gay community subcultures (cf Southgate and Hopwood[21]). This also might be true of attitudes toward the off-label use of EDMs.

Anxiety and depression are associated with self-esteem,[22,23] social withdrawal,[24] and erectile dysfunction.[25] EDM use can override these factors by providing increased confidence and relieving sexual performance anxiety.

Despite its role in HIV risk behaviors and transmission, few studies have described the characteristics of GBM who use EDMs, the history and frequency of their use, and their motivations for using EDMs.[2,4] These studies show that EDM use tends to be associated more often with sexual pleasure than with erectile dysfunction and, hence, their strong association with HIV risk behaviors and transmission.

AIM

In this study, we used baseline data from a cohort of Australian GBM to investigate the prevalence and contexts of, and motivations for, phosphodiesterase type 5 inhibitor EDM use and its relation to sexual risk behavior.

METHODS

Procedures

The Following Lives Undergoing Change (FLUX) Study is an online prospective observational study of Australian GBM. The methods are described in greater detail elsewhere.[26] The FLUX Study aimed to:

- Identify individual and contextual factors associated with initiation and cessation of drug use and changes over time in patterns of sexual and drug use behaviors among GBM.
- Describe the relation between social and community norms and drug use behaviors and beliefs among GBM.
- Describe the role of particular aspects of gay community sexual and social life, and participation in these, in relation to attitudes and beliefs about drug use and drug use behaviors.

We developed sophisticated and automated procedures specific to this study.[26]

In brief, participants were recruited from August 2014 through July 2015 through gay community websites and online media, Facebook, mobile phone applications, and gay sexual networking websites. Ethical approval was provided by the human research ethics committee of the University of New South Wales (Sydney, Australia).

Measurements

The online baseline questionnaire included demographic items, questions on sexual identity, HIV testing history and self-reported serostatus, sexual behavior with men, and attitudes and beliefs about drug use. Men described their lifetime and recent (ie, previous 6 months) use of licit and illicit drugs and the frequency and methods of EDM use. They also were asked about the reasons for their use of EDMs, including whether they used it to "enhance sex." We also included our previously used measurement of social engagement with gay men[27] and the measurement of sexual sensation seeking.[17] To address intensive sex partying,[16] we included questions about group sex and using drugs for sex or to enhance sex ("party and play" or "chemsex").

The Generalized Anxiety Disorder Assessment (GAD7),[28] a seven-item self-report questionnaire screening for generalized anxiety disorders, and the Patient Health Questionnaire,[29] a nine-item self-report questionnaire that screens for depression, were included.

Participants and Sample

Men at least 16 years 6 months old who lived in Australia were eligible for participation if they identified as gay or bisexual or

had sex with another man in the previous year. No incentives were provided to promote enrollment. Overall, 4,306 people clicked on the study website, and 2,943 completed the online consent form; 2,250 completed the minimum data requirements for the online questionnaire.

Analysis

Descriptive statistics were used to characterize the types of men who used EDMs. For univariate analyses of whether they had used EDMs in the previous 6 months and whether they had used EDMs at least weekly, we included age, education, cultural background, social engagement with gay men, sexual identification, relationship status, HIV status, and sexual risk behavior. We used a type I error of 5% for these analyses.

Categorical variables were analyzed using the Pearson χ^2 test. Post hoc testing controlling for familywise error for the Pearson χ^2 test was conducted in accordance with Beasley and Schumacker[30] and García-Pérez and Nunez-Anton.[31] Continuous variables were analyzed using one-way analysis of variance. Assumptions of normality were satisfactory as determined by the central limit theory. The Tukey post hoc honest significant difference test controlling for familywise errors was used to compare all possible pairs of means.

To estimate statistical associations, we used a binary logistic backward stepwise multiple regression analysis to control for confounding factors and presented adjusted odds ratios (aORs) and 95% CIs. Associations with a P value less than .10 in the univariate logistic regression were included in the multivariate analyses. Data were analyzed using SPSS 24 (IBM Corp, Armonk, NY, USA).

RESULTS

Characteristics of Sample

A total of 2,250 GBM completed the survey. The median age was 33.0 years (range = 16–81 years). More than half the participants (52.4%) were university educated. Almost half were in managerial (15.5%) or professional (26.8%) employment (Table 1). Participants predominantly identified as gay (88.4%), 8.8% identified as bisexual, and 2.7% identified as heterosexual or other. Most participants were of Anglo-Celtic background (72.0%). Most men had been tested for HIV (80.3%), with 7.6% reporting that they were positive for HIV. Half (50.4%) indicated they were in a relationship with another man, 25.9% reported that most of their friends were gay men, and 18.4% spent much of their free time with gay friends.

Prevalence

Two thirds (67.7%) reported no history of any EDM use in their lifetime. Of those who used any EDM (including sildenafil citrate, tadalafil, and vardenafil), approximately 1 in 10 participants (11.1%) had last used an EDM more than 6 months previously. In the previous 6 months, 11.5% reported using an

EDM less than monthly, 5.3% reported using an EDM at least monthly, and 4.5% reported using an EDM at least weekly (Table 1). Of those who used an EDM in the previous 6 months, the types used were sildenafil citrate (88.3%), tadalafil (76.2%), and vardenafil (19.0%). Most (55.0%) reported obtaining the medication other than by a prescription from a doctor, with the most common method being online procurement (33.8%), followed by a casual male sex partner (17.9%) and a regular fuckbuddy (15.6%).

Univariate Associations

Older men used EDMs more recently ($P < .001$) and more often ($P < .001$). Men who ever used EDMs had higher levels of education. Approximately one in five men who had used EDMs was positive for HIV. HIV-positive men were more likely to have ever used an EDM ($P < .001$), whereas untested men were less likely to have ever used an EDM ($P < .001$). Most (82.2%) who used an EDM in the previous 6 months reported having at least some friends who also used EDMs, whereas 76.9% of men who never used an EDM reported having no friends who used EDMs. Men who recently used an EDM were more socially engaged with other gay men ($P = .013$) and they had higher scores on the measurement of sexual sensation seeking ($P = .022$).

Approximately one fourth (26.2%) reported having more than 10 male sex partners in the previous 6 months (Table 2). One third (35.4%) had had sex with a "fuckbuddy," more than half with a casual partner (59.5%) and 33.4% with a "boyfriend." Approximately one fourth reported CLAI with their boyfriend, and approximately 1 in 20 reported CLAI with any fuckbuddies or with any casual partners.

Most (68.8%) reported having used illicit drugs in the previous 6 months, with amyl nitrite (52.9%), cannabis (35.4%), and crystal methamphetamine (32.4%) being the most common drugs reported (Table 2). Of those who used illicit drugs, 55.6% reported having used "party drugs to enhance their sexual experiences."

The more recently, and more frequently, men used EDMs, the larger the number of sexual partners they were likely to report in the previous 6 months and the more likely they were to have had sex with fuckbuddies and with casual partners (Table 2). More recent and frequent EDM users also were more likely to report CLAI with these partner types; nearly half the men (42.6%) who used EDMs weekly reported CLAI with fuckbuddies and half (56.4%) reported CLAI with casual partners. The more recently, and more frequently, men used EDMs, the more likely they were to report having engaged in group sex in the previous 6 months.

Those who used EDMs more frequently were significantly more likely to use most illicit drugs compared with those who used EDMs less frequently or did not use EDMs (Table 2). Those who had used illicit drugs to enhance sexual pleasure were more likely to report recent EDM use than were those who had not used them for this purpose.

Table 1. Characteristics of sample according to use of EDM (N = 2,250)

	Never used EDM (n = 1,523)	Used EDM >6 mo ago (n = 249)	Used EDM less than monthly in previous 6 mo (n = 258)	Used EDM approximately monthly in previous 6 mo (n = 119)	Used EDM at least weekly in previous 6 mo (n = 101)
Age (y), median (range)	26 (16—76)	36 (20—67)	38 (17—69)	45 (20—81)	51 (18—81)
Age (y), n (%)[‡]					
≥20	328 (21.5)[§]	2 (0.8)[§]	4 (1.6)[§]	1 (0.8)[§]	2 (2.0)[§]
21—30	698 (45.8)[§]	60 (24.1)[§]	61 (23.6)[§]	11 (9.2)[§]	9 (8.9)[§]
31—40	276 (18.1)[§]	90 (36.1)[§]	87 (33.7)[§]	30 (25.2)	12 (11.9)
41—50	130 (8.5)[§]	51 (20.5)	63 (24.4)[§]	43 (36.1)[§]	27 (26.7)[§]
>50	91 (6.0)[§]	46 (18.5)[§]	43 (16.7)	34 (28.6)[§]	51 (50.5)[§]
Cultural background, n (%)[‡]					
Anglo-Celtic	1,051 (69.0)[§]	181 (72.7)	201 (77.9)	98 (82.4)	89 (88.1)[§]
Other	429 (28.2)[§]	63 (25.3)	53 (20.5)	20 (16.8)	11 (10.9)[§]
Not stated	43 (2.8)	5 (2.0)	4 (1.6)	1 (0.8)	1 (1.0)
Education, n (%)[‡]					
Less than university level	775 (50.9)[§]	97 (39.0)	107 (41.5)	35 (29.4)[§]	49 (48.5)
Undergraduate level	463 (30.4)	89 (35.7)	87 (33.7)	35 (29.4)	24 (23.8)
Postgraduate level	282 (18.5)[§]	62 (24.9)	61 (23.6)	49 (41.2)[§]	28 (27.7)
Not stated	3 (0.2)	1 (0.4)	3 (1.2)	0 (0.0)	0 (0.0)
Occupation, n (%)[‡]					
Managerial	205 (13.5)[§]	49 (19.7)	47 (18.2)	24 (20.2)	24 (23.8)
Professional	362 (23.8)[§]	90 (36.1)[§]	80 (31.0)	45 (37.8)	26 (25.7)
Other white collar	240 (15.8)	28 (11.2)	38 (14.7)	11 (9.2)	10 (9.9)
Other	150 (9.8)	34 (13.7)	31 (12.0)	12 (10.1)	7 (6.9)
Not in work	566 (37.2)[§]	48 (19.3)[§]	62 (24.0)[§]	27 (22.7)	34 (33.7)
HIV status, n (%)[‡]					
HIV+	36 (2.4)[§]	36 (14.5)[§]	52 (20.2)[§]	30 (25.2)[§]	17 (16.8)[§]
HIV−	1,057 (69.4)[§]	205 (82.3)[§]	194 (75.2)	87 (73.1)	79 (78.2)
Unknown or untested	430 (28.2)[§]	8 (3.2)[§]	12 (4.7)[§]	2 (1.7)[§]	5 (5.0)[§]
In relationship with regular partner, n (%)					
Not in relationship	766 (50.3)	124 (49.8)	120 (46.5)	53 (44.5)	52 (51.5)
In relationship	757 (49.7)	125 (50.2)	138 (53.5)	66 (55.5)	49 (48.5)
GAD, n (%)					
None or minimal	752 (55.0)	144 (63.7)	140 (59.6)	72 (64.9)	52 (57.1)
Mild	353 (25.8)	42 (18.6)	64 (27.2)	24 (21.6)	24 (26.4)
Moderate	151 (11.0)	23 (10.2)	22 (9.4)	10 (9.0)	6 (6.6)
Moderately severe	112 (8.2)	17 (7.5)	9 (3.8)	5 (4.5)	9 (9.9)
PHQ					
None or minimal	555 (39.8)[§]	113 (49.6)	107 (46.9)	56 (52.3)	47 (49.5)
Mild	414 (29.7)	57 (25.0)	67 (29.4)	28 (26.2)	22 (23.2)
Moderate	213 (15.3)	24 (10.5)	30 (13.2)	15 (14.0)	11 (11.6)
Moderately severe	119 (8.5)	21 (9.2)	15 (6.6)	3 (2.8)	10 (10.5)
Severe	92 (6.6)	13 (5.7)	9 (3.9)	5 (4.7)	5 (5.3)
Gay social engagement, mean (SD)[‡]	3.16 (1.59)	3.94 (1.54)	4.04 (1.51)	4.53 (1.47)	4.32 (1.70)
Never	—	−0.78 (0.11)[§]	−0.87 (0.10)[§]	−1.37 (0.14)[§]	−1.15 (0.17)[§]
Used EDM >6 mo ago	0.78 (0.11)[§]	—	−0.10 (0.14)	−0.59 (0.17)[§]	−0.38 (0.20)
Used EDM less than monthly in previous 6 mo	0.87 (0.10)[§]	0.10 (0.14)	—	−0.49 (0.16)[§]	−0.28 (0.19)

(continued)

Table 1. Continued

	Never used EDM (n = 1,523)	Used EDM >6 mo ago (n = 249)	Used EDM less than monthly in previous 6 mo (n = 258)	Used EDM approximately monthly in previous 6 mo (n = 119)	Used EDM at least weekly in previous 6 mo (n = 101)
Used EDM approximately monthly in previous 6 mo	1.37 (0.14)[§]	0.59 (0.17)[§]	0.49 (0.16)[§]	—	0.21 (0.22)
Used EDM at least weekly in previous 6 mo	1.15 (0.17)[§]	0.38 (0.20)	0.28 (0.19)	−0.21 (0.22)	—
Sexual sensation-seeking, mean (SD)[‡]	28.2 (6.47)	30.0 (5.84)	31.0 (5.78)	32.8 (5.65)	32.0 (6.44)
Never	—	−1.82 (0.43)[§]	−2.8 (0.42)[§]	−4.62 (0.57)[§]	−3.81 (0.67)[§]
Used EDM >6 mo ago	1.82 (0.43)[§]	—	−1.03 (0.55)	−2.80 (0.67)[§]	−2.0 (0.75)
Used EDM less than monthly in previous 6 mo	2.84 (0.41)[§]	1.03 (0.55)[§]	—	1.77 (0.66)	−0.97 (0.75)
Used EDM approximately monthly in previous 6 mo	4.62 (0.57)[§]	2.80 (0.67)[§]	1.77 (0.66)	—	0.80 (0.84)
Used EDM at least weekly in previous 6 mo	3.81 (0.67)[§]	2.00 (0.75)	0.97 (0.75)	−0.80 (0.84)	—

EDM = erectile dysfunction medication; GAD = Generalized Anxiety Disorder Assessment; PHQ = Patient Health Questionnaire.
[‡]$P < .001$.
[§]Statistically significant; adjusted for familywise error.

Reasons for Use

Of all men who had used an EDM in the previous 6 months, the most common reasons cited for its use were to maintain an erection for longer (63.6%) and make it easier to attain an erection (56.1%). Those who used an EDM monthly or less frequently in the previous 6 months also were more likely to cite the need to counter the effects of other drugs (40.6%) as reasons for its use. GBM who used EDMs at least weekly were more likely to cite difficulties getting an erection (53.5%) as reasons for its use (Table 3).

Covariates of EDM Use in Previous 6 Months

In univariate analyses, GBM who were older, of Anglo-Celtic background, university educated, reported being positive for HIV, and more socially engaged with gay men were significantly more likely to have used an EDM in the previous 6 months (Table 4). EDM use in the previous 6 months also was associated with lower scores on the GAD scales, higher scores on the sexual sensation-seeking scale, having more sex partners, having group sex, reporting CLAI with casual partners and fuckbuddies, and using "party drugs" to enhance sex.

In the multivariate analysis, being older, being positive for HIV, being more socially engaged with gay men, scoring higher on the sexual sensation-seeking scale, having engaged in group sex, engaging in CLAI with fuckbuddies, and using drugs to enhance sex were independently associated with EDM use in the previous 6 months (Table 4).

Covariates of at Least Weekly EDM Use

In univariate analyses, GBMs who were older, of Anglo-Celtic background, university educated, had more sex partners, and had CLAI with casual partners were significantly more likely to have used an EDM weekly compared with those who used an EDM less frequently in the previous 6 months (Table 4). At least weekly use of EDM also was associated with higher scores on the GAD.

In a multivariate analysis, being older, having engaged in CLAI with casual partners, and scoring higher on the GAD were independently associated with weekly EDM use in the previous 6 months (Table 4).

Concurrent Polydrug Use With EDM

In a separate multivariate analysis looking only at concurrent polydrug use with EDM, any use of an EDM in the previous 6 months was independently associated with the use of amyl nitrite (aOR = 2.58; 95% = 2.01−3.30; $P < .001$), γ-hydroxybutyrate (aOR = 3.36; 95% = 2.19−5.12; $P < .001$),

Table 2. Sexual behavior and illicit drug use in previous 6 months according to use of EDM (N = 2,250)

	Never used EDM (n = 1,523)	Used EDM >6 mo ago (n = 249)	Used EDM less than monthly in previous 6 mo (n = 258)	Used EDM approximately monthly in previous 6 mo (n = 119)	Used EDM at least weekly in previous 6 mo (n = 101)
Number of sexual partners, median (quartiles)[‡]	2 (1–8)	5 (1–15)	10 (3–25)	14 (5–30)	20 (5–50)
Number of sexual partners, n (%)					
No partner	207 (13.6)[§]	24 (9.6)	8 (3.1)[§]	1 (0.8)[§]	2 (2.0)
≤10	979 (64.3)[§]	143 (57.4)	108 (41.9)	60 (50.4)[§]	56 (55.4)[§]
>10	292 (19.2)[§]	74 (29.7)	108 (41.9)[§]	60 (50.4)[§]	56 (55.4)[§]
Not stated	45 (3.0)	8 (3.2)	8 (3.1)	6 (5.0)	4 (4.0)
Sex with boyfriends, n (%)					
No boyfriend	994 (65.3)	149 (59.8)	157 (60.9)	64 (53.8)	64 (63.4)
No anal intercourse	37 (2.4)	6 (2.4)	9 (3.5)	3 (2.5)	3 (3.0)
Condom use only	65 (4.3)	7 (2.8)	7 (2.7)	7 (5.9)	6 (5.9)
Any condom-less anal intercourse	382 (25.1)	79 (31.7)	77 (29.8)	39 (32.8)	24 (23.8)
Not stated	45 (3.0)	8 (3.2)	8 (3.1)	6 (5.0)	4 (4.0)
Sex with fuckbuddy, n (%)[‡]					
No fuckbuddies	1,040 (68.3)[§]	143 (57.4)	118 (45.7)[§]	44 (37.0)[§]	38 (37.6)[§]
No anal intercourse	38 (2.5)	8 (3.2)	7 (2.7)	4 (3.4)	3 (3.0)
Condom use only	167 (11.0)	26 (10.4)	35 (13.6)	11 (9.2)	13 (12.9)
Any condom-less anal intercourse	233 (15.3)[§]	64 (25.7)	90 (34.9)[§]	54 (45.4)[§]	43 (42.6)[§]
Not stated	45 (3.0)	8 (3.2)	8 (3.1)	6 (5.0)	4 (4.0)
Sex with casual partners, n (%)[‡]					
No casual partners	688 (45.2)[§]	77 (30.9)	41 (15.9)[§]	19 (16.0)[§]	14 (13.9)[§]
No anal intercourse	83 (5.4)[§]	25 (10.0)	20 (7.8)	14 (11.8)	6 (5.9)
Condom use only	378 (24.8)	59 (23.7)	73 (28.3)	31 (26.1)	20 (19.8)
Any condom-less anal intercourse	329 (21.6)[§]	80 (32.1)	116 (45.0)[§]	49 (41.2)[§]	57 (56.4)[§]
Not stated	45 (3.0)	8 (3.2)	8 (3.1)	6 (5.0)	4 (4.0)
Group sex, n (%)[‡]					
No group sex	1,124 (73.8)[§]	151 (60.6)	115 (44.6)[§]	49 (41.2)[§]	35 (34.7)[§]
Any group sex	310 (20.4)[§]	83 (33.3)	129 (50.0)[§]	63 (52.9)[§]	58 (57.4)[§]
Not stated	89 (5.8)	15 (6.0)	14 (5.4)	7 (5.9)	8 (7.9)
Recent illicit drug use, n (%)[‖]					
No recent drug use[‡]	345 (22.7)[§]	50 (20.1)	26 (10.1)[§]	9 (7.6)[§]	14 (13.9)
Used amyl nitrite[‡]	373 (24.5)[§]	96 (38.6)	139 (53.9)[§]	65 (54.6)[§]	49 (48.5)[§]
Used cannabis[‡]	412 (27.1)[§]	80 (32.1)	100 (38.8)[§]	37 (31.1)	32 (31.7)
Used ecstasy[‡]	204 (13.4)[§]	63 (25.3)[§]	77 (29.8)[§]	33 (27.7)[§]	20 (19.8)
Used methamphetamine or amphetamine (speed)[‡]	69 (4.5)[§]	25 (10.0)	26 (10.1)	7 (5.9)	8 (7.9)
Used cocaine[‡]	135 (8.9)[§]	49 (19.7)	57 (22.1)	24 (20.2)	16 (15.8)
Used crystal methamphetamine[‡]	70 (4.6)[§]	44 (17.7)[§]	84 (32.6)[§]	40 (33.6)[§]	31 (30.7)[§]
Used GHB[‡]	31 (2.0)[§]	21 (8.4)	53 (20.5)[§]	31 (26.1)[§]	20 (19.8)[§]
Used ketamine[‡]	31 (2.0)[§]	11 (4.4)	18 (7.0)	13 (10.9)[§]	12 (11.9)[§]
Used LSD[†]	50 (3.3)[§]	14 (5.6)	11 (4.3)	2 (1.7)[§]	4 (4.0)[§]
Heroin[¶]	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	1 (1.0)

(continued)

Table 2. Continued

	Never used EDM (n = 1,523)	Used EDM >6 mo ago (n = 249)	Used EDM less than monthly in previous 6 mo (n = 258)	Used EDM approximately monthly in previous 6 mo (n = 119)	Used EDM at least weekly in previous 6 mo (n = 101)
Used drugs to enhance sex, n (%)[‡]					
Never	1,418 (93.1)[§]	192 (77.1)[§]	164 (63.6)[§]	68 (57.1)[§]	63 (62.4)[§]
Once	39 (2.6)[§]	25 (10.0)[§]	15 (5.8)	9 (7.6)	4 (4.0)
More than once	66 (4.3)[§]	32 (12.9)	79 (30.6)[§]	42 (35.3)[§]	34 (33.7)[§]

EDM = erectile dysfunction medication; GHB = γ-hydroxybutyrate; LSD = lysergic acid diethylamide.
[†]$P < .01$; [‡]$P < .001$.
[§]Statistically significant; adjusted for familywise error.
[‖]Items are not mutually exclusive; could have used multiple drugs.
[¶]Numbers are too small to interpret.

and crystal methamphetamine (aOR = 3.52; 95% = 2.51−4.92; $P < .001$).

DISCUSSION

Most men in the FLUX Study had never used an EDM. Men who used an EDM more recently and more often tended to be somewhat older. The age distribution of EDM use was similar to what has been found elsewhere in that older men were more likely to use an EDM and to use it more frequently.[13] Although older men were more likely to use an EDM in our sample, other studies have found that younger men also experience erectile dysfunction and sometimes use an EDM to treat that condition.[32] Jannini et al[32] found that 1 in 20 younger men in their sample (18−39 years old) reported erectile dysfunction, but only about half were using an EDM. Some younger men in our sample might have had erectile dysfunction, but the differences we observed in the use of EDM also might reflect differences in our sample of mostly gay men and how EDMs are used in some gay subcultures.

Although EDM use is intended to treat erectile dysfunction, many men use EDMs without having such a medical condition.[1−5] Nonetheless, it is likely that those who do have erectile dysfunction would tend to use an EDM on a more frequent basis. The reasons men gave for their use of EDMs appear to support this. Although weekly and less frequent users of EDMs cited "maintaining an erection" and "make it easier to get hard" as reasons for their EDM use, those who used EDM at least weekly cited "difficulty in attaining or maintaining an erection" as a reason for their EDM use. Although we cannot definitively determine whether men in our sample had erectile dysfunction, there is clear evidence to suggest men were using EDMs for sex partying, in which EDMs are usually used to extend their sexual capacity and to counter the effect of other drugs.

In this sample, EDMs appeared to be used primarily to enhance aspects of intensive sex partying: to maintain an erection for longer and to counter the effects of other drugs on the ability to attain and maintain an erection. Users of EDMs also were more likely to engage in those practices that have been described as aspects of intensive sex partying. Our data support the previous contention that, in the context of intensive sex partying, GBM often use EDMs to enhance and extend the sexual

Table 3. Reasons for use of EDM in previous 6 months (n = 478)

	Used EDM in previous 6 mo (n = 377 [78.95]), n (%)	Used EDM at least weekly in previous 6 mo (n = 101 [21.1%]), n (%)	Total (n = 478), n (%)
To counter effects of other drugs	153 (40.6)	32 (31.7)	185 (38.7)
To make condom use easier	77 (20.4)	29 (28.7)	106 (22.2)
To see what it was like[‡]	64 (17.0)	1 (1.0)	65 (13.6)
To make it easier to "get hard"*	200 (53.1)	68 (67.3)	268 (56.1)
Someone else wanted me to use it	23 (6.1)	2 (2.0)	25 (5.2)
For fun[‡]	120 (31.8)	10 (9.9)	130 (27.2)
To maintain erection longer*	230 (61.0)	74 (73.3)	304 (63.6)
Difficulty attaining or maintaining erection[‡]	117 (31.0)	54 (53.5)	171 (35.8)
Needs EDM to take insertive position[†]	50 (13.3)	25 (24.8)	75 (15.7)

EDM = erectile dysfunction medication.
*$P < .05$; [†]$P < .01$; [‡]$P < .001$.

Table 4. Associations with use of erectile dysfunction medication

| | Any use in previous 6 mo vs no use in previous 6 mo (n = 2,250) | | | | At least weekly use in previous 6 mo vs less frequent use in previous 6 mo (n = 478) | | | |
| | Univariate analysis | | Multivariate analysis | | Univariate analysis | | Multivariate analysis | |
	OR (95% CI)	P value for trend	aOR (95% CI)	P value for trend	OR (95% CI)	P value for trend	aOR (95% CI)	P value for trend
Continuous variables, n (%)								
Socially engaged with other gay men	1.46 (1.37–1.57)	<.001	1.20 (1.11–1.31)	<.001	1.05 (0.91–1.22)	.481		
Sensation-seeking scale	1.09 (1.07–1.11)	<.001	1.04 (1.02–1.07)	<.001	1.01 (0.97–1.05)	.563		
Binary categorical variables, n (%)								
>35 y old	6.05 (4.86–7.53)	<.001	4.86 (3.73–6.33)	<.001	3.71 (2.03–6.78)	<.001	4.28 (2.17–8.43)	<.001
Anglo-Celtic background	1.89 (1.47–2.43)	<.001			1.94 (1.01–3.71)	.047		
University education	1.43 (1.16–1.76)	.001			0.66 (0.43–1.03)	.069		
HIV+	6.17 (4.46–8.52)	<.001	2.53 (1.71–3.75)	<.001	0.73 (0.41–1.30)	.280		
Severe PHQ	0.67 (0.41–1.10)	.113			1.27 (0.45–3.63)	.651		
Severe GAD	0.63 (0.40–0.99)	.048			2.60 (1.09–6.22)	.037	3.78 (1.47–9.75)	.006
>10 partners	3.39 (2.74–4.19)	<.001			1.55 (1.00–2.41)	.053		
Relationship with regular partner	1.18 (0.94–1.47)	.151			0.80 (0.52–1.24)	.317		
Condom-less anal intercourse with fuckbuddies	3.19 (2.56–3.99)	<.001	1.75 (1.32–2.33)	<.001	1.20 (0.77–1.87)	.424		
Condom-less anal intercourse with casual partners	2.89 (2.34–3.57)	<.001			1.66 (1.07–2.59)	.024	1.83 (1.13–2.96)	.015
Group sex	3.85 (3.11–4.75)	<.001	1.74 (1.32–2.29)	<.001	1.30 (0.83–2.02)	.246		
Used drugs to enhance sex	6.17 (4.83–7.88)	<.001	3.89 (2.86–5.30)	<.001	0.97 (0.61–1.52)	.878		
Used amyl nitrite*	3.97 (3.17–4.98)	<.001			0.77 (0.47–1.24)	.273		
Used marijuana*	1.51 (1.21–1.88)	<.001			0.82 (0.50–1.32)	.409		
Used ecstasy*	2.29 (1.79–2.92)	<.001			0.60 (0.35–1.04)	.068		
Used methamphetamine or amphetamine (speed)*	1.75 (1.19–2.57)	.004			0.90 (0.40–2.01)	.789		
Used cocaine*	2.33 (1.78–3.07)	<.001			0.69 (0.38–1.25)	.218		
Used crystal methamphetamine*	7.64 (5.82–10.04)	<.001			0.875 (0.54–1.42)	.587		
Used GHB*	9.64 (6.78–13.71)	<.001			0.80 (0.47–139)	.434		
Used ketamine*	4.26 (2.75–6.60)	<.001			1.52 (0.75–3.09)	.247		
Used LSD*	1.01 (0.59–1.75)	.963			1.15 (0.37–3.60)	.814		
Used heroin*	7.42 (0.67–82.03)	.102			3.84 (0.24–61.89)	.343		

aOR = adjusted odds ratio; GAD = Generalized Anxiety Disorder Assessment; GHB = γ-hydroxybutyrate; LSD = lysergic acid diethylamide; OR = odds ratio; PHQ = Patient Health Questionnaire.
*Omitted from multivariate model because of possible multicollinearity.

experience and to counter the effects of other party drugs.[1,14] Although some GBM, particularly those who use an EDM at least weekly, might do so for specific medical conditions involving erectile dysfunction, much of the use in our sample appears to be at least as often for "recreational" as it is for therapeutic purposes.

Peer influence and social connection appear to be factors associated with the use of EDMs by GBM. Those who used an EDM recently were significantly more likely than non-users to socialize with friends who also used EDMs. Those who were more socially engaged with other gay men were significantly more likely to use EDMs. Overall, EDM use appears to be relatively common among GBM, and most of those who used an EDM reported having gay friends who also used it, suggesting that EDM use is fairly normalized among GBM. Fewer than one in five GBM who did not use an EDM themselves reported having friends who used it. In addition, more sexually active men and those who participated in intensive sex partying were particularly likely to report EDM use in the previous 6 months.

HIV-positive men tend to be older[33] and are more likely to be involved in subcultures in which intensive sex partying occurs,[16,34] which are associated with EDM use. Nonetheless, self-reported HIV-positive status was not independently associated with at least weekly EDM use. This suggests that the use of EDMs for erectile dysfunction might be no more common among HIV-positive GBM than among other men and that they are at least as likely to be using EDMs recreationally.

Men who used an EDM in the previous 6 months reported fewer symptoms of anxiety and depression than those who did not use EDMs. However, those who used EDMs at least weekly reported more symptoms of anxiety than those who used EDMs less frequently. Our data provide no evidence of depression among users of EDMs overall, but those who used EDMs on a more frequent basis might be subject to symptoms of anxiety. Our data cannot determine whether these symptoms are related to their use of EDMs or, possibly, to the reasons for their more frequent use of EDMs. Those who used EDMs more frequently were more likely to cite erectile dysfunction as a reason for their use of EDMs, and erectile dysfunction has been associated with poor mental health outcomes.[35,36] In contrast, those men who use EDMs less frequently appeared less likely to do so for therapeutic purposes and they tended to have lower scores on depression and anxiety than the men who used EDMs at least weekly or the men who never used EDMs.

LIMITATIONS AND STRENGTHS

We did not use a standardized tool to determine a diagnosis of erectile dysfunction in our sample. However, participants were asked for their reasons for EDM use, including whether they experienced erectile difficulties. Future studies of EDM use among GBMs should consider including standardized tools in addition to detailed investigation of the use of EDMs within gay community sex partying subcultures. Participants in this study were broadly similar to other samples of Australian GBMs.[37,38] Nonetheless, it was a volunteer online convenience sample and might not be representative of all GBM in Australia. Extrapolating these findings to other contexts might be limited by differences between Australia and other locations. Also, this was a cross-sectional analysis of baseline data from a cohort study and, as such, it is not possible to determine any causative or temporal relations in the data.

The FLUX Study is Australia's first large-scale study specifically looking at drug use among GBM among whom prevalence is known to be higher than in the general population. It includes comprehensive detailed data on history of use and how and why men use drugs. Our large community-based national sample is geographically dispersed and includes men of all ages and those who are engaged and those who are not engaged with gay community life. Our online methodology potentially decreases social desirability bias in reporting illegal or stigmatized behaviors.[39–41]

CONCLUSION

Although some GBMs use EDMs specifically for erectile dysfunction, many also use EDMs to enhance their sexual experiences. Often this occurs in the context of intensive sex partying, which can include risky sexual behavior. GBM who use EDMs also use illicit drugs at higher rates compared with those who do not use EDMs. The use of EDMs in the context of intensive sex partying (which includes the combined use of EDMs and illicit drugs), with the associated potential for increased risk of HIV transmission, indicates a need to consider the use of EDMs among GBM in HIV prevention. Specifically, there is a need for health promotion initiatives for men who engage in intensive sex partying to address the potential of EDMs to amplify the risk of sexually transmissible infection, including HIV, transmission. These initiatives need to acknowledge the emic value of the EDM within particular sexual cultures, its relation to CLAI, and how this might conflict with harm minimization approaches.

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3.1.4   Chapter three summary

While the majority of gay and bisexual men in this sample had never used erectile dysfunction medications, those who did mainly appeared to be using them recreationally, often in the context of chemsex. Nonetheless, some men who used erectile dysfunction medications on a weekly basis may have been doing so for therapeutic purposes.

Use of erectile dysfunction medications was associated with use of illicit drugs and sexual behaviours that are in turn associated with HIV infection. These included condomless anal intercourse with casual partners, engaging in group sex, and using illicit drugs to engage in chemsex. Factors associated with use of erectile dysfunction medications in this sample are similar to factors associated with the use of illicit drugs for chemsex found in other studies,[1,13-20] including use of methamphetamine.[1,20]

Prestage et al. (2009) identified use of both methamphetamine and erectile dysfunction medications as predicting subsequent HIV infection in the *HIM Study*. Despite being based on the findings from the *HIM Study,* the *Australian PrEP Guidelines,*[21,22] only specify the use of methamphetamine as a criterion for access. Neither use of erectile dysfunction medications nor any other illicit drug was included in the *Australian PrEP Guidelines*.

Chapter Four

Casting a wider net

4.1 Use of gamma-hydroxybutyrate to engage in chemsex and its associations with HIV risk behaviours

4.1.1 Publication details

4.1.2 Thesis aims related to this chapter

Thesis aim 2: Describe the characteristics of Australian gay and bisexual men who engage in chemsex and the types of drugs used.

Thesis aim 3: Describe the extent to which men who engage in chemsex also engage in behaviours that may represent potential HIV risk.

4.1.3 Chapter four in context

In Australia, use of gamma-hydroxybutyrate among gay and bisexual men has been steadily increasing over time.[4] Prior to the analysis reported in this chapter, there had been little investigation of the use of gamma-hydroxybutyrate specifically for its association with HIV risk behaviours.

I describe the characteristics of gay and bisexual men who use gamma-hydroxybutyrate to engage in chemsex before the widespread availability of PrEP in Australia. I also explore factors that may represent potential HIV risk, and whether use of illicit drugs other than methamphetamine might be linked to chemsex networks and therefore potentially play a role in HIV infection.

Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men – results from the Flux Study

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Abstract. **Background**: Gamma-hydroxybutyrate (GHB) use among gay and bisexual men (GBM) has increased in recent years. It is commonly cited as a sexual-enhancement drug. There is, however, little evidence for factors associated with GHB use or the consequences of its use among GBM. **Aim**: Factors associated with GHB use, its relationship to sexual risk behaviour, and the contexts, consequences, and motivations for its use were examined. **Methods**: The Following Lives Undergoing Change (Flux) Study is an online prospective observational study of Australian GBM. At baseline, a total of 3190 GBM provided details about their use of GHB. Data on frequency, methods, pleasures and consequences of their drug use, alongside key demographic variables were collected. **Results**: Mean age was 35.0 years. One in five men (19.5%) had a history of GHB use and 5.4% reported use within the past 6 months, with 2.7% having used it monthly or more frequently. Overdose had been experienced by 14.7%, this was more common among men who used GHB at least monthly. Being HIV-positive, having more gay friends, greater social engagement with gay men who use drugs, a greater number of sexual partners, group sex, and condomless anal intercourse with casual partners were independently associated with GHB use in the past 6 months. Greater social engagement with gay men who use drugs and group sex were independently associated with at least monthly use. More frequent GHB use was independently associated with experiencing overdose among GHB users. **Conclusion**: Most men used GHB infrequently and it was often used explicitly to enhance sexual experiences, often in the context of intensive sex partying. Men who used GHB frequently, were at greater risk of overdose and other negative health outcomes. GHB use should be considered alongside other drugs that have been implicated in sexual risk behaviour and HIV transmission. Harm-reduction interventions need to consider the particular impact of frequent GHB use.

Introduction

Globally, gay and bisexual men (GBM) use most illicit drugs, including gamma-hydroxybutyrate (GHB), at higher rates than their heterosexual male counterparts.[1–7] Use of GHB, in particular, has been increasing among GBM in recent years,[8,9] specifically for sexual purposes.[10–12] Its increasing use has been accompanied by growing concerns about overdose and other negative health outcomes.[13]

Also known as liquid ecstasy, fantasy, G, and Gina, GHB was originally developed as an anaesthetic,[14–16] but its applications

were limited by adverse side-effects, including vomiting and seizures.[17] Known effects of using GHB include, but are not limited to, euphoria,[18–20] increased libido,[10–12,21,22] lowered inhibitions[11,22] and loss of motor control.[20,23] The euphoric and stimulating effects of GHB were discovered by recreational users in the mid-1990s.[13] GHB is usually swallowed in liquid form in non-alcoholic beverages, as mixing with alcohol can be dangerous.[20,24,25] Nonetheless, injecting and rectal administration (known as shafting or shelving) of this drug is not unknown. As a central nervous system depressant,[26] GHB has a high overdose

liability, particularly when used in combination with alcohol and other depressants.[13]

Overdose from GHB has become a particular problem.[27–29] The UK coroner noted a 119% rise in GHB-related deaths between 2014 and 2015, with one person, on average, dying from a GHB-related overdose every 12 days.[30] Although GHB has a high overdose liability, overdoses are not always identified, even through autopsy, and are undercounted.[31,32] Some evidence suggests high rates of overdose among GBM users of GHB.[28,33]

In Australia, the use of GHB has fluctuated over time but has been increasing in recent years.[34] In particular, among Australian GBM, GHB use has increased from an estimated 9.8% in 2004 to 13.1% in 2011.[9] Within the Sydney gay community, increased use of GHB has been associated with declining use of ecstasy.[35] Sexual motives have been explicitly ascribed to the use of certain drugs, including crystal methamphetamine,[39] among GBM.[7,36–38] The use of GHB has also been associated with sexual motivation.[11,12]

Using drugs to enhance sex is colloquially referred to as chemsex (chemical sex) or 'party n play'[40,41] and has been associated with sexual risk behaviours and HIV infection among GBM.[37,42–49] Discussions about chemsex often frame drugs as the drivers of 'risky' sex.[41,50,51]

Intensive sex partying describes interrelated practices that involve: being highly sexually active; greater involvement in gay community social and sexual networks; group sex; condomless anal intercourse (CLAI); and use of 'party drugs' to intensify bodily pleasure.[52] Sexual behaviour and HIV risk reduction among GBM has been influenced by gay community norms regarding understandings of pleasure and HIV risk.[53,54] Drug use among GBM, particularly in relation to harm reduction practices, can similarly reflect normative values within specific gay community subcultures.[55]

Drugs commonly cited as being used in intensive sex-partying contexts include: crystal methamphetamine; amyl nitrite; and erectile dysfunction medication (EDM).[36,48] GHB is also commonly cited as a sexual-enhancement drug,[10–12,21,22] so its use also likely applies to intensive sex partying contexts, but there is little specific evidence of the role of GHB in intensive sex partying or of its impact on sexual risk behaviours.

Drug use, particularly dependent drug use, and sexual risk behaviour have often been associated with poor mental health outcomes.[51,56] As well as being at a greater risk of HIV infection, and using drugs at higher rates than their heterosexual counterparts, GBM also have higher rates of anxiety and depression.[57–60] The possible relationship between GHB use and mental health, and its role in drug overdose, among GBM is unknown.

Aim

In this paper, we use baseline data from a cohort of Australian GBM to investigate factors associated with the use of GHB, its relationship to sexual risk behaviour, including chemsex in particular, and the contexts, consequences, and motivations for its use.

Methods
Procedures

The Following Lives Undergoing Change (Flux) Study is an entirely online automated prospective observational study of Australian GBM. Participants were recruited between August 2014 and July 2017 through Facebook, gay community websites and online media, mobile phone applications, and gay sexual networking websites.

Potential participants were directed to the study website for enrolment, where they were provided details of the study and what was required for participation. Informed consent was obtained online and stored separately to their de-identified survey responses. The baseline self-completed questionnaire included ~200 questions. No incentives were offered for participation at baseline. The methods are described in detail elsewhere.[61] Ethical approval was granted by the Human Research Ethics Committee of UNSW Sydney (HC14075).

Measures

The online baseline questionnaire included demographic items, questions on sexual identity and social networks, HIV testing history and self-reported serostatus, sexual behaviour with men, and attitudes and beliefs about drug use. Men reported their sexual behaviour in the past 6 months with three categories of partner types:[62] 'boyfriends' (a regular committed partner with whom they maintained a romantic relationship); 'fuckbuddies' (non-romantic regular partners); and casual partners. With each partner type they reported whether they had engaged in anal intercourse and whether they had used a condom for anal intercourse. Men described their lifetime and recent (i.e. past 6 months) use of licit and illicit drugs, including GHB, as well as the method and frequency of recent use (e.g. once or twice in the past 6 months, at least monthly, weekly, or daily). They were also asked about their history of having been on a GHB 'drug binge', defined as using continuously over a period of at least 48 h. There were also questions about the reasons for their use of GHB, including whether they used it to 'enhance sex', and the perceived consequences of their drug use, including items such as meeting new friends, becoming sick, and (self-defined) 'unsafe sex'. Subjective experiences of overdose were included. Participants were asked if they had ever overdosed, overdosed once, or more than once, in relation to all party drugs, including GHB. A definition of overdose was provided.

The scale measuring Social Engagement with Gay Men, a previously used measure of social connectedness with gay men was included, and is based on two items, the proportion of friends who are gay men and the amount of free time spent with gay male friends.[63] Higher scores indicated greater social engagement with gay men. We also included a modified version of this scale to measure social engagement with gay friends who use drugs with two equivalent items, the proportion of gay friends who use drugs and the amount of free time spent with gay friends who use drugs.

To address intensive sex partying,[52] questions about group sex and party and play (chemsex) sessions were also included. The Generalised Anxiety Disorder Assessment, a seven-item self-report measure, assesses symptoms of generalised anxiety disorder,[64] and the Patient Health Questionnaire, a nine-item self-report measure, assesses symptoms of depression.[65]

Participants and sample

Men, who lived in Australia and were aged 16.5 years or more, were eligible for participation if they identified as gay or bisexual or had sex with another man in the previous year. During 2014, 753 men were recruited, with a further 1461 recruited in 2015, and 1039 in 2017. Overall, 3253 men completed the minimum data requirements for the online questionnaire. There were 63 men who did not respond to questions about their GHB use and were excluded from this analysis, leaving a sample of 3190 men. Compared with the 3190 men included here, the 63 excluded men were less likely to be tested for HIV (1.6% *v.* 17.3%; $P < 0.01$), more likely to be HIV-positive (20.6% *v.* 6.2%; $P < 0.001$), and reported more sex partners in the past 6 months (mean = 33.3 *v.* mean = 14.7; $P = 0.001$) but were otherwise similar.

Analysis

Data were analysed using SPSS ver. 24 software (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used to characterise the types of men who used GHB. For univariate analyses of whether participants had used GHB in the past 6 months, and, separately, of whether they had used GHB at least monthly, we included: age, cultural background, education, occupation, HIV testing history and serostatus, social engagement with gay men and with gay friends who use drugs, relationship status, sexual risk behaviour, and licit and illicit drug use. Categorical variables were analysed using Pearson's χ^2 test, and continuous variables were analysed using one-way analysis of variance. Assumptions of normality were satisfactory as determined by the central limit theory. We used type I error of 5% for these analyses.

We compared all men who had not used GHB in the past 6 months with all those who had used GHB within the past 6 months. Also, among men who had used GHB within the past 6 months, we compared men who reported having used GHB at least monthly or more often with those who had used it less than monthly. In a separate analysis to estimate the statistical associations for overdose among men who had used GHB within the past 6 months, we compared men who reported having experienced drug overdose with those who had not experienced an overdose.

To estimate statistical associations, we used a binary logistic backward stepwise multiple regression analysis to control for confounding factors and presented the adjusted odds ratios and 95% confidence intervals. Univariate associations with a *P*-value of less than 0.10 in univariate analyses were included in the multivariate analyses. Multivariate associations with a *P*-value of less than 0.05 were retained in the final model.

Results

Characteristics of the sample

The mean age of the 3190 men was 35.0 years (s.d. 13.3; Table 1). The majority of participants identified as gay or homosexual (88.3%), were of Anglo-Celtic background (71.3%), were university-educated (54.5%) and in full-time employment (56.8%). Most men (82.3%) had been tested for HIV and 6.2% reported they had tested HIV-positive. More than

a quarter (29.0%) reported that most of their friends were gay and 19.1% spent much of their free time with gay friends.

Approximately one-third (34.5%) of men reported having more than 10 male sex partners in the past 6 months, and one in five (19.5%) had engaged in group sex (Table 2). One-third (34.7%) indicated they had a regular partner (or boyfriend). More than one-third (37.9%) reported sex with fuckbuddies and nearly two-thirds (61.6%) reported sex with casual partners.

The majority (52.7%) of men reported having used illicit drugs in the past 6 months (Table 2). Commonly used drugs included amyl nitrite (35.1%), cannabis (30.0%), ecstasy (17.7%), cocaine (14.0%), and crystal methamphetamine (12.0%). About one in six (16.9%) reported using drugs to enhance their sexual experiences. More than one-third (36.4%) had used EDM in the past 6 months.

GHB use

Most (80.4%) had no lifetime history of GHB use, but 19.5% reported having ever used it. One in nine participants (11.4%) had last used GHB more than 6 months ago, and 5.4% reported using GHB within the past 6 months, including 2.7% who reported using it at least monthly. Men that enrolled during 2015 had somewhat lower rates of GHB use ($P < 0.001$).

Compared with men who had never used GHB, those who had used GHB were more likely to be university-educated and in professional or managerial employment (Table 1). They were also more likely to have ever tested for HIV and to report a HIV-positive serostatus. Men who used GHB at least monthly in the past 6 months were slightly younger than those who had used it less than monthly. Men who used GHB tended to be more socially engaged with other gay men in general and with other gay men who use drugs specifically. No statistical associations were observed between use of GHB, ever or recently, and scores on the measures of depression and anxiety.

Men who had used GHB reported a greater number of sexual partners in the past 6 months than those who had not used GHB (Table 2). They were also more likely to have engaged in CLAI with boyfriends, fuckbuddies, and casual partners, and to have engaged in group sex. Men who used GHB were more likely to have used most illicit drugs and to report having used drugs to enhance sex, and they were more likely to have used EDM. Notably, most recent users of GHB also reported having used crystal methamphetamine and amyl nitrite.

Overall, one in six (16.4%, $n = 524$) reported that they considered their gay friends' use of GHB as at least 'somewhat acceptable,' including 6.0% ($n = 192$) who indicated that it was 'very acceptable.' Among men who had never used GHB, 1.8% ($n = 45$) reported that their friends' use of GHB was very acceptable. This was true of 30.8% ($n = 53$) of men who had used GHB less than monthly in the past 6 months, and 44.8% ($n = 39$) of men who had used GHB at least monthly ($P < 0.001$).

Among men who had used GHB in the past 6 months, the three most common ways of obtaining GHB were from a dealer (43.6%), from gay friends (29.3%) or from a sex partner (10.8%; Table 3). More than half the men (58.3%)

Table 1.   Characteristics of sample according to use of with gamma-hydroxybutyrate (GHB; *n* = 3190)
* *P* < 0.05; ** *P* < 0.01; *** *P* < 0.001

Characteristics *n* (%)	Never used GHB *n* = 2566 (80.4%)	Used GHB more than 6 months ago *n* = 365 (11.4%)	Used GHB less than monthly in past 6 months *n* = 172 (5.4%)	Used GHB at least monthly in past 6 months *n* = 87 (2.7%)
Age (years)***				
Mean (s.d.)**	34.4 (14.0)	37.3 (10.0)	38.0 (10.3)	36.4 (10.2)
≤ 20	393 (15.3)	2 (0.5)	2 (1.2)	1 (1.1)
21–30	900 (35.1)	99 (27.1)	43 (25.0)	29 (33.3)
31–40	494 (19.3)	138 (37.8)	61 (35.5)	29 (33.3)
41–50	355 (13.8)	81 (22.2)	47 (27.3)	19 (21.8)
Over 50	423 (16.5)	45 (12.3)	19 (11.0)	9 (10.3)
Year of recruitment***				
2014	572 (22.3)	108 (29.6)	46 (26.7)	22 (25.3)
2015	1188 (46.3)	138 (37.8)	57 (33.1)	21 (24.1)
2017	806 (31.4)	119 (32.6)	69 (40.1)	44 (50.6)
Cultural background				
Anglo-Celtic	1804 (70.3)	280 (76.7)	124 (72.1)	67 (77.0)
Other	749 (29.2)	83 (22.7)	47 (27.3)	20 (23.0)
Not stated	13 (0.5)	2 (0.5)	1 (0.6)	0 (0.0)
Education level*				
Less than university level	1195 (46.6)	154 (42.2)	58 (33.7)	37 (42.5)
Undergraduate level	789 (30.7)	108 (29.6)	60 (34.9)	28 (32.2)
Postgraduate level	578 (22.5)	102 (27.9)	53 (30.8)	22 (25.3)
Not stated	4 (0.2)	1 (0.3)	1 (0.6)	0 (0.0)
Occupation***				
Managerial	382 (14.9)	95 (26.0)	34 (19.8)	20 (23.0)
Professional	687 (26.8)	120 (32.9)	54 (31.4)	33 (37.9)
Other white collar	364 (14.2)	46 (12.6)	23 (13.4)	6 (6.9)
Other	274 (10.7)	41 (11.2)	19 (11.0)	8 (9.2)
Not in work	822 (32.0)	54 (14.8)	40 (23.3)	19 (21.8)
Did not answer	37 (1.4)	9 (2.5)	2 (1.2)	1 (1.1)
Tested for HIV***				
Never tested	537 (20.9)	13 (3.6)	2 (1.2)	1 (1.1)
Tested	2022 (78.8)	347 (95.1)	170 (98.8)	86 (98.9)
Did not answer	7 (0.3)	5 (1.4)	0 (0.0)	0 (0.0)
HIV status***				
HIV-positive	102 (4.0)	54 (14.8)	27 (15.7)	14 (16.1)
HIV-negative	1899 (74.0)	291 (79.7)	142 (82.6)	72 (82.8)
Unknown or untested	565 (22.0)	20 (5.5)	3 (1.7)	1 (1.1)
Patient Health Questionnaire depression status				
Minimal	1025 (39.9)	149 (40.8)	78 (45.3)	31 (35.6)
Mild	631 (24.6)	93 (25.5)	52 (30.2)	22 (25.3)
Moderate	328 (12.8)	46 (12.6)	16 (9.3)	11 (12.6)
Moderately severe	210 (8.2)	24 (6.6)	11 (6.4)	5 (5.7)
Severe	146 (5.7)	22 (6.0)	5 (2.9)	5 (5.7)
Did not answer	226 (8.8)	31 (8.5)	10 (5.8)	13 (14.9)
Generalised Anxiety Disorder anxiety status				
Minimal anxiety	1331 (51.9)	191 (52.3)	103 (59.9)	38 (43.7)
Mild anxiety	544 (21.2)	89 (24.4)	43 (25.0)	21 (24.1)
Moderate anxiety	253 (9.9)	32 (8.8)	10 (5.8)	12 (13.8)
Severe anxiety	186 (7.2)	22 (6.0)	5 (2.9)	5 (5.7)
Did not answer	252 (9.8)	31 (8.5)	11 (6.4)	11 (12.6)
Relationship status				
Not in a relationship	1298 (50.6)	179 (49.0)	87 (50.6)	47 (54.0)
In a relationship	1268 (49.4)	186 (51.0)	85 (49.4)	40 (46.0)
Social engagement with gay menmean (s.d.)				
Socially engaged with other gay men***	3.3 (1.6)	4.0 (1.5)	4.6 (1.5)	5.0 (1.4)
Socially engaged with other gay men who use drugs***	1.9 (1.5)	3.2 (1.5)	4.2 (1.5)	4.9 (1.4)

Table 2. Sexual and drug-use behaviours in past 6 months according to use of gamma-hydroxybutyrate (GHB; *n* = 3190)
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Sexual behaviour and drug use *n* (%)	Never used GHB *n* = 2566 (80.4%)	Used GHB more than 6 months ago *n* = 365 (11.4%)	Used GHB less than monthly in past 6 months *n* = 172 (5.4%)	Used GHB at least monthly in past 6 months *n* = 87 (2.7%)
Number of sexual partners***				
Mean (s.d.)***	11.8 (32.7)	16.6 (27.7)	41.9 (99.5)	39.8 (49.1)
No partner	309 (12.0)	20 (5.5)	0 (0.0)	0 (0.0)
Up to 10	1428 (55.7)	179 (49.0)	48 (27.9)	17 (19.5)
More than 10	759 (29.6)	156 (42.7)	122 (70.9)	63 (72.4)
Not stated	70 (2.7)	10 (2.7)	2 (1.2)	7 (8.0)
Sex with boyfriends**				
No boyfriend	1685 (65.7)	237 (64.9)	108 (62.8)	50 (57.5)
No anal intercourse	74 (2.9)	4 (1.1)	2 (1.2)	3 (3.4)
Sex with condoms only	97 (3.8)	12 (3.3)	4 (2.3)	0 (0.0)
Any condomless anal intercourse	640 (24.9)	102 (27.9)	56 (32.6)	27 (31.0)
Not stated	70 (2.7)	10 (2.7)	2 (1.2)	7 (8.0)
Sex with fuckbuddy***				
No fuckbuddies	1586 (61.8)	202 (55.3)	75 (43.6)	32 (36.8)
No anal intercourse	68 (2.7)	9 (2.5)	1 (0.6)	1 (1.1)
Sex with condoms only	266 (10.4)	28 (7.7)	14 (8.1)	0 (0.0)
Any condomless anal intercourse	576 (22.4)	116 (31.8)	80 (46.5)	47 (54.0)
Not stated	70 (2.7)	10 (2.7)	2 (1.2)	7 (8.0)
Sex with casual partners***				
No casual partners	1012 (39.4)	100 (27.4)	17 (9.9)	5 (5.7)
No anal intercourse	191 (7.4)	19 (5.2)	7 (4.1)	0 (0.0)
Sex with condoms only	571 (22.3)	69 (18.9)	31 (18.0)	13 (14.9)
Any condomless anal intercourse	722 (28.1)	167 (45.8)	115 (66.9)	62 (71.3)
Not stated	70 (2.7)	10 (2.7)	2 (1.2)	7 (8.0)
Group sex***				
No group sex	2147 (83.7)	273 (74.8)	100 (58.1)	41 (47.1)
Any group sex	419 (16.3)	92 (25.2)	72 (41.9)	46 (52.9)
Used drugs to enhance sex***				
Never	2386 (93.0)	230 (63.0)	28 (16.3)	7 (8.0)
Once	61 (2.4)	31 (8.5)	24 (14.0)	3 (3.4)
More than once	119 (4.6)	104 (28.5)	120 (69.8)	77 (88.5)
Used erectile dysfunction medication***				
Never	1867 (72.8)	123 (33.7)	26 (15.1)	14 (16.1)
Less than weekly	562 (21.9)	223 (61.1)	124 (72.1)	51 (58.6)
At least weekly	137 (5.3)	19 (5.2)	22 (12.8)	22 (25.3)
Illicit recent drug use[A]				
Used amyl nitrite***	692 (27.0)	221 (60.5)	132 (76.7)	76 (87.4)
Used cannabis***	629 (24.5)	187 (51.2)	96 (55.8)	44 (50.6)
Used ecstasy***	251 (9.8)	144 (39.5)	114 (66.3)	56 (64.4)
Used meth/amphetamine (speed)***	84 (3.3)	36 (9.9)	33 (19.2)	19 (21.8)
Used cocaine***	202 (7.9)	116 (31.8)	80 (46.5)	49 (56.3)
Used crystal methamphetamine	83 (3.2)	103 (28.2)	121 (70.3)	76 (87.4)
Used ketamine***	30 (1.2)	28 (7.7)	37 (21.5)	37 (42.5)
Used lysergic acid diethylamide (LSD)***	61 (2.4)	24 (6.6)	16 (9.3)	9 (10.3)
Used heroin[B]***	0 (0.0)	1 (0.3)	2 (1.2)	2 (2.3)

[A]Items are not mutually exclusive (i.e. participant could have used multiple drugs).
[B]Numbers too small to interpret.

used their GHB in one dose, and 40.9% spaced their GHB use over a few hours.

Of those who had used GHB in the past 6 months, most (54.1%) indicated that they had never been on a GHB drug binge (Table 3). One in thirteen (7.7%) indicated that the last time they had a GHB drug binge was more than 6 months ago, 25.1% had binge-used GHB less than monthly in the past 6 months and 13.1% had done so at least monthly.

Table 3.   Context of recent gamma-hydroxybutyrate (GHB) use. *n* = 259
* *P* < 0.05; ** *P* < 0.01; *** *P* < 0.001

Characteristics of GHB use *n* (%)	Used GHB less than monthly in past 6 months *n* = 172 (66.4%)	Used GHB at least monthly in past 6 months *n* = 87 (33.6%)
Usual source for obtaining GHB*		
Dealer	64 (37.2)	49 (56.3)
Gay friends	55 (32.0)	21 (24.1)
Sex partner	20 (11.6)	8 (9.2)
Other (mobile phone applications, online sites, straight friends, boyfriend)	33 (19.2)	9 (10.3)
Usage on a single occasion		
Used in a single dose	106 (61.6)	45 (51.7)
Spaced over a few hours	65 (37.8)	41 (47.1)
Did not answer	1 (0.6)	1 (1.1)
Binge use***		
Never binge used GHB	105 (61.0)	26 (29.9)
Last binge used GHB more than 6 months ago	16 (9.3)	4 (4.6)
Binge used GHB less than monthly	41 (23.8)	24 (27.6)
Binge used GHB at least monthly	4 (2.3)	30 (34.5)
Did not answer	6 (3.5)	3 (3.4)
Overdose experience*		
Never overdosed	108 (62.8)	39 (44.8)
Overdosed once	39 (22.7)	25 (28.7)
Overdosed more than once	23 (13.4)	19 (21.8)
Did not answer	2 (1.2)	4 (4.6)
Reasons for use[A]		
It makes me feel horny*	50 (29.1)	29 (33.3)
It was available	42 (24.4)	23 (26.4)
To lose my inhibitions*	37 (21.5)	26 (29.9)
For fun**	28 (16.3)	29 (33.3)
I wanted to feel connected to the other guys*	19 (11.0)	16 (18.4)
Someone else wanted me to use it	21 (12.2)	12 (13.8)
To see what it was like	22 (12.8)	4 (4.6)
Make it easier for me to get fucked***	10 (5.8)	16 (18.4)
To try something different	21 (12.2)	4 (4.6)
I wanted the guy I was having sex with to take charge	10 (5.8)	8 (9.2)
To counter the effects of other drugs**	6 (3.5)	9 (10.3)
Didn't know what it was at the time	1 (0.6)	0 (0.0)

[A]Items are not mutually exclusive (i.e. participant could have cited multiple reasons).

Covariates of GHB use

Men who were older and who were employed in a managerial position were more likely to have used GHB in the past 6 months (Table 4). Compared with men who reported being HIV-negative, HIV-positive men were more likely to have recently used GHB, whereas men who had not been tested or whose HIV status was unknown were less likely to have done so. Greater social engagement with gay friends who use drugs was associated with use of GHB in the past 6 months. Men who reported a greater number of sexual partners, had engaged in group sex, reported CLAI with their boyfriend or fuckbuddy, or reported any anal intercourse (with or without condoms) with casual partners were more likely to have used GHB in the past 6 months.

In multivariate analysis, being HIV-positive, being more socially engaged with other gay men who use drugs, having a greater number of sexual partners, group sex, and CLAI with casual partners were independently associated with GHB use in the past 6 months (Table 4). Not knowing one's HIV status was independently associated with having not recently used GHB.

Among men who had used GHB at least monthly or more frequently in the past 6 months, greater social engagement with other gay men who use drugs and having engaged in group sex were independently associated with monthly or more frequent GHB use (Table 4).

Consequences

Overall, 10.5% of men reported having ever experienced a drug overdose involving any party drug (including GHB). Whereas 5.5% of men who had never used GHB had experienced an overdose, nearly half (40.9%) of those who had used GHB in the past 6 months reported overdosing at least once (*P* < 0.05). This included 16.2% who self-reported overdosing more than once.

Table 4. Associations with use of gamma-hydroxybutyrate (GHB)

OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; I, insufficient cases for analysis; PHQ, Patient Health Questionnaire; GAD, Generalised Anxiety Disorder; GBM, gay and bisexual men; CLAI, condomless anal intercourse

Characteristics n (%)	No use in the previous six months v. any use in the previous six months. n = 3190								Less than monthly use in the previous six months v. monthly use in the previous six months. n = 259							
	Univariate analysis				Multivariate analysis				Univariate analysis				Multivariate analysis			
	OR	CI 95%		P	aOR	CI 95%		P	OR	CI 95%		P	aOR	CI 95%		P
		Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper	
Year of enrolment in survey																
2014	1								1							
2015	0.59	0.42	0.83	0.002					0.77	0.38	1.57	0.473				
2017	1.22	0.89	1.68	0.215					1.33	0.71	2.51	0.373				
Age	1.02	1.01	1.02	0.002					0.98	0.96	1.01	0.226				
Education																
Less than university level	1								1							
Undergraduate level	1.39	1.03	1.88	0.031					0.73	0.40	1.35	0.315				
Postgraduate level	1.57	1.14	2.15	0.005					0.65	0.34	1.24	0.192				
Did not answer	2.84	0.33	24.55	0.343					I	I	I	I				
Occupation																
Other white collar	1								1							
Manager	1.601	1.000	2.561	0.050					1.40	0.52	3.77	0.510				
Professional	1.524	0.985	2.359	0.059					1.45	0.57	3.69	0.434				
Other	1.212	0.703	2.089	0.489					0.62	0.18	2.10	0.442				
Not working									1.13	0.42	3.04	0.811				
Did not answer	0.922	0.270	3.145	0.897					1.19	0.09	15.04	0.894				
Testing for HIV																
Never tested	1								1							
Tested	19.81	6.32	62.07	<0.001					1.01	0.09	11.32	0.992				
HIV status																
HIV-negative	1				1				1							
HIV-positive	2.69	1.86	3.90	<0.001	1.63	1.03	2.56	0.035	1.02	0.51	2.07	0.950				
Don't know or unsure	0.01	0.26	0.02	<0.001	0.17	0.06	0.47	0.001	0.66	0.07	6.43	0.719				
PHQ depression status																
Minimal	1								1							
Mild	1.10	0.81	1.50	0.543					0.87	0.28	2.72	0.817				
Moderate	0.75	0.50	1.20	0.259					0.93	0.29	3.00	0.904				
Moderately severe	0.74	0.43	1.27	0.270					1.51	0.41	5.59	0.535				
Severe	0.64	0.33	1.25	0.192					2.20	0.43	11.22	0.343				
GAD anxiety status																
Minimal anxiety	1								1							
Mild anxiety	1.09	0.80	1.49	0.58					0.37	0.10	1.35	0.131				
Moderate anxiety	0.83	0.52	1.33	0.44					0.49	0.13	1.87	0.296				
Severe anxiety	0.52	0.27	1.00	0.05					1.20	0.27	5.36	0.811				
Social engagement with other GBM who use drugs	2.31	2.11	2.53	<0.001	2.16	1.96	2.38	<0.001	1.42	1.17	1.71	<0.001	1.43	1.18	1.74	0.000
Sexual behaviours																
Number of sex partners	1.01	1.01	1.02	<0.001	1.00	1.00	1.01	0.007	1.00	1.00	1.00	0.858				

Table 4.   *(continued)*

| Characteristics n (%) | No use in the previous six months v. any use in the previous six months. n = 3190 | | | | | | | | Less than monthly use in the previous six months v. monthly use in the previous six months. n = 259 | | | | | | | |
| | | Univariate analysis CI 95% | | | | Multivariate analysis CI 95% | | | | Univariate analysis CI 95% | | | | Multivariate analysis CI 95% | | |
	OR	Lower	Upper	P	aOR	Lower	Upper	P	OR	Lower	Upper	P	aOR	Lower	Upper	P
Group sex	3.96	3.05	5.53	<0.001	1.88	1.36	2.60	<0.001	1.56	0.93	2.62	0.094	1.71	1.00	2.93	0.049
Sex with fuckbuddies																
No sex	1								1							
No anal sex	0.43	0.11	1.79	0.248					2.34	0.14	38.64	0.551				
Sex with condoms only	0.80	0.45	1.41	0.432					1	–	–	1				
Any condomless sex	3.07	2.34	4.02	<0.001					1.38	0.80	2.38	0.253				
Sex with casual partners																
No partner	1				1				1							
No anal sex	1.69	0.71	3.99	0.236					1.43	0.43	4.68	0.559				
Sex with condoms only	3.48	2.06	5.85	<0.001					1.83	0.65	5.21	0.255				
Any condomless sex	10.06	6.41	15.81	<0.001	3.43	2.07	5.70	<0.001								
CLAI with boyfriend																
No partner	1								1							
No anal sex	0.78	0.31	1.95	0.596					3.24	0.53	20.0	0.206				
Sex with condoms only	0.45	0.16	1.23	0.118					1	–	–	1				
Any condomless sex	1.36	1.03	1.80	0.030					1.04	0.59	1.84	0.889				

In multivariate analysis, frequent (at least monthly) use of GHB (adjusted odds ratio 1.82; 95% confidence interval 1.08 – 3.01; $P < 0.05$) was independently associated with having experienced any drug overdose. In 2017, men were asked specifically about overdosing on GHB and 34.2% of recent GHB users reported overdosing on GHB specifically.

The most commonly cited harm that users of GHB ascribed as a consequence of their drug use was 'unsafe sex' (Fig. 1). Compared with men who used GHB less than monthly in the past 6 months, those who had used it at least monthly or more often reported more physical health consequences as a result of their drug use, such as needing medical attention, having accidentally hurt themselves, and reported more negative impacts on their social connections, such as friendship break-ups.

Among men who had used GHB in the past 6 months, common reasons ascribed for its use included: it made them feel sexually aroused (30.5%); it was available (25.1%); and it would help them lose their inhibitions (24.3%; Table 3). Compared with less frequent GHB users, men who used GHB at least monthly or more often were more likely to report they used it for fun ($P < 0.01$), to counter the effects of other drugs ($P < 0.01$), to feel connected to other men ($P < 0.01$), to lose their inhibitions ($P < 0.05$), and to make it easier to be the receptive partner during anal intercourse ($P < 0.001$).

Most men ascribed pleasurable outcomes as reasons for their GHB use, commonly related to sex and partying (Fig. 1). Compared with less frequent GHB users, those who had used GHB at least monthly more often ascribed positive outcomes to their drug use, such as developing closer connections and meeting new friends.

Discussion

In this sample, men who used GHB appeared to do so primarily in the context of intensive sex partying. They were highly sexually active, closely involved in gay community social and sexual networks, and tended to engage in group sex and CLAI. They often cited sexual enhancement as a primary reason for using GHB. Men who used GHB were also more likely to have used other party drugs, particularly crystal methamphetamine and amyl nitrite, as well as EDM, all drugs that have been linked to intensive sex partying[39,45] and associated with HIV infection.[48] Our data indicate that GBM use GHB for similar purposes, in similar circumstances, and with similar consequences to other party drugs. Users of GHB in our study were particularly vulnerable to the risk of drug overdose. Frequent users were more likely to experience a range of negative health and interpersonal outcomes compared with those who used it less than monthly.

Peer influences and social acceptability within gay community networks play a key role in drug using behaviours,[55] and this appears to apply equally to use of GHB among the men in our study. Indeed, those who used GHB, and particularly those who used it more frequently, were more likely to report that its use tended to be considered acceptable among their gay friends. Unsurprisingly, men who were more socially engaged with other gay men who used drugs were more likely to use GHB themselves.

Fig. 1. Reported consequences of recent drug use among men who had recently used with gamma-hydroxybutyrate (GHB). Men who had not used GHB in the past 6 months were not included.* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Among men who used GHB overall, there was little evidence of any association with poor mental health outcomes. In fact, men who had used GHB in the past 6 months reported fewer symptoms of depression than did those who had not used it. Previous studies of drug use among Australian GBM have similarly found little association with poor mental health.[39,45,66] Peer-support, active and satisfying sex lives and greater social connection with gay men have been shown to counter poor mental health.[67,68] Men who used GHB tended to be more socially engaged with other gay men, which may have countered some of the effects of anxiety and depression.

As with other drugs, more frequent use of GHB could be an indicator of dependent use. Self-reported overdose was not uncommon in this sample, particularly among men who used GHB monthly or more frequently. Rates of overdose reported in this sample were similar to those found elsewhere.[28] Both physical and socially harmful consequences were also associated with monthly or more frequent use of GHB.

However, this cross-sectional analysis cannot determine causality between GHB use and any of these negative outcomes. Longitudinal analysis of changes in drug using behaviours, negative outcomes, and mental health over time is needed to provide a clearer understanding of how these factors may be interrelated.

Our findings indicate that GHB is a key drug in chemsex among GBM. Harm reduction needs to target more frequent users of GHB, who risk multiple negative outcomes, including overdose. On the other hand, many participants reported that they derived clear, if subjective, benefits from GHB use, particularly in relation to sexual enjoyment. Interventions need to acknowledge that some men appear to use GHB functionally, or

at least to experience its use as functional, and seek to ensure that these men are provided with the tools to ensure that their use does not become problematic. In particular, given the strong role of peer norms and social connections within gay drug-using networks, harm reduction can utilise these networks to develop interventions that are appropriate to both the perceived and actual needs of individual GHB users within them.

Limitations and strengths

Although the men who participated in our study were similar to other samples of Australian GBM,[6,9] ours was a volunteer, online convenience sample. As such, findings may not be representative of all Australian GBM. Also, this cross-sectional analysis cannot determine causative or temporal relationships in the data. Given that this was an observational self-report study, rates of overdose were limited to subjective experiences. Future studies should consider linking hospital records to participant responses to verify the accuracy of self-reported drug-related overdoses in this population.

Flux is the first Australian cohort study to specifically examine drug use, in detail, among GBM. This large, community-based national sample is geographically dispersed and includes men of all ages and both those that are engaged and those not engaged with gay community life. Our online methodology potentially reduces social desirability bias in reporting illegal or stigmatised behaviours.[69–71]

Conclusions

Although the absolute percentage of GHB use was somewhat low compared with use of other drugs within the sample, it was

high in comparison to rates of GHB use in other populations. Nonetheless, most participants reported infrequent use, often explicitly to enhance sexual experiences. Our findings indicate that GHB is commonly used among GBM who engage in chemsex for intensive sex partying purposes. Men who used GHB were also strongly connected to networks of drug-using gay friends.

GHB use among GBM should be considered alongside crystal methamphetamine and other drugs that have been implicated in sexual risk behaviour and HIV infection. Gay community norms and peer influence appear to play a role in influencing the use of GHB. Interventions to reduce risk in intensive sex partying networks therefore need to consider the role of GHB.

Men who used GHB more frequently were often at risk of potentially harmful consequences, particularly overdose. Social networks of drug-using friends can potentially play a key role in responding appropriately in harmful situations. Interventions that take advantage of gay community affiliations and social connections to promote harm reduction among frequent users of GHB are needed.

Conflicts of interest

The authors declare no conflicts of interest.

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4.1.4 Chapter four summary

Most men did not use gamma-hydroxybutyrate at study baseline. Among those who did, most used gamma-hydroxybutyrate infrequently (once or twice in the previous six months). Nonetheless, when it was used, it was often explicitly to enhance sexual experiences, usually in the context of chemsex.

Those who used gamma-hydroxybutyrate engaged in behaviours that have been strongly associated with HIV infection. These behaviours were similar to what was found reported in **chapter 2** about use of erectile dysfunction medications, and to previously published findings on methamphetamine use.[3,5,23,24] These included greater numbers of sexual partners, engaging in group sex, and condomless anal intercourse with casual partners.

Based on what I found with erectile dysfunction medications and gamma-hydroxybutyrate use, it is evident that methamphetamine is not the only drug used by gay and bisexual men to engage in chemsex, nor is it the only drug associated with behaviours that represent a risk of HIV transmission in this population. The results highlight two potential limitation in the *Australian PrEP Guidelines.* Firstly, methamphetamine is the only drug-related criterion for access to PrEP. However, it is evident that drugs, other than methamphetamine, are used to enhance sexual pleasure. The guidelines were based on data collected in the early to mid-2000s,[1] when gamma-hydroxybutyrate use attracted less attention. Therefore, they may not reflect current HIV risk behaviours. Second, most gay and bisexual men reported infrequently drug use in the previous six months (once or twice). The *Australian PrEP Guidelines* specify

high-risk behaviours in the previous six months. This questions the sensitivity of the *Australian PrEP Guidelines* and their potential accuracy.

Identifying gaps within key populations

5.1 Factors associated with the non-use of PrEP among high-risk men

5.1.1 Publication details

Hammoud MA, Vaccher S, Jin F, Bourne A, Maher L, Holt M, Bavinton BR, Haire B, Degenhardt L, Grulich A. HIV pre-exposure prophylaxis (PrEP) uptake among gay and bisexual men in Australia and factors associated with the nonuse of PrEP among eligible men: Results from a prospective cohort study. Journal of Acquired Immune Deficiency Syndromes 2019; 81(3): e73-e84

5.1.2 Thesis aims related to this chapter

Thesis aim 4: Measure the incidence of PrEP uptake among gay and bisexual men, and describe uptake and non-uptake of PrEP among men who engage in chemsex.

Thesis aim 5: Identify factors associated with use of PrEP as a harm reduction strategy.

5.1.3 Chapter five in context

Through the previous chapters, I have demonstrated how use of licit and illicit drugs, other than methamphetamine, are associated with behaviours that correspond to the *Australian PrEP Guidelines* before the widespread availability of PrEP.[21,22]

At the time of this analysis, access to PrEP had become increasingly available in Australia. In this chapter, I identify factors that predict the use of PrEP through longitudinal analysis. I explore which gay and bisexual men have initiated PrEP, and the contexts in which some gay and bisexual men who are eligible for PrEP are not using PrEP. I describe the incidence of PrEP uptake, and factors predicting its initiation. I also identify characteristics associated with non-uptake of PrEP among gay and bisexual men in Australia who meet the eligibility criteria.

HIV Pre-exposure Prophylaxis (PrEP) Uptake Among Gay and Bisexual Men in Australia and Factors Associated With the Nonuse of PrEP Among Eligible Men: Results From a Prospective Cohort Study

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Background: HIV pre-exposure prophylaxis (PrEP) is a highly effective biomedical HIV prevention strategy, yet some gay and bisexual men (GBM) who are eligible to access PrEP are not using it. We report the incidence of PrEP uptake, factors predicting its initiation, and identify characteristics associated with nonuptake of PrEP among Australian GBM who meet the eligibility criteria.

Methods: The Following Lives Undergoing Change (Flux) Study is a national, online, prospective observational study among GBM focusing on licit and illicit drug use. Participants (N = 1257) responded to baseline and 6-monthly follow-up questionnaires. Incidence per 100 person-years and incidence rate ratios of PrEP initiation are presented. Multivariate Poisson regression was used to examine associations with PrEP initiation and logistic regression to examine associations with nonuptake of PrEP among eligible GBM.

Results: Among GBM who met the eligibility criteria, 69.8% of men did not commence PrEP. Factors independently associated with nonuptake of PrEP were younger age, living in an Australian state without a PrEP trial, lower social engagement with other gay men,

less use of illicit party drugs or use of illicit party drugs for sex, and less likely to have engaged in HIV sexual risk behaviors such as group sex or any condomless anal intercourse.

Conclusions: Despite meeting formal eligibility criteria for PrEP, men who were relatively less sexually active or less socially connected were less likely to initiate PrEP. Men who did not initiate PrEP may assess their risk as insufficient relative to others to warrant using PrEP because they engaged in less frequent "risky" behaviors.

Key Words: eligible, gay bisexual men, HIV, incidence, PrEP, prevention

(J Acquir Immune Defic Syndr 2019;81:e73–e84)

INTRODUCTION

In Australia, gay and bisexual men (GBM) account for the majority (~70%) of new HIV diagnoses.[1] Over the past 10 years, there has been a 21.0% decrease in HIV notifications among Australian born GBM.[1] However, among notifications due to male-to-male sexual contact, the proportion who were Asian born GBM increased from 28.0% in 2008 to 52.0% in 2017 but remained stable among GBM from other countries.[1] Despite increasing levels of HIV testing, and higher and earlier treatment coverage among those diagnosed with HIV,[2] new HIV diagnoses in Australia were stable in the decade to 2017.[1]

The coformulation of tenofovir disoproxil fumarate and emtricitabine (FTC) as pre-exposure prophylaxis (PrEP) is a highly effective biomedical HIV prevention strategy.[3,4] Australia's National HIV Strategy prioritizes GBM for HIV prevention, and PrEP has recently been approved for public subsidy in Australia, ensuring that individuals at high risk of HIV have affordable access.[5,6] Before this, several Australian jurisdictions made PrEP available to high-risk individuals through large-scale implementation studies[7–9]; substantial reductions in HIV diagnoses have since been described in New South Wales.[6,10,11]

The national eligibility criteria for access to PrEP for GBM include at least 1 episode of any of the following in the previous 3 months: condomless anal intercourse (CAI)

with an HIV-positive regular partner not on treatment or with detectable viral load; receptive CAI with a casual partner (R-CAIC); diagnosis of a rectal sexually transmitted infection or infectious syphilis; or methamphetamine use. Cross-sectional surveys have shown that most men who have commenced PrEP meet prescribing guidelines.[12] GBM who meet these criteria, herein described as "PrEP-eligible," are at highest risk of HIV seroconversion.[13–15]

Australian behavioral surveillance finds that PrEP use increased from 2% to 24% among HIV-negative GBM between 2013 and 2017.[16] During the same period, among men who were HIV negative or untested and not on PrEP, the proportion who reported having engaged in R-CAIC remained steady at 19.6%.

Although PrEP use has rapidly increased among Australian GBM and financial barriers have been reduced within the Australian health system by recent public subsidy, many PrEP-eligible men are not accessing it.[16] To date, there have been limited data on community-based cohort studies that examine PrEP uptake in individual GBM,[17] none of which assessed uptake against PrEP eligibility criteria. Little is known about the influence of social, community, and interpersonal factors on initiation.

In this paper, we use data from a prospective observational cohort of GBM in Australia to:

- Estimate incidence of uptake and factors predicting PrEP initiation, and
- Identify factors associated with the nonuptake of PrEP among PrEP-eligible men.

METHODS

Study Design and Procedure

The Following Lives Undergoing Change (Flux) Study is an ongoing national, online, prospective observational study among GBM to examine the prevalence, incidence, and contexts of licit and illicit drug use. The primary aim of Flux was to identify individual and contextual factors associated with initiation of licit and illicit drug use and changes over time in patterns of sexual and drug use behaviors among GBM. The study protocol has been published previously.[18]

Participants

Men were eligible to participate in the study if they were at least 16 years and 6 months of age; identified as gay or bisexual, or had sex with a man in the past 12 months; and lived in Australia. Use of licit or illicit drugs or knowledge about PrEP was not requirements for participation. Participants were recruited between September 25, 2014, and July 5, 2015, through Facebook, gay community websites and online media, mobile phone applications, and gay sexual networking websites. At enrolment, online informed consent was obtained from all participants. No compensation was offered for participation in this study.

Procedures

Baseline and 6-monthly follow-up questionnaires were completed online using computer-assisted self-interviewing software.[18] Demographic items included country of birth, ethnicity, state of residence, education, and employment status. Social engagement with gay men was assessed using a scale with 2 items (proportion of friends who are gay men and amount of free time spent with gay male friends), where higher scores indicated greater social engagement with gay men.[19] HIV status was self-reported. HIV-negative/untested men reported use of PrEP ("daily, every other day, or before and after sex"). Men reported their use of methamphetamine and their sexual behavior in the previous 6 months. Three categories of sex partners were included: "boyfriends" (a regular committed partner with whom they maintained a romantic relationship); "fuckbuddies" (nonromantic regular partners); and casual partners.[20] GBM who reported a regular committed partner were also asked about their partner's HIV serostatus and, if HIV positive, whether they were on treatment.

Statistical Analysis

Data were right-censored to account for participants who left the study before PrEP initiation or did not provide any follow-up data. Right censoring allows for all accrued follow-up time to be included in the analysis but acknowledges that the "time to event," in this case, PrEP initiation, may not occur for some individuals.[21] Analyses included all men who completed at least 1 follow-up questionnaire, reported an HIV-negative/unknown serostatus, and reported no PrEP use at baseline. Participants with missing data included in this analysis were noted accordingly and included in the denominator. Baseline characteristics were summarized by PrEP eligibility and initiation status. Analyses focused on the following factors: demographic and behavioral characteristics reported at preceding follow-up questionnaires associated with subsequent PrEP initiation; and factors associated with the nonuse of PrEP among PrEP-eligible men over a 24-month period. PrEP initiation was defined as the first 6-month period of PREP use following a baseline report of no PrEP use.

Based on the Australian PrEP prescribing guidelines,[15] PrEP eligibility for this sample was defined as any CAI with a regular HIV-positive partner not on treatment or with detectable viral load; any R-CAIC of HIV-positive or unknown status; any methamphetamine use; or rectal gonorrhoea, rectal chlamydia, or infectious syphilis diagnosis in the past 6 months. The clinical guidelines use a 3-month period because most data collected in Australian clinic settings are for that time period.[15] However, the Health in Men study on which the guidelines were based used a 6-month time period,[13] as is commonly reported in behavioral research.[22] The Flux Study used measures that were drawn from the Health in Men study and hence also used a 6-month time period. The level of HIV risk for sexual behavior in this study was categorized using a previously used classification system, ranging from lowest risk to highest risk (no such partner, no

anal sex with this type of partner, consistent condom use, insertive-only CAI, and any R-CAIC).[12]

To determine what factors were associated with the initiation of PrEP, time-varying variables reported in the previous questionnaire were considered as predictors for PrEP initiation. Bivariate Poisson regression was used to examine the associations between PrEP initiation, and incidence rate ratios per 100 person-years (100 PY) and their corresponding 95% confidence intervals (CIs) were presented. Predictors with a *P* value <0.10 in bivariate analyses were included in multivariable analyses.

Multivariable Poisson regression models were then constructed to allow adjustment for confounding factors. Multivariate associations with a *P* value of <0.05 were retained in the final model. To estimate statistical associations of PrEP-eligible men who did not initiate PrEP, bivariate regression was used to examine the associations between noninitiators and their PrEP-using counterparts. Odds ratios (ORs) and their corresponding 95% CI were presented. Predictors with a *P* value <0.10 in bivariate analyses were included in the multivariable analyses.

Binary logistic backward stepwise multiple regression analysis was used to control for confounding factors and presented as adjusted ORs (aORs) and 95% CI. Multivariate associations with a *P* value of <0.05 were retained in the final model. The year of study visit and state of residence were included in both models to account for increasing availability of PrEP over time, and differential availability of, and information about PrEP in different Australian states and territories. Data were analyzed using Stata version 15 (StataCorp, TX).

RESULTS

Overall, 1695 men were enrolled during 2014–2015, of whom 1377 (81.2%) provided the minimum data required for follow-up. Men who reported an HIV-positive serostatus (n = 134; 7.9%) or any PrEP use (n = 16; 0.9%) at baseline were excluded from analysis. The following analyses were restricted to the remaining 1257 men who were HIV negative or untested at baseline.

At baseline, the mean age of the sample was 33.6 years (SD 12.3). Participants predominantly identified as gay (90.4%) or bisexual (7.2%) and most (84.6%) had been tested for HIV in the previous 6 months. Most (83.6%) reported having tested HIV negative, with 16.4% not knowing or being unsure of their HIV status. The majority of men in the sample were of Anglo-Celtic background (76.0%), university educated (58.9%), and in full-time (58.3%) or part-time (12.9%) employment. One in 4 (27.6%) reported that most of their friends were gay, and 19.7% spent most of their free time with gay friends (Table 1).

Most (91.3%) reported sex with a man in the previous 6 months, and 41.5% reported having more than 10 male sex partners in the previous 6 months. One in 5 (20.0%) had engaged in group sex in the previous 6 months. Two-fifths (37.9%) indicated they had a regular partner (or "boyfriend"), 36.6% reported sex with a fuckbuddy, and more than half

(63.3%) reported sex with casual partners in the previous 6 months. In the previous 6 months, 15.3% used drugs to enhance their sexual experiences. Most (84.4%) lived in an Australian state where a large PrEP trial had commenced before 2017.

Prevalence of PrEP Use

Within the total sample of 1257 men who reported never having used PrEP at baseline, the proportion of men who reported current use of PrEP increased from 0.0% to 18.0% at 24 months (*P* trend <0.001). A total of 226 initiated PrEP during follow-up. Thirty-two men (2.5%) initiated by 6 months and an additional 2.6% (n = 33), 4.0% (n = 50), and 8.8% (n = 111) by 12, 18, and 24 months, respectively. The overall incidence of PrEP use within the whole sample was 11.57 per 100 PY (95% CI: 10.00 to 13.40). Over the 24 months of follow-up, 20 men (3.6%) discontinued PrEP use after having previously initiated it after baseline. Overall, 8.8% of GBM did not meet the eligibility criteria but nonetheless initiated PrEP, and 9.5% of GBM met the eligibility criteria and initiated PrEP.

Predictors and Incidence of PrEP Initiation

In bivariate analysis, the incidence of initiation was higher among GBM who were older. Among men aged 16–24 years, the incidence of initiation was 9.0 per 100 PY (95% CI: 6.51 to 12.61). This increased to 25.88 per 100 PY (95% CI: 10.72 to 70) among men aged 40 years and older (*P* trend <0.01).

The incidence of initiation was higher among men who lived in a state where a large-scale PrEP project had commenced before 2017 (12.7 per 100 PY; 95% CI: 10.9 to 14.9) compared with GBM not living in other jurisdictions (7.0 per 100 PY; 95% CI: 4.7 to 10.9) (*P* trend = 0.012) (Table 2).

The incidence of PrEP initiation among those who did not use any illicit party drugs in the previous 6 months was 8.82 per 100 PY (95% CI: 6.9 to 11.2). Among those who reported using any illicit party drugs in the previous 6 months, but not for sex, the incidence of initiation was 9.52 per 100 PY (95% CI: 7.3 to 12.5), and among those who used any illicit party drugs specifically for sex, it was 25.45 per 100 PY (95% CI: 19.7 to 32.9) (*P* trend <0.001).

The incidence rate of PrEP initiation was higher among men who engaged in group sex (23.07 per 100 PY; 95% CI: 18.9 to 28.1) compared with GBM who did not engage in group sex (7.12 per 100 PY; 95% CI: 0.5 to 0.9) (*P* <0.001).

For those who reported insertive-only CAI with a fuckbuddy, the incidence rate for PrEP initiation was 21.60 per 100 PY (95% CI: 13.0 to 35.8) but was 35.9 per 100 PY (95% CI: 27.9 to 46.3) among those who reported receptive CAI with a fuckbuddy (*P* trend <0.001).

In multivariable analysis, PrEP initiation was more likely in more recent years. The incidence of PrEP initiation increased from 2.06 per 100 PY (95% CI: 1.08 to 3.90) in 2016 to 7.24 (95% CI: 3.97 to 13.19) per 100 PY in 2017 (*P* trend <0.001).

TABLE 1. Baseline Characteristics Comparing Eligible and Noneligible Men and Their PrEP Initiation Status (N = 1257)

N (%)	Did Not Meet the Eligibility criteria*		Met the Eligibility Criteria*		Total, 1257
	Did Not Initiate PrEP	Initiated PrEP After Baseline	Did Not Initiate PrEP	Initiated PrEP After Baseline	
	788 (62.7)	110 (8.8)	243 (19.3)	116 (9.2)	
Age					
16–24	238 (30.2)	21 (19.1)	76 (31.3)	18 (15.5)	353 (28.1)
25–29	148 (18.8)	21 (19.1)	45 (18.5)	20 (17.2)	234 (18.6)
30–39	191 (24.2)	37 (33.6)	61 (25.1)	32 (27.6)	321 (25.5)
40–84	211 (26.8)	31 (28.2)	61 (25.1)	46 (39.7)	349 (27.8)
Country of birth					
Australia	649 (82.4)	90 (81.8)	197 (81.1)	92 (79.3)	1028 (81.8)
Oceania (excl. Australia)	21 (2.7)	1 (0.9)	13 (5.3)	2 (1.7)	37 (2.9)
Asia	28 (3.6)	4 (3.6)	3 (1.2)	8 (6.9)	43 (3.4)
North America	18 (2.3)	1 (0.9)	5 (2.1)	2 (1.7)	26 (2.1)
South/Central America	2 (0.3)	0 (0.0)	0 (0.0)	2 (1.7)	4 (0.3)
Europe	45 (5.7)	8 (7.3)	13 (5.3)	10 (8.6)	76 (6.0)
Middle East	2 (0.3)	1 (0.9)	0 (0.0)	0 (0.0)	3 (0.2)
Africa	6 (0.8)	1 (0.9)	4 (1.6)	0 (0.0)	11 (0.9)
Did not answer	17 (2.2)	4 (3.6)	8 (3.3)	0 (0.0)	29 (2.3)
Ethnicity					
Anglo-Celtic	595 (75.5)	77 (70.0)	195 (80.2)	94 (81.0)	961 (76.5)
Aboriginal or Torres Strait Islander	20 (2.5)	1 (0.9)	3 (1.2)	3 (2.6)	27 (2.1)
Others	173 (22.0)	32 (29.1)	45 (18.5)	19 (16.4)	269 (21.4)
State of residence					
New South Wales and ACT	341 (43.3)	62 (56.4)	95 (39.1)	64 (55.2)	562 (44.7)
Victoria	182 (23.1)	24 (21.8)	67 (27.6)	28 (24.1)	301 (23.9)
Queensland	127 (16.1)	17 (15.5)	39 (16.0)	15 (12.9)	198 (15.8)
Others	138 (17.5)	7 (6.4)	42 (17.3)	9 (7.8)	196 (15.6)
Education					
Less than university educated	320 (40.6)	34 (30.9)	120 (49.4)	43 (37.1)	517 (41.1)
University educated	468 (59.4)	76 (69.1)	123 (50.6)	73 (62.9)	740 (58.9)
Employment status					
Not in employment	236 (29.9)	27 (24.5)	57 (23.5)	32 (27.6)	352 (28.0)
Part-time employed	96 (12.2)	15 (13.6)	40 (16.5)	11 (9.5)	162 (12.9)
Full-time employed	456 (57.9)	68 (61.8)	146 (60.1)	73 (62.9)	743 (59.1)
Socially engaged with other gay men	3.43 (1.55)	4.00 (1.67)	3.54 (1.65)	4.44 (1.53)	3.58 (1.60)
Not at all	67 (8.5)	6 (5.5)	24 (9.9)	6 (5.2)	103 (8.2)
A little	321 (40.9)	29.1	89 (36.6)	21 (18.1)	463 (36.9)
Mostly	202 (25.7)	22 (20.0)	55 (22.6)	27 (23.3)	306 (24.4)
Very much	195 (24.8)	50 (45.5)	75 (30.9)	62 (53.4)	382 (30.5)
Methamphetamine use					
No recent use (including never used)	788 (100.0)	110 (100.0)	115 (47.3)	59 (50.9)	1072 (85.3)
Recent use	0 (0.0)	0 (0.0)	128 (52.7)	57 (49.1)	185 (14.7)
Reasons for party drug use					
No recent drug use (including never used)	677 (85.9)	80 (72.7)	97 (39.9)	46 (39.7)	900 (71.6)
Recent drug use (not for sex)	69 (8.8)	16 (14.5)	60 (24.7)	20 (17.2)	165 (13.1)
Recent drug use (used to enhance sex)	42 (5.3)	14 (12.7)	86 (35.4)	50 (43.1)	192 (15.3)
No. of recent sex partners					
No sex partners	98 (12.4)	9 (8.2)	2 (0.8)	0 (0.0)	109 (8.7)
1 sex partner	229 (29.1)	14 (12.7)	20 (8.2)	2 (1.7)	265 (21.1)
Up to 10	325 (41.2)	42 (38.2)	121 (49.8)	38 (32.8)	526 (41.8)
Up to 50	124 (15.7)	40 (36.4)	94 (38.7)	64 (55.2)	322 (25.6)
More than 50	12 (1.5)	5 (4.5)	6 (2.5)	12 (10.3)	35 (2.8)
Group sex					
No group sex	671 (85.2)	78 (70.9)	190 (78.2)	67 (57.8)	1006 (80.0)
Recent group sex	117 (14.8)	32 (29.1)	53 (21.8)	49 (42.2)	251 (20.0)

TABLE 1. (*Continued*) Baseline Characteristics Comparing Eligible and Noneligible Men and Their PrEP Initiation Status (N = 1257)

N (%)	Did Not Meet the Eligibility criteria*		Met the Eligibility Criteria*		
	Did Not Initiate PrEP	Initiated PrEP After Baseline	Did Not Initiate PrEP	Initiated PrEP After Baseline	Total,
	788 (62.7)	110 (8.8)	243 (19.3)	116 (9.2)	1257
Sex with a casual partner					
No casual partner	393 (49.9)	29 (26.4)	33 (13.6)	6 (5.2)	461 (36.7)
No anal intercourse	113 (14.3)	30 (27.3)	20 (8.2)	7 (6.0)	170 (13.5)
Consistent condom use	205 (26.0)	31 (28.2)	19 (7.8)	12 (10.3)	267 (21.2)
Insertive-only condomless anal intercourse	61 (7.7)	15 (13.6)	22 (9.1)	8 (6.9)	106 (8.4)
Receptive condomless anal intercourse	0 (0.0)	0 (0.0)	148 (60.9)	82 (70.7)	230 (18.3)
Did not answer	16 (2.0)	5 (4.5)	1 (0.4)	1 (0.9)	23 (1.8)
Sex with fuckbuddies					
No fuckbuddies	557 (70.7)	65 (59.1)	131 (53.9)	44 (37.9)	797 (63.4)
No anal intercourse	49 (6.2)	10 (9.1)	12 (4.9)	8 (6.9)	79 (6.3)
Consistent condom use	69 (8.8)	8 (7.3)	13 (5.3)	5 (4.3)	95 (7.6)
Insertive-only condomless anal intercourse	38 (4.8)	6 (5.5)	12 (4.9)	9 (7.8)	65 (5.2)
Receptive condomless anal intercourse	66 (8.4)	20 (18.2)	75 (30.9)	50 (43.1)	211 (16.8)
Did not answer	9 (1.1)	1 (0.9)	0 (0.0)	0 (0.0)	10 (0.8)
Sex with boyfriend					
No boyfriend	475 (60.3)	62 (56.4)	162 (66.7)	81 (69.8)	780 (62.1)
No anal intercourse	28 (3.6)	4 (3.6)	4 (1.6)	1 (0.9)	37 (2.9)
Consistent condom use	46 (5.8)	3 (2.7)	7 (2.9)	1 (0.9)	57 (4.5)
Any condomless anal intercourse with an HIV-negative partner or an HIV-positive partner with an unknown, undetectable serostatus, or is on treatment	236 (29.9)	41 (37.3)	69 (28.4)	32 (27.6)	378 (30.1)
Any condomless anal intercourse with an HIV-positive partner (detectable viral load or not on treatment)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.9)	2 (0.2)
Did not answer	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.2)

*Percentages represent total in column. ACT, The Australian Capital Territory.

The incidence of initiation was higher among those who were socially engaged with other gay men (2.12 per 100 PY; 95% CI: 0.86 to 5.20) compared with GBM who had no, or little social engagement with other gays (*P* trend <0.001).

The incidence of initiation was higher among men who had recently used methamphetamine (1.50 per 100 PY; 95% CI: 1.10 to 2.05) compared with men who had never used or reported no recent use (*P* trend <0.001).

PrEP initiation was also associated with having a higher number of sexual partners. Compared with GBM who had 1 sex partner in the previous 6 months, GBM who had up to 10 sexual partners in the previous 6 months had a PrEP incidence rate of 3.78 per 100 PY (95% CI: 2.75 to 22.73). The incidence rate increased to 7.91 per 100 PY (95% CI: 2.75 to 22.73) and 8.03 per 100 PY (95% CI: 2.40 to 26.87) when GBM had up to 50 and over 50 sexual partners in the previous 6 months, respectively (*P* trend <0.001).

Among GBM who engaged in insertive-only CAI with casual partners, this incidence rate was 1.75 per 100 PY (95% CI: 0.87 to 3.51). The incidence of PrEP initiation was higher among GBM who engaged in R-CAIC (2.46 per 100 PY; 95% CI: 1.29 to 4.67) (*P* trend <0.001).

Among those who reported having any condomless sex with an HIV-positive boyfriend who had a detectable viral load or was not on treatment, the PrEP incidence rate was 14.74 per 100 PY (95% CI: 28.83) (*P* trend <0.001).

Prevalence of Eligibility

Among the 1257 men who reported never having used PrEP at baseline, 43.7% (n = 549) were eligible for PrEP during the study. At baseline, 28.6% (n = 359) men were PrEP-eligible, 26.7% (n = 335) were PrEP-eligible by 6 months, 24.1% GBM (n = 303) by 12 months 22.8% (n = 287) by 18 months, and 329 (n = 26.2%) by 24 months (Fig. 1).

Among men who were eligible for PrEP at baseline, 30.2% (n = 166) initiated PrEP during follow-up, leaving 383 PrEP-eligible men who did not initiate PrEP. The overall incidence of PrEP use among PrEP-eligible men was 19.5 per 100 PY (95% CI: 16.4 to 23.1).

Associations With Nonuse of PrEP Among Eligible Men

By definition, PrEP-eligible men had engaged in behaviors consistent with the PrEP eligibility criteria either at

TABLE 2. Incidence Rate Ratios per 100 Person-Years for PrEP Initiation (N = 1257)

				95% CI		Univariate Associations				Multivariate Associations			
			Incidence per			Incidence	95% CI			Incidence	95% CI		
Factor	Person-Years	Incidence	100 Person-Years	Lower	Upper	Rate Ratio	Lower	Upper	P Trend	Rate Ratio	Lower	Upper	P Trend
Year of visit									<0.001				<0.001
2015	330.25	12	3.63	2.01	6.40	1				1			
2016	821.62	66	8.03	6.31	10.22	2.21	1.20	4.07		2.06	1.08	3.90	
2017	386.34	100	25.88	21.28	31.49	7.12	3.95	12.84		7.24	3.97	13.19	
Age									0.012				
16–24	399.06	36	9.02	6.51	12.61	1							
25–29	297.15	28	9.42	6.51	13.65	1.04	0.66	1.66					
30–39	399.17	53	13.28	10.14	17.38	1.47	0.99	2.19					
40–84	442.83	61	13.78	10.72	17.70	1.53	1.04	2.25					
Country of birth									0.168				
Australia	1267.70	144	11.36	9.65	13.37	1							
Oceania (excl. Australia)	43.88	3	6.84	2.21	21.20	0.60	0.19	1.90					
Asia	47.95	10	20.85	11.22	38.76	1.84	1.02	3.29					
North America	36.81	2	5.43	1.35	2.17	0.48	0.12	1.91					
South/Central American	6.17	2	32.44	8.11	1.30	2.86	0.77	10.57					
Europe	83.56	13	15.56	9.03	26.8	1.37	0.81	2.33					
Middle East	4.57	1	21.86	3.08	1.55	1.92	0.41	8.96					
Africa	11.99	1	8.34	1.17	5.92	0.73	0.10	5.15					
Did not answer	35.58	2	5.62	1.17	5.92	0.49	0.13	1.87					
Ethnicity									0.711				
Anglo-Celtic	1185.60	133	11.22	119.46	13.30	1							
Aboriginal or Torres Strait Islander	30.17	4	13.26	4.98	35.33	1.18	0.51	2.75					
Others	322.44	41	12.72	9.36	17.29	1.13	0.82	1.56					
State of residence									0.027				
New South Wales and ACT	635.28	88	13.85	11.24	17.07	1							
Victoria	371.73	46	13.37	9.27	16.52	0.89	0.64	1.25					
Queensland	221.01	22	9.95	6.55	15.12	0.72	0.43	1.11					
Others	310.19	22	7.01	4.67	10.77	0.51	0.32	0.81					
Education									0.371				
Less than university educated	547.61	58	10.59	8.19	13.70	1							
University educated	990.60	120	12.11	10.13	14.49	1.14	0.85	1.54					
Employment status									0.055				
Not in employment	351.47	29	8.25	5.73	11.87	1							
Part-time employed	219.51	23	10.48	6.96	15.77	1.27	0.75	2.15					
Full-time employed	967.23	126	13.03	10.94	15.51	1.58	1.07	2.32					
Socially engaged with other gay men									<0.001				<0.001
Not at all	94.93	5	5.27	2.19	12.65	1				1			
A little	583.02	35	6.00	4.31	8.36	1.14	0.46	2.83		0.94	0.37	2.37	
Mostly	372.70	42	11.27	8.33	15.25	2.14	0.87	5.26		1.34	0.54	3.36	
Very much	487.56	96	19.69	16.12	24.05	3.74	1.57	8.92		2.12	0.86	5.20	
Methamphetamine use									<0.001				0.012
No recent use (including never used)	1323.30	126	9.52	8.00	13.34	1				1			
Recent use	214.91	52	24.20	18.44	31.75	2.54	1.90	3.40		1.50	1.10	2.05	

TABLE 2. (*Continued*) Incidence Rate Ratios per 100 Person-Years for PrEP Initiation (N = 1257)

Factor	Person-Years	Incidence	Incidence per 100 Person-Years	95% CI Lower	95% CI Upper	Incidence Rate Ratio	95% CI Lower	95% CI Upper	P Trend	Incidence Rate Ratio	95% CI Lower	95% CI Upper	P Trend
						Univariate Associations				**Multivariate Associations**			
Reasons for party drug use									<0.001				
No recent drug use (including never used)	759.91	67	8.82	6.94	11.20	1							
Recent drug use (not for sex)	546.50	52	9.52	7.25	12.49	1.08	0.76	1.53					
Recent drug use (used to enhance sex)	231.80	59	25.45	19.72	32.85	2.89	2.10	3.94					
No. of recent sex partners									<0.001				<0.001
1 sex partner	351.83	6	1.71	0.77	3.80	1				1			
Up to 10	669.38	61	9.11	7.09	11.71	5.34	2.31	12.34		3.78	1.35	10.61	
Up to 50	317.38	85	26.78	21.65	32.13	15.70	6.86	35.97		7.91	2.75	22.73	
More than 50	18.30	9	49.18	25.59	94.53	28.84	10.99	75.68		8.03	2.40	26.87	
Group sex									<0.001				
No group sex	1109.12	79	7.12	5.71	88.80	1							
Recent group sex	429.09	99	23.07	18.95	28.10	3.24	2.45	4.29					
Sex with a casual partner									<0.001				<0.001
No casual partner	595.05	16	2.69	1.65	4.39	1				1			
No anal intercourse	181.25	14	0.77	4.57	13.04	2.87	1.42	5.82		0.81	0.36	1.84	
Consistent condom anal intercourse	276.97	19	0.69	4.38	10.75	2.55	1.32	4.92		0.96	0.44	2.09	
Insertive-only condomless anal intercourse	156.36	31	19.83	13.94	28.19	7.37	4.09	13.30		1.75	0.87	3.51	
Any receptive condomless anal intercourse	295.78	95	32.12	26.27	39.27	11.95	7.06	20.20		2.46	1.29	4.67	
Did not answer	32.80	3	9.15	2.95	28.37	3.40	1.00	11.58		1.38	0.35	5.41	
Sex with fuckbuddies									<0.001				
No fuckbuddies	1177.97	91	7.73	6.29	9.49	1							
No anal intercourse	47.88	3	6.27	2.02	19.43	0.81	0.26	2.51					
Consistent condom use	69.31	7	10.10	4.81	21.18	1.01	0.62	2.74					
Insertive-only condomless anal intercourse	69.46	15	21.60	13.02	35.82	2.80	1.71	4.57					
Any receptive condomless anal intercourse	167.04	60	35.92	27.89	4.63	4.65	3.43	6.29					
Did not answer	6.55	2	30.54	7.64	1.22	3.95	1.14	13.71					
Sex with boyfriend									<0.001				<0.001
No boyfriend	733.30	96	13.09	10.72	16.00	1				1			
No anal intercourse	77.49	4	5.16	1.94	13.75	0.39	0.15	1.03		0.77	0.33	1.81	
Consistent condom use	104.71	3	2.87	0.92	8.89	0.22	0.07	0.68		0.32	0.12	1.22	

TABLE 2. (*Continued*) Incidence Rate Ratios per 100 Person-Years for PrEP Initiation (N = 1257)

						Univariate Associations				Multivariate Associations			
			Incidence per 100 Person-Years	95% CI		Incidence Rate Ratio	95% CI		*P* Trend	Incidence Rate Ratio	95% CI		*P* Trend
Factor	Person-Years	Incidence		Lower	Upper		Lower	Upper			Lower	Upper	
Any condomless anal intercourse with an HIV-negative partner or an HIV-positive partner with an unknown, undetectable serostatus, or is on treatment	619.05	74	11.95	9.52	15.01	0.91	0.68	1.22		1.31	0.97	1.76	
Any condomless sex with an HIV-positive partner (detectable or not on treatment)	1.13	1	88.60	12.48	628.97	6.76	3.87	11.81		14.74	7.53	28.86	
Did not answer	2.53	0	—	—	—	—	—	—		—	—	—	

ACT, The Australian Capital Territory.

baseline or during follow-up. However, they did not report these behaviors during every follow-up period, and those who did not initiate PrEP were less likely to report these behaviors consistently between survey visits than those who did initiate PrEP. Hence, PrEP-eligible men who did not initiate PrEP were less likely to consistently report either R-CAIC or CAI with an HIV-positive regular partner who had a detectable viral load or was not on treatment between survey rounds. They were also less likely to have engaged in other HIV risk behaviors such as use of drugs for sex or group sex during each follow-up period. PrEP-eligible men who did not initiate PrEP reported fewer sexual partners compared with men who initiated PrEP (Table 3).

In multivariate analysis among PrEP-eligible men, those who did not initiate PrEP were less likely to report a study visit in recent years. PrEP initiation in 2016 decreased from aOR: 0.08 (95% CI: 0.63 to 0.02) to aOR: 0.02 (95% CI: 0.00 to 0.18) in 2017 (*P* trend <0.001).

PrEP initiation was less likely among men living in an Australian state that had not commenced a PrEP trial before 2017 (aOR: 2.11; 95% CI: 1.16 to 3.85) and who were less socially engaged with other gay men (aOR: 0.78; 95% CI: 0.68 to 0.91). Men who did not initiate PrEP were also less likely to have used drugs to enhance sexual pleasure (aOR: 0.57; 95% CI: 0.32 to 1.00). Men who were eligible for PrEP but did not initiate were less likely to report group sex (aOR: 0.59; 95% CI: 0.37 to 0.93) or any CAI (aOR: 0.20; 95% CI: 0.10 to 0.41) (*P* < 0.001) compared with eligible men who did initiate PrEP.

DISCUSSION

GBM in this cohort who initiated PrEP were likely to report having engaged in behaviors that corresponded with the Australian PrEP eligibility guidelines. Nonetheless, most PrEP-eligible men had not yet initiated PrEP. These men were
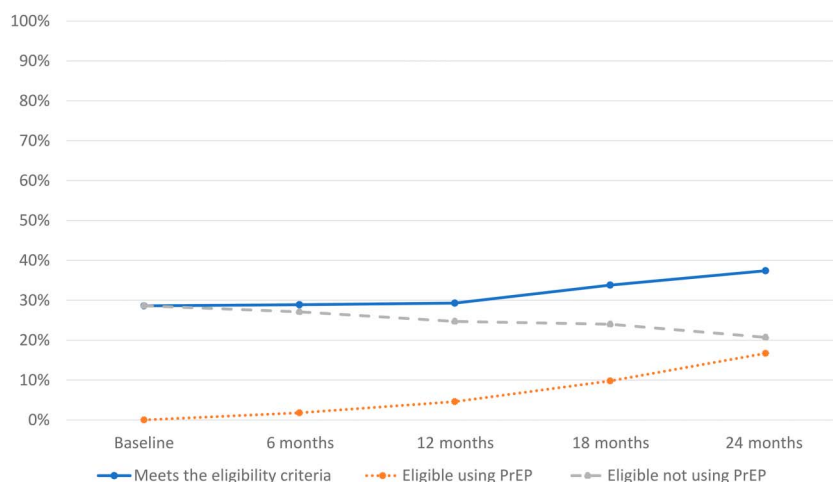
FIGURE 1. Prevalence of PrEP use and eligibility.

TABLE 3. Factors Associated With Noninitiation of PrEP Among Men Who Are Eligible for PrEP (n = 560)

Factor	OR	95% CI Lower	95% CI Upper	*P*	aOR	95% CI Lower	95% CI Upper	*P*
Year of visit								
2015	1				1			
2016	0.09	0.01	0.66	0.019	0.08	0.01	0.63	0.016
2017	0.03	0.00	0.24	0.001	0.02	0.00	0.18	<0.001
Age								
16–24	1				1			
25–29	0.45	0.26	0.78	0.005	0.54	0.28	1.03	0.062
30–39	0.48	0.28	0.84	0.010	0.44	0.23	0.83	0.012
40–84	0.39	0.23	0.67	0.001	0.60	0.32	1.13	0.115
Country of birth								
Australia	1							
Oceania (excl. Australia)	2.54	0.74	8.77	0.140				
Asia	0.34	0.13	0.88	0.026				
North America	1.48	0.30	7.23	0.626				
South/Central American	—	—	—	—				
Europe	0.70	0.35	1.39	0.306				
Middle East	1.69	0.19	15.30	0.638				
Africa	4.24	0.54	33.42	0.171				
Ethnicity								
Anglo-Celtic	1							
Aboriginal or Torres Strait Islander	0.73	0.17	3.11	0.674				
Others	1.13	0.71	1.80	0.609				
State of residence								
New South Wales and ACT	1				1			
Victoria	1.49	0.96	2.33	0.077	1.30	0.77	2.19	0.331
Queensland	1.78	0.97	3.29	0.064	1.30	0.65	2.62	0.463
Others	2.20	1.30	3.73	0.003	2.11	1.16	3.85	0.014
Education								
Less than university educated	1							
University educated	0.67	0.46	0.98	0.038				
Employment status								
Not in employment	1							
Part-time employed	1.35	0.67	2.74	0.401				
Full-time employed	0.82	0.52	1.30	0.406				
Socially engaged with other gay men	0.71	0.63	0.81	<0.001	0.78	0.68	0.91	0.001
Methamphetamine use								
No recent use (including never used)	1							
Recent use	1.12	0.76	1.63	0.570				
Reasons for party drug use								
No recent drug use (including never used)	1				1			
Recent drug use (not for sex)	0.47	0.29	0.77	0.003	0.37	0.21	0.64	<0.001
Recent drug use (used to enhance sex)	0.48	0.30	0.78	0.003	0.57	0.32	1.00	0.049
No. of recent sex partners								
1 sex partner	1							
Up to 10	0.28	0.12	0.68	0.005				
Up to 50	0.13	0.05	0.32	0.000				
More than 50	0.09	0.03	0.26	<0.001				
Group sex								
No group sex	1				1			
Recent group sex	0.35	0.24	0.51	<0.001	0.59	0.37	0.93	0.025
Sex with a casual partner								
No casual partner	1				1			

TABLE 3. (*Continued*) Factors Associated With Noninitiation of PrEP Among Men Who Are Eligible for PrEP (n = 560)

Factor	OR	95% CI Lower	95% CI Upper	*P*	aOR	95% CI Lower	95% CI Upper	*P*
No anal intercourse	0.28	0.12	0.65	0.003	0.45	0.18	1.14	0.092
Consistent condom use	0.46	0.20	1.04	0.063	0.51	0.21	1.25	0.143
Insertive-only condomless anal intercourse	0.17	0.08	0.37	<0.001	0.21	0.09	0.51	0.001
Any receptive condomless anal intercourse	0.15	0.08	0.27	<0.001	0.20	0.10	0.41	0.000
Did not answer	0.19	0.05	0.74	0.017	0.14	0.03	0.63	0.011
Sex with fuckbuddies								
No fuckbuddies	1							
No anal intercourse	1.20	0.42	3.39	0.731				
Consistent condom anal intercourse	1.47	0.58	3.72	0.421				
Insertive-only condomless anal intercourse	1.09	0.44	2.66	0.857				
Any receptive condomless anal intercourse	0.68	0.44	1.03	0.070				
Did not answer	0.53	0.12	2.43	0.416				
Sex with boyfriend								
No boyfriend	1							
No anal intercourse	1.20	0.42	3.39	0.731				
Consistent condom use	1.47	0.58	3.72	0.421				
Any condomless sex with an HIV-negative partner or an HIV-positive partner with an unknown, undetectable serostatus, or is on treatment	1.09	0.44	2.66	0.857				
Any condomless sex with an HIV-positive partner (detectable or not on treatment)	0.68	0.44	1.03	0.070				
Did not answer	0.53	0.12	2.43	0.416				

ACT, The Australian Capital Territory.

younger than those who initiated PrEP and tended to be less socially connected to other gay men. They also lived in states where PrEP trials had not commenced before 2017. However, many eligible men who did not initiate PrEP did not consistently engage in behaviors corresponding to the eligibility criteria over time and seemed to do so less often compared with eligible men who initiated PrEP.

The rapid rate of PrEP initiation in this sample mirrors the increasing prevalence of PrEP use found in Australian behavioral surveillance among GBM,[16] coinciding with the roll-out of large-scale PrEP implementation projects throughout Australia.[7–9] The Flux Study commenced before PrEP was listed for national subsidy and before the commencement of any of the large-scale Australian PrEP studies. Flux was neither a PrEP demonstration project nor it focused on PrEP use. Accessing PrEP was therefore not a condition for participation in this study, so participant characteristics may be more likely to reflect GBM living in Australia more broadly—a mix of PrEP users and nonusers, with varying eligibility for PrEP.

In recent years, a growing number of PrEP implementation studies across Australia and internationally have made PrEP more accessible, with approval for national subsidy likely to further increase uptake. Unsurprisingly, PrEP initiation increased over time in our sample, and living in an Australian state where a large PrEP trial had commenced before 2017 was a predictor of initiation. Among eligible men, those who lived outside an Australian state where a large PrEP trial had commenced were less likely to initiate

PrEP compared with their PrEP-initiating counterparts. In this regard, our sample reflects the unequal access to PrEP around Australia at the time of data collection.

Regardless of these access issues, younger age was independently associated with being less likely to initiate PrEP. This is also true among eligible men who did not initiate PrEP. Younger age has often been associated with lesser engagement with health care.[23] Being younger is also associated with being less socially connected to gay community, and in our data, being more socially connected with gay men was also predictive of PrEP uptake. These data reinforce the pivotal role gay community networks have played in HIV-risk reduction throughout the epidemic facilitating access to information and reinforcing social norms.[19,24] The Diffusion of Innovations theory suggests that innovations tend to spread more quickly through tightly bonded networks of similar people.[25] Gay community affiliations and social connections offer such an opportunity because they can promote PrEP as a harm-reduction strategy, particularly in the context of sexually adventurous networks of GBM.[26] These sorts of peer networks can be used to disseminate information and normalize new prevention technologies such as PrEP.

Behaviors previously associated with HIV infection, such as R-CAIC, using drugs to enhance sex ("chemsex"), group sex, and higher numbers of partners,[13,19,27–29] were also associated with PrEP initiation. Among eligible men who did not initiate PrEP, although they had engaged in these behaviors, they did so less frequently and reported engaging in these behaviors less consistently over time. In this sample,

GBM who used methamphetamine were more likely to initiate PrEP, and among eligible men, those who did not initiate PrEP were less likely to report drug use than were those who had initiated PrEP. Elsewhere, we have found that men who engage in chemsex have increasingly introduced PrEP into their drug use regime to mitigate against the risk of HIV infection in what would otherwise be considered a high HIV risk environment.[26]

Furthermore, GBM who reported to have more than 50 sexual partners in the previous 6-month period had an eight-fold increased likelihood of PrEP initiation compared with men who reported fewer partners. Although the number of sexual partners was not independently associated with PrEP initiation among PrEP-eligible men, those who did not use PrEP were nonetheless less likely to have engaged in group sex and had fewer partners than did those who used PrEP. Overall, men who initiated PrEP were likely to have engaged in behaviors that met the eligibility criteria for PrEP access; however, not all men whose behaviors met these criteria subsequently initiated PrEP. Indeed, many men who reported having engaged in these behaviors did not do so either as consistently or at the same rates as the men who did initiate PrEP. For some of these men, their decision not to initiate PrEP may be based on a reasonable assessment of their current risk profile. For others, however, it may reflect misconceptions about the levels of risk required to make use of PrEP worthwhile. Although the Australian National PrEP Prescribing Guidelines determine eligibility based on reported risk behaviors, they do not report the frequency of these risk behaviors. However, our data indicate that some high-risk men were engaging in these behaviors less often or inconsistently, thereby raising concerns about the sensitivity of the National PrEP prescribing guidelines and their potential accuracy. The guidelines may need a more nuanced approach to the application of the criteria. In some cases, it may be that some men underestimate their level of risk, but it may also be that the use of a single episode of risk behavior as indicative of eligibility for PrEP may be an overestimation of their likelihood of engaging in risk behaviors on an ongoing basis. Nonetheless, it seems that lack of intimate partner knowledge is a key facilitator in HIV seroconversion,[28] and thus, even oneoff events can pose HIV transmission risk that might otherwise be protected by PrEP.

Limitations and Strengths

As a voluntary online convenience sample, this sample may not be representative of all GBM living in Australia. Nonetheless, those who participated in our study were similar to other samples of Australian GBM. Inherent in all self-report data, recall bias and social desirability bias may be evident.[16,22] Our automated online methodology, however, can reduce social desirability bias in reporting illegal or stigmatized behaviors.[30,31]

Recent findings suggest that stigma, belief, and self-efficacy are important considerations for PrEP initiation.[32] Further research exploring men's reasoning for use and nonuse of PrEP is needed.

CONCLUSIONS

Most GBM who initiated PrEP in this study met the Australian behavioral eligibility criteria before PrEP initiation. However, not all men who met these eligibility criteria engaged in those behaviors as consistently as others. Although some men were eligible on previous rounds, their risk behaviors and eligibility status did not remain consistent over time compared with those who remained eligible. Furthermore, despite meeting the formal eligibility criteria for PrEP, men who did not initiate PrEP were less socially connected to other gay men. Their perception of their own level of risk compared with other gay men, and their relative lack of social connection, may influence their decisions about the need to use PrEP.

Men who are more or less socially engaged with gay community may also hold differing perceptions of social norms about or perceived acceptability of PrEP, as well as differing understandings of the level of risk required to warrant use of PrEP. Representations of PrEP users as sexually irresponsible, such as through the concept of "Truvada whores,"[33] may reinforce misconceptions about when PrEP use is appropriate and mitigate against more complete coverage in at-risk populations. On the other hand, the consistency and frequency of engaging in behaviors that correspond to the eligibility criteria varies over time, suggesting that the application of PrEP eligibility guidelines may need greater nuance than has been the case.

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5.1.4 Chapter five summary

Prior to PrEP initiation, gay and bisexual men who initiated PrEP reported behaviours that corresponded with the *Australian PrEP Guidelines*.[21,22] Among PrEP-eligible men, there was a rapid uptake of PrEP among men who engaged in chemsex. However, there was a large proportion of men who met the behavioural eligibility criteria but did not subsequently initiate PrEP. After controlling for all other variables, use of methamphetamine predicted PrEP initiation. As previously discussed, recent methamphetamine use is one of the eligibility criteria for PrEP access in Australia, so these results were not surprising.

Of more interest were the differences observed among PrEP-eligible men between those that initiated PrEP and those who did not. Restricting the analysis to PrEP-eligible men, these results demonstrated that, although having previously engaged in behaviours that make them high risk of HIV, they were doing so less frequently, and less consistently, than their PrEP using counterparts. Moreover, PrEP-eligible men who initiated PrEP were no more likely to report recent methamphetamine use than PrEP-eligible men who did not initiate PrEP. On the other hand, after controlling for all other variables, PrEP-eligible men who did not initiate PrEP were less likely to report using *any* drugs to engage in chemsex. That is, those who initiated PrEP were more likely to report use of any illicit drugs to engage in chemsex, rather than methamphetamine specifically.

A nuanced approach to harm reduction

6.1 PrEP as a harm reduction strategy among gay and bisexual men who engage in chemsex

6.1.1 Publication details

Hammoud MA, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Prestage G. The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe. International Journal of Drug Policy 2018; 55: 197-204.

6.1.2 Thesis aims related to this chapter

Thesis aim 4: Measure the incidence of PrEP uptake among gay and bisexual men, and describe uptake and non-uptake of PrEP among men who engage in chemsex.

Thesis aim 5: Identify factors associated with use of PrEP as a harm reduction strategy.

6.1.3   Chapter six in context

Prestage et al. (2009) have previously demonstrated the increased likelihood of HIV acquisition among men who used both erectile dysfunction medication and methamphetamine in the context of chemsex. Given that the *HIM Study* had already identified the concurrent use of crystal methamphetamine and erectile dysfunction medications as a strong predictor for HIV infection (Table 1.2),[1] **chapter 6** explores whether men at higher risk of HIV by using both drugs concurrently, use PrEP to mitigate against the risks of HIV.

From 2017, PrEP became more available in Australia, first through demonstration projects and personal importation,[25] and more recently through public subsidy.[26,27] In this chapter, I build on my PhD supervisors' previous work,[1] to investigate whether gay and bisexual men who concurrently use erectile dysfunction medication and methamphetamine were also using PrEP to mitigate against those same risks of HIV infection identified through the *HIM Study*.[1] This analysis explored whether gay and bisexual men who engage in chemsex had commenced using PrEP as it became more widely available.
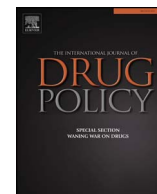
Commentary

The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe

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ABSTRACT

Introduction: Gay and bisexual men (GBM) often use illicit drugs to enhance sexual pleasure, commonly referred to as 'chemsex' or 'party n play'. In particular, the use of methamphetamine and Viagra™, and other erectile dysfunction medications, both together and separately are strongly predictive of subsequent HIV infection. Truvada™, as pre-exposure prophylaxis (PrEP), virtually eliminates HIV transmission during condomless anal intercourse (CLAI). HIV-negative GBM in intensive sex partying networks may be adding PrEP to their drug regimen to actively reduce the possibility of HIV transmission during chemsex.
Aim: We describe the prevalence and context of concurrent use of methamphetamine, Truvada™ (or its generic formulations), and Viagra™ or other erectile dysfunction medication (collectively, MTV).
Method: The *Following Lives Undergoing Change* study is an online prospective observational study of licit and illicit drug use among Australian GBM. Between January and July 2017, 1831 GBM provided details about their use of MTV. Binary logistic multiple regression analysis were used to estimate adjusted odds ratios (aOR) and associated 95% confidence intervals (95%CI).
Results: Concurrent MTV use was reported by 6.0% of participants; 3.1% used methamphetamine and Viagra™ or other erectile dysfunction medication ('MV only') and 11.2% used Truvada™ as PrEP ('T only'). In multivariate analysis, compared to use of 'MV only', MTV was independently associated with CLAI with casual partners (aOR = 6.78;95%CI = 1.42–32.34) and 'fuckbuddies' (aOR = 3.47;95%CI = 1.41–8.56) in the previous six months. Compared to use of 'T only', MTV was independently associated with being older (aOR = 3.95;95%CI = 1.55–10.03) and engaging in group sex (aOR = 3.31;95%CI = 1.82–6.00). Greater social engagement with other gay men (aOR = 1.44;95%CI = 1.18–1.76) and having more sexual partners (aOR = 2.30;95%CI = 1.10–4.82) were independently associated with use of MTV compared to use of 'MV only' or 'T only'.
Conclusion: GBM in intensive sex partying networks are increasingly adding PrEP alongside other drugs they use to enhance sexual experiences. Interventions that promote the use of PrEP during chemsex could mitigate HIV risk.

1 Introduction

Gay and bisexual men (GBM) often use illicit drugs to enhance sexual pleasure, particularly in the context of 'chemsex' or 'party n play'[1]; (Ahmed et al., 2016; Bourne, Reid, Hickson, Torres-Rueda, Steinberg, et al., 2015; Bourne, Reid, Hickson, Torres-Rueda, Weatherburn, 2015; Bui et al., 2018). Chemsex involves the use of drugs to maximise the potential for intense bodily pleasure while engaging in sex partying, often involving multiple partners. Intensive sex partying involves these chemsex practices, often including condomless anal intercourse (CLAI), in the context of greater involvement in gay community social and sexual networks (Hurley & Prestage, 2009).

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[1] The terms 'chemsex' and 'party-n-play' both refer to using drugs to enhance sexual pleasure. While the use of these terms varies across countries, both refer to the same practice. Although 'party n play' has tended to be more commonly used in Australia, for the purposes of this paper, we use 'chemsex'.

Intensive sex partying practices occur within the context of sexually adventurous networks and tend to be associated with HIV infection (Kippax et al., 1998).

Within the setting of intensive sex partying networks (Hurley & Prestage, 2009), chemsex has been associated with HIV sexual risk behaviours (Bourne, Reid, Hickson, Torres-Rueda, Weatherburn, 2015; Prestage et al., 2007), possibly because intensive sex partying networks facilitate an environment of heightened sexual activity in which sexually transmissible infections, including HIV, may be more common. In particular, the use of methamphetamine and Viagra™, and other erectile dysfunction medications, both together and separately has been found to be strongly predictive of subsequent HIV infection (Fisher, Reynolds, & Napper, 2010; Prestage, Jin et al., 2009; Swearingen & Klausner, 2005).

The drugs associated with chemsex are location specific (Bourne, Reid, Hickson, Torres-Rueda, Steinberg et al., 2015; Bourne, Reid, Hickson, Torres Rueda, & Weatherburn, 2014; Buchacz et al., 2005; Hammoud et al., 2017). In Australia, methamphetamine is commonly used during chemsex (Prestage et al., in press) but other drugs can include gamma hydroxybutyrate (Hammoud et al., 2017), cocaine, ketamine, and mephedrone (Bourne et al., 2014). These drugs are used to increase the levels of sexual excitement and reduce inhibitions. In this context, men often also use Viagra™ and other erectile dysfunction medication, usually off-label, specifically to enhance and extend their sexual functioning or to overcome the erectile dysfunction that often accompanies methamphetamine use (Hammoud, Jin, Lea, Maher, & Prestage, 2017; Fisher et al., 2010). While most drug use has been found to be associated with sexual risk behaviour among GBM (Prestage, 2009; Prestage et al., 2007; Prestage, Grierson, Bradley, Hurley, & Hudson, 2009), the particular use of these two drugs, separately and concurrently (using both drugs within a specified time period, but not necessarily on the same occasion), has been independently associated with HIV seroconversion (Prestage, Jin, et al., 2009).

Peer norms and socialisation play a key role in drug-using behaviours. The use of drugs such as methamphetamine, gamma hydroxybutyrate, and erectile dysfunction medication is strongly associated with social engagement with other gay men who use drugs (Hammoud et al., 2017; Hammoud, Jin, Lea et al., 2017; Prestage et al., in press). The links between the use of these drugs and HIV risk have generated considerable attention about the phenomenon of chemsex, including concerns about its role in gay communities, and calls for new harm reduction approaches to prevent increases in HIV transmissions or drug-use effects (Bourne, Reid, Hickson, Torres-Rueda, Steinberg et al., 2015; Bourne et al., 2014).

The co-formulation of emtricitabine and tenofovir (Truvada™), and its generic formulations when used as PrEP, is a highly effective biomedical HIV prevention strategy (Fonner et al., 2016; Kennedy & Fonner, 2016). Among GBM, in a sub-analysis of a trial cohort, the use of seven pills/week resulted in a 99% HIV risk reduction, whilst four pills/week was associated with a 96% risk reduction (Anderson et al., 2012). Event-based dosing has been shown to be equally as effective as daily dosing in GBM, with two recent randomised trials reporting a risk reduction of 86%, and their open label extensions and subsequent analyses reporting a value closer to 99% (Molina et al., 2015; Molina, Charreau et al., 2017).

Truvada™, as pre-exposure prophylaxis (PrEP), virtually eliminates the possibility of HIV transmission during condomless anal intercourse (CLAI) (Kennedy & Fonner, 2016). HIV-negative GBM who use both methamphetamine and Viagra™ may be adding Truvada™ to their drug regimen to actively reduce the possibility of HIV transmission in the context of chemsex.

Through implementation studies, there has been a rapid roll out of PrEP among Australian GBM, particularly during 2016–2017: Prevalence of PrEP use has risen from 1.4% in 2014 to 13.9% in 2017 among GBM in Sydney (Hull et al., 2017). The introduction of PrEP in

Australia, alongside ongoing suppression of viral load at a population level (Rodger et al., 2016) and other HIV prevention strategies, has resulted in a rapid decrease in new HIV infections among GBM in New South Wales, Australia's most populous state (NSW Ministry of Health, 2017).

PrEP offers an opportunity for an HIV prevention strategy that could be usefully deployed by men who engage in chemsex (Murphy, 2015). PrEP offers practical benefits over condom-based HIV protection in intensive sex partying contexts, in that it is taken orally once daily, and is not linked to individual risk events. To date, there are few quantitative data to indicate the prevalence of concurrent use of methamphetamine, PrEP, and erectile dysfunction medication among GBM, or whether those who participate in intensive sex partying networks are utilising biomedical HIV prevention strategies such as PrEP (Kurtz, Buttram, & Surratt, 2014).

2 Aim

In this paper, we use data from an online cohort study of licit and illicit drug use among Australian GBM to describe the prevalence of concurrent use of methamphetamine, Truvada™ (or its generic formulations), and Viagra™ or other erectile dysfunction medication (collectively, MTV). We also describe the prevalence of concurrent use of methamphetamine and Viagra™ or other erectile dysfunction medication without use of PrEP ('MV only'), and the prevalence of use of Truvada™ or its generic formulations alone, without use of either methamphetamine or erectile dysfunction medication ('T only'). Methamphetamine and Viagra™, or other erectile dysfunction medication have not been assessed alongside these combinations as both have previously been reported using data from this study (Hammoud, Jin, Lea et al., 2017; Prestage et al., in press). We examine factors that distinguish men who use MTV from men who use 'MV only' and from men who use 'T only'. Finally, we investigate the relationship between each of these patterns of use and sexual risk behaviour, and intensive sex partying.

3 Methods

3.1 Procedure

The *Following Lives Undergoing Change* (Flux) Study is an ongoing, online prospective observational cohort study of licit and illicit drug use among Australian GBM. The Flux Study examines the prevalence, incidence, and context of licit and illicit drug use, and their associated motivations, pleasures, and harms. Methods have been described in greater detail elsewhere (Hammoud, Jin, Degenhardt et al., 2017).

Participants were recruited between August 2014 and July 2017 through Facebook, gay community websites and online media, mobile phone applications, and gay sexual networking websites. Participants provided informed consent and ethical approval was granted by the Human Research Ethics Committee of UNSW Sydney (HC14075).

After baseline, follow-up questionnaires were completed biannually. Invitations to participate in each follow up round were sent via email or text messaging.

3.2 Measures

The baseline and follow-up surveys included: demographic items, questions on sexual identity and social networks, HIV testing history and self-reported HIV serostatus, sexual behaviour with men, and attitudes and beliefs about drug use. Men also indicated how much they were affiliated with specific gay community tribal subcultures (Prestage et al., 2015), with responses of 'Not at all', 'Somewhat', and 'Very much'. Subcultures include 'sex pigs', those who enjoy a range of sexual experiences that are more adventurous (Mowlabocus, 2016), and 'party boys', characterised as those who barhop and cruise for sex (Griffin,

Table 1

Characteristics of non HIV positive men according to use of MTV. N = 1831.

N (%)	No use of any of these 3 drugs 1008 (55.1)	Any use of V, M, TV, MT 451 (24.6)	T only 205 (11.2)	MV only 57 (3.1)	MTV 110 (6.0)
Age***					
Mean (SD)***	33.6 (12.4)	43.8 (13.9)	37.2 (11.1)	42.1 (11.6)	42.3 (9.3)
≤ 30	520 (51.6)	95 (21.1)	57 (27.8)	11 (19.3)	12 (10.9)
31–40	234 (23.2)	108 (23.9)	79 (38.5)	13 (22.8)	36 (32.7)
41–50	124 (12.3)	89 (19.7)	40 (19.5)	17 (29.8)	43 (39.1)
Over 50	130 (12.9)	159 (35.3)	29 (14.1)	16 (28.1)	19 (17.3)
Cultural background					
Anglo-Celtic	721 (71.5)	347 (76.9)	148 (72.2)	46 (80.7)	83 (75.5)
Aboriginal or Torres Strait Islander	21 (2.1)	4 (0.9)	2 (1.0)	1 (1.8)	1 (0.9)
Other	263 (26.1)	100 (22.2)	55 (26.8)	9 (15.8)	26 (23.6)
Not stated	3 (0.3)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)
Education***					
Less than university level	411 (40.8)	166 (36.8)	74 (36.1)	22 (38.6)	29 (26.4)
University educated	595 (59.0)	285 (63.2)	131 (63.9)	35 (61.4)	81 (73.6)
Not stated	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Occupation***					
Managerial	121 (12.0)	77 (17.1)	39 (19.0)	14 (24.6)	35 (31.8)
Professional	265 (26.3)	145 (32.2)	68 (33.2)	18 (31.6)	33 (30.0)
Other white collar	130 (12.9)	46 (10.2)	22 (10.7)	5 (8.8)	11 (10.0)
Other	81 (8.0)	42 (9.3)	25 (12.2)	3 (5.3)	10 (9.1)
Not in work	263 (26.1)	85 (18.8)	38 (18.5)	8 (14.0)	16 (14.5)
Did not answer	148 (14.7)	56 (12.4)	13 (6.3)	9 (15.8)	5 (4.5)
HIV Status***					
HIV-negative	610 (60.5)	395 (87.6)	200 (97.6)	43 (75.4)	108 (98.2)
Unknown/untested	398 (39.5)	56 (12.4)	5 (2.4)	14 (24.6)	2 (1.8)
In a relationship with regular partner					
Not in a relationship	606 (60.2)	278 (61.6)	130 (63.4)	31 (54.4)	65 (59.1)
In a relationship	401 (39.8)	173 (38.4)	75 (36.6)	26 (45.6)	45 (40.9)
Patient Health Questionnaire (PHQ-9)					
Minimal	445 (44.1)	221 (49.0)	100 (48.8)	27 (47.4)	51 (46.4)
Mild	253 (25.1)	116 (25.7)	46 (22.4)	12 (21.1)	30 (27.3)
Moderate	105 (10.4)	37 (8.2)	27 (13.2)	7 (12.3)	16 (14.5)
Moderately severe	79 (7.8)	40 (8.9)	13 (6.3)	4 (7.0)	3 (2.7)
Severe	48 (4.8)	16 (3.5)	12 (5.9)	1 (1.8)	4 (3.6)
Did not answer	78 (7.7)	21 (4.7)	7 (3.4)	6 (10.5)	6 (5.5)
Generalized Anxiety Disorder (GAD7)					
Minimal anxiety	543 (53.9)	274 (60.8)	115 (56.1)	35 (61.4)	73 (66.4)
Mild anxiety	229 (22.7)	87 (19.3)	47 (22.9)	12 (21.1)	19 (17.3)
Moderate anxiety	95 (9.4)	47 (10.4)	20 (9.8)	4 (7.0)	7 (6.4)
Severe anxiety	65 (6.4)	20 (4.4)	14 (6.8)	2 (3.5)	7 (6.4)
Did not answer	76 (7.5)	23 (5.1)	9 (4.4)	4 (7.0)	4 (3.6)
Socially engaged with other gay men***	3.3 (1.5)	4.2 (1.5)	4.2 (1.5)	3.9 (1.7)	5.0 (1.3)
Sexual sensation seeking scale***	28.3 (5.9)	31.3 (5.5)	31.9 (5.4)	32.7 (5.3)	33.7 (5.0)
Drug use sensation seeking scale***	18.0 (5.3)	20.8 (7.4)	19.4 (6.1)	28.6 (7.3)	27.6 (7.3)

*p < 0.05.
**p < 0.01.
***p < 0.001.

2017). Men reported their sexual behaviour in the previous six months with their 'boyfriend' (regular committed partner with whom they maintain a romantic relationship), 'fuckbuddies' (non-romantic regular partners), and casual partners (Bavinton et al., 2016; Down, Ellard, Bavinton, Brown, & Prestage, 2017).

Men reported their use of licit and illicit drugs in the previous six months. For methamphetamine-type drugs ('crystal' or 'speed') and erectile dysfunction medication, they were asked how often they used these drugs in the previous six months (e.g., daily, weekly, monthly, less than monthly). For PrEP, they were asked whether they used it only before and after having sex, and whether they continued to use PrEP after having sex. We included a previously used measure of social connectedness with gay men, based on two items measuring the proportion of friends who are gay men; and the amount of free time spent with gay male friends (Zablotska, Holt, & Prestage, 2012). Intensive sex partying practices (Hurley & Prestage, 2009) were addressed by questions about group sex, number of sexual partners, and using drugs for sex.

The Generalized Anxiety Disorder Assessment (GAD7), a seven-item self-report measure that assesses symptoms of anxiety (Spitzer, Kroenke, Williams, & Löwe, 2006), and the Patient Health Questionnaire (PHQ9), a nine-item self-report measure that assesses symptoms of depression (Kroenke, Spitzer, & Williams, 2001) were also included.

3.3 Participants and sample

Men who lived in Australia and were aged sixteen years and six months or above were eligible for participation in the Flux Study if they were gay- or bisexual-identified or had sex with another man in the previous year. Recruitment included: 753 enrolments during 2014; 1461 enrolments during 2015, and 1039 enrolments during 2017. In total, 3253 GBM provided sufficient data at baseline for analysis.

Of 1954 respondents who provided either baseline or follow-up data in 2017, 6.3% reported a HIV-positive serostatus and were excluded from this analysis. A total of 1831 non-HIV-positive men provided data in 2017.

This analysis only includes 1831 responses provided, either at baseline or during follow-up, during 2017, the year in which PrEP became widely available in Australia (Holt, 2017).

Table 2

Sexual and drug use behaviours in the previous 6 months of non HIV positive men according to use of MTV. N = 1831.

N (%)	No use of any of these 3 drugs 1008 (55.1)	Any use of V, M, TV, MT 451 (24.6)	T only 205 (11.2)	MV only 57 (3.1)	MTV 110 (6.0)
Identify as part of sex pig networks ***					
No	846 (83.9)	315 (69.8)	144 (70.2)	37 (64.9)	47 (42.7)
Yes	107 (10.6)	102 (22.6)	50 (24.4)	19 (33.3)	55 (50.0)
Did not answer	55 (5.5)	34 (7.5)	11 (5.4)	1 (1.8)	8 (7.3)
Identify as part of sex club and party networks ***					
No	779 (77.3)	300 (66.5)	152 (74.1)	31 (54.4)	40 (36.4)
Yes	171 (17.0)	115 (25.5)	42 (20.5)	25 (43.9)	61 (55.5)
Did not answer	58 (5.8)	36 (8.0)	11 (5.4)	1 (1.8)	9 (8.2)
Number of sexual partners ***					
Mean (SD) ***	7.5 (35.4)	21.4 (34.0)	25.3 (33.0)	25.0 (33.9)	45.9 (65.2)
No partner	149 (14.8)	12 (2.7)	0 (0.0)	2 (3.5)	0 (0.0)
Up to 10	660 (65.5)	190 (42.1)	63 (30.7)	25 (43.9)	11 (10.0)
Over 10	186 (18.5)	243 (53.9)	142 (69.3)	30 (52.6)	98 (89.1)
Not stated	13 (1.3)	6 (1.3)	0 (0.0)	0 (0.0)	1 (0.9)
Sex with boyfriends *					
No boyfriend	559 (55.5)	271 (60.1)	131 (63.9)	28 (49.1)	66 (60.0)
No anal intercourse	44 (4.4)	16 (3.5)	1 (0.5)	2 (3.5)	2 (1.8)
Condom use only	57 (5.7)	13 (2.9)	6 (2.9)	1 (1.8)	1 (0.9)
Any condomless anal intercourse	335 (33.2)	145 (32.2)	67 (32.7)	26 (45.6)	40 (36.4)
Not stated	13 (1.3)	6 (1.3)	0 (0.0)	0 (0.0)	1 (0.9)
Sex with fuckbuddy ***					
No boyfriend	795 (78.9)	225 (49.9)	87 (42.4)	40 (70.2)	41 (37.3)
No anal intercourse	20 (2.0)	8 (1.8)	4 (2.0)	2 (3.5)	2 (1.8)
Condom use only	61 (6.1)	27 (6.0)	9 (4.4)	2 (3.5)	3 (2.7)
Any condomless anal intercourse	119 (11.8)	185 (41.0)	105 (51.2)	13 (22.8)	63 (57.3)
Not stated	13 (1.3)	6 (1.3)	0 (0.0)	0 (0.0)	1 (0.9)
Sex with casual partner ***					
No boyfriend	494 (49.0)	80 (17.7)	23 (11.2)	14 (24.6)	4 (3.6)
No anal intercourse	80 (7.9)	33 (7.3)	9 (4.4)	10 (17.5)	3 (2.7)
Condom use only	208 (20.6)	82 (18.2)	23 (11.2)	10 (17.5)	4 (3.6)
Any condomless anal intercourse	213 (21.1)	250 (55.4)	150 (73.2)	23 (40.4)	98 (89.1)
Not stated	13 (1.3)	6 (1.3)	0 (0.0)	0 (0.0)	1 (0.9)
Party n play ***					
Never used drugs/no recent drug use	874 (86.7)	273 (60.5)	167 (81.5)	2 (3.5)	3 (2.7)
Once	17 (1.7)	64 (14.2)	5 (2.4)	22 (38.6)	42 (38.2)
More than once	6 (0.6)	14 (3.1)	0 (0.0)	16 (28.1)	59 (53.6)
Did not answer	111 (11.0)	100 (22.2)	33 (16.1)	17 (29.8)	6 (5.5)
Group sex ***					
No	846 (83.9)	276 (61.2)	103 (50.2)	27 (47.4)	21 (19.1)
Yes	162 (16.1)	175 (38.8)	102 (49.8)	30 (52.6)	89 (80.9)
Used drugs for sex ***					
Never	256 (25.4)	140 (31.0)	56 (27.3)	9 (15.8)	3 (2.7)
Used drugs for sex	46 (4.6)	107 (23.7)	14 (6.8)	47 (82.5)	107 (97.3)
Did not answer	706 (70.0)	204 (45.2)	135 (65.9)	1 (1.8)	0 (0.0)
Used drugs for group sex ***					
Never	275 (27.3)	184 (40.8)	64 (31.2)	31 (54.4)	18 (16.4)
Used drugs for group sex	24 (2.4)	58 (12.9)	6 (2.9)	25 (43.9)	92 (83.6)
Did not answer	709 (70.3)	209 (46.3)	135 (65.9)	1 (1.8)	0 (0.0)

*p < 0.05.

**p < 0.01.

***p < 0.001.

3.4 Analysis

Data were analysed using SPSS™ version 24 software. Missing data were recoded accordingly (e.g., did not answer, no recent drug use, etc.). Descriptive statistics were used to characterise the types of men who used the various combinations of MTV. For univariate analysis of whether participants have used MTV, we included: age, cultural background, education, social engagement with other gay men, sexual and sexual risk behaviours. Categorical variables were analysed using Pearson's chi-square test, and continuous variables were analysed using one-way analysis of variance. We used Type I error of 5% for these analyses.

Analysis was restricted to GBM who reported a HIV-negative serostatus. Prevalence trends on 'T only', 'MV only', and MTV were reported using data from 2014 to 2017. Analysis for associations were restricted to participants who provided recent data in 2017 on: concurrent use of MTV; 'MV only'; 'T only'; any combination of MTV; or no use of these three drugs. We compared men who used MTV, to men who used 'MV only', and seperately to men who used 'T only'.

To estimate statistical associations, we used a binary logistic backward stepwise multiple regression analysis to control for confounding factors and presented the Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI). Associations with a p-value of less than 0.10 in univariate analyses were included in the multivariate analyses.

4 Results

4.1 Characteristics of the sample

The mean age of the 1831 men included in this analysis was 37.3 (SD 13.2) years. They predominantly identified as gay (89.0%) and most (86.2%) had been tested for HIV. The majority of men in the sample were of Anglo-Celtic background (73.5%), and were university educated (61.6%) (Table 1). Almost half were in managerial (15.6%) or
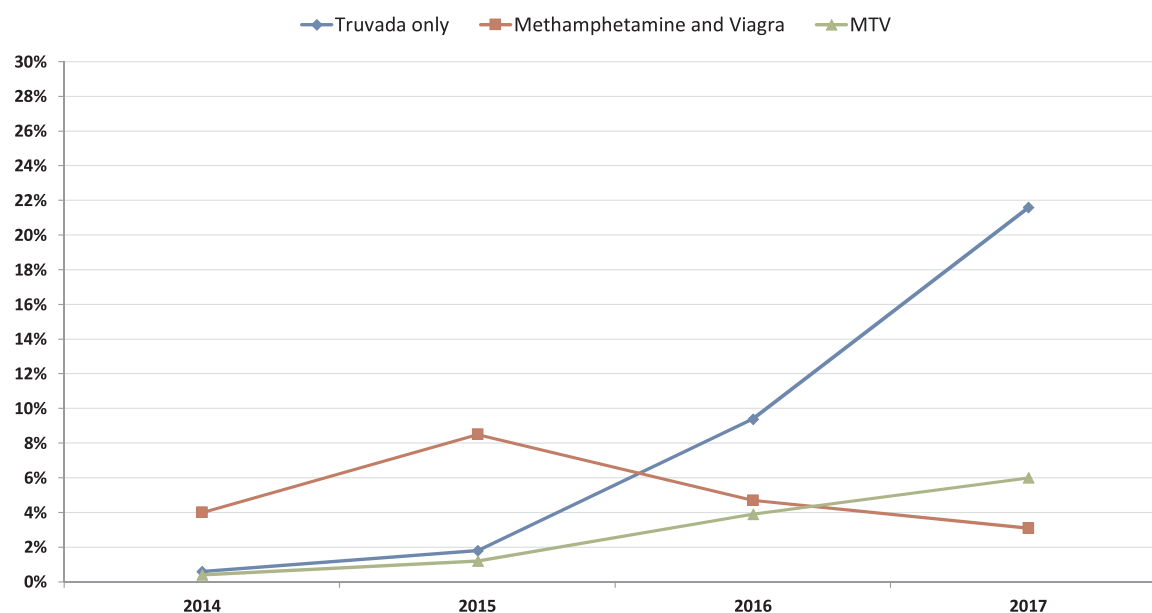
Fig. 1. MTV prevalence over time. Categories are mutually exclusive.

professional (28.9%) employment. One in three (34.0%) reported that most of their friends were gay and 57.4% spend much of their free time with gay friends.

Most (91.1%) reported sex with a man in the previous six months, and 38.2% reported having more than ten male sex partners in the previous six months (Table 2). About one in three (30.5%) had engaged in group sex. 39.3% indicated they had a regular partner (or 'boyfriend'), one-third (34.1%) reported sex with 'fuckbuddies', and more than half (65.4%) reported sex with casual partners.

Almost one in five (18.2%) identified at least somewhat affiliated with a 'sex pig' subculture and 22.6% identified at least somewhat with a 'party boy' subculture. In the previous six months, 13.4% reported engaging in a 'party n play' session, 17.5% used party drugs for sex, and 11.2% used party drugs for group sex. Most (71.7%) of those who had used PrEP reported having at least some friends who also used it, and 38.0% of the men who had not used PrEP reported also having friends who had used it.

4.2 Changes in use of MTV over time

Among 2037 men who responded to a survey in 2014, 13.3% reported use of methamphetamine and 18.8% reported use of erectile dysfunction medication. Among 1831 men who responded in 2017, these proportions were 14.5% and 28.3% respectively. Regarding PrEP use, among respondents in 2014, 1.0% reported use of PrEP (Fig. 1). By 2017, 27.6% reported using PrEP. The concurrent use of methamphetamine and erectile dysfunction medication has decreased from 2014 to 2017 from 4.5% to 3.1%, whilst the concurrent use of MTV increased from 1.9% to 6.0%.

4.3 MTV use in 2017

In 2017, 6.0% of participants reported the concurrent use of MTV. One in nine (11.2%) had used 'T only' and 3.1% had used 'MV only'. One in four (24.6%) used any combination of these drugs and half (55.1%) had not recently used either methamphetamine, PrEP, or erectile dysfunction medications.

The results of the regression analyses can be found in Table 3. In univariate analyses, compared to men who used 'MV only', men who reported MTV use were more likely to be more socially engaged with other gay men. MTV use was also more likely to occur in conjunction

with having had more than ten sexual partners, group sex, and CLAI both with casual partners and with fuckbuddies in the previous six months. In multivariate analysis, compared to men who used 'MV only', being more socially engaged with other gay men remained independently associated with the concurrent use of MTV. Having more than ten sexual partners, and CLAI with casual partners and fuckbuddies in the previous six months were also independently associated with MTV.

In univariate analyses, compared to men who used 'T only', MTV use was more likely to occur among men who were older and more socially engaged with other gay men (Table 3). MTV use was also more likely to occur in conjunction with having more than ten sexual partners, group sex, and CLAI with casual partners. In multivariate analysis, compared to men who used 'T only', being older and being more socially engaged with other gay men remained significantly associated with MTV use, as did having more than ten sexual partners and engaging in group sex.

5 Discussion

For the first time, these data show the increasing concurrent use of methamphetamines, Viagra™ and other erectile dysfunction medications, and Truvada™ as PrEP among Australian GBM. These findings may have significant implications for intensive sex partying networks, which thus serve as potential harm reduction targets.

Incorporating PrEP into sexual and drug use practices offers a highly efficacious harm reduction strategy for GBM who use drugs to enhance their sexual pleasure. Men in our sample who used methamphetamine and erectile dysfunction medication were highly engaged in gay community life, were highly sexually active, and tended to engage in group sex and in CLAI with casual partners − all behaviours that have been previously shown to be associated with HIV acquisition (Prestage, Jin, et al., 2009). The men who used both of these drugs concurrently while also using PrEP − thus, MTV − were significantly more sexually active and more likely to engage in sexual risk behaviour.

GBM who used MTV were older compared to men who used 'T only'. No age differences were observed between use of 'MV only' and use of MTV, suggesting that any age differences are probably specific to the use of erectile dysfunction medication. Previous research has also shown that older men, including older GBM, are more likely to use erectile dysfunction medication; both during chemsex (Crosby &

Table 3
Associations with use of MTV.

n (%)	MV vs. MTV n = 167							T vs. MTV n = 315							
	Univariate analysis				Multivariate analysis				Univariate analysis				Multivariate analysis		
	OR	CI 95 Lower–Upper		p	aOR	CI 95 Lower–Upper		p	OR	CI 95 Lower–Upper		p	aOR	CI 95 Lower–Upper		p
Characteristics																
Age																
≤30	1								1				1			
31–40	2.54	0.90	7.15	0.08					2.17	1.04	4.52	0.04	2.38	1.08	5.24	0.03
41–50	2.32	0.86	6.25	0.10					5.11	2.40	10.89	< 0.01	4.94	2.20	11.11	< 0.01
> 50	1.09	0.38	3.12	0.88					3.11	1.33	7.28	0.01	3.95	1.55	10.03	< 0.01
Anglo-Celtic	0.74	0.33	1.62	0.44					1.18	0.70	2.01	0.53				
University educated	1.76	0.89	3.47	0.11					1.58	0.95	2.63	0.08				
Occupation	1.27	0.66	2.42	0.48					1.48	0.93	2.38	0.10				
Socially engaged with other gay man	1.60	1.27	2.02	< 0.01	1.60	1.19	2.13	< 0.01	1.47	1.23	1.77	< 0.01	1.44	1.18	1.76	< 0.01
Sexual behaviours																
More than 10	7.35	3.32	16.25	< 0.01	2.99	1.00	8.91	0.05	3.62	1.86	7.07	< 0.01	2.30	1.10	4.82	0.03
Group sex	3.81	1.89	7.72	< 0.01					4.28	2.47	7.41	< 0.01	3.31	1.82	6.00	< 0.01
CLAI with fuckbuddies																
No partner	1				1				1							
No anal	0.98	0.13	7.27	0.98	0.37	0.04	3.78	0.40	1.06	0.19	6.03	0.95				
Condom only	1.46	0.23	9.23	0.69	3.49	0.38	32.34	0.27	0.70	0.18	2.75	0.62				
Any condomless sex	4.73	2.26	9.90	< 0.01	3.47	1.41	8.56	0.01	1.27	0.78	2.07	0.33				
CLAI with casual partners																
No partner	1				1				1							
No anal	1.05	0.19	5.76	0.94	0.71	0.09	5.26	0.73	1.92	0.36	10.32	0.45				
Condom only	1.40	0.28	6.98	0.68	0.98	0.13	7.19	0.98	1.00	0.22	4.49	1.00				
Any condomless sex	14.91	4.49	49.53	< 0.01	6.78	1.42	32.34	0.02	3.76	1.26	11.19	0.02				
CLAI with boyfriend																
No partner	1								1							
No anal	0.424	0.06	3.16	0.40					3.97	0.35	44.58	0.26				
Condom only	0.424	0.03	7.02	0.55					0.33	0.04	2.81	0.31				
Any condomless sex	0.653	0.34	1.27	0.21					1.19	0.73	1.94	0.50				

DiClemente, 2004; Hammoud, Jin, Lea et al., 2017) and for erectile dysfunction purposes (Shamloul & Ghanem, 2013). Erectile dysfunction medication use by men who also use methamphetamine may be specifically to prolong sexual pleasure in a chemsex encounter. Elsewhere, we have found little relationship between age and methamphetamine use (Prestage et al., in press). However, most studies of PrEP use among GBM have found an association between age and PrEP use, with older men more likely to take up PrEP (Snowden, Chen, McFarland, & Raymond, 2016).

Overall, PrEP use increased over time. This, which was not unexpected given the increasing access to PrEP through its mass roll out among GBM in Australia via large-scale PrEP implementation studies (Grulich, 2017), and elsewhere (Molina et al., 2015; Molina, Pialoux et al., 2017).

Compared to use of 'MV only' or 'T only', use of MTV was associated with being more socially engaged with other gay men. Most men in this sample reported having gay friends who use PrEP, but PrEP use was more common among men who used PrEP themselves. So, peer networks may play an important role in disseminating information and normalising new prevention technologies, in the same way as they appear to play a role in normalising the use of methamphetamine and erectile dysfunction medication (Lea et al., 2015).

Use of MTV was associated with sexual risk behaviours. Although men who used 'MV only' and men who used 'T only' were also highly sexually active and very likely to engage in CLAI, both with casual partners and with fuckbuddies, men who used MTV were significantly more likely to engage in each form of risk behaviour. What particularly distinguishes the men who are most likely to engage in these behaviours is that they concurrently use MTV. They are more likely to use the combination of all three of these drugs rather than either PrEP alone or the combination of methamphetamine and erectile dysfunction medication without PrEP. This represents a useful introduction of biomedical prevention into the drug use regimen commonly found in intensive sex partying contexts.

While the concurrent use of 'MV only' has declined in recent years, MTV and 'T only' have increased. This suggests that GBM who engage in chemsex appear to be including PrEP in their drug regimens, presumably to prevent risk of HIV infection.

5.1 Limitations and strengths

Although this cohort was a volunteer, online convenience sample, those who participated in our study were similar to other samples of Australian GBM and internationally (Lea et al., 2013; McCormack et al., 2016; Roxburgh, Lea, de Wit, & Degenhardt, 2016; Weatherburn et al., 2013); however, findings may not be representative of all Australian GBM, or of GBM internationally. Further research among specific subsamples of GBM that are few in number or may be underrepresented in our sample are needed. Relatively small sample sizes applied specifically to the analyses of MV vs. MTV and CLAI with casual partners. These specific analyses were of men who have been demonstrated to be at highest risk of HIV infection in the absence of PrEP use and are therefore of key interest for HIV prevention (Jin et al., 2009; Wright et al., 2017).

As with all cross-sectional analysis, causative or temporal relationships in the data could not be determined. This analysis was unable to determine the reasons why GBM who were using MV only were not using PrEP. Although our data could describe the concurrent use of these three drugs (methamphetamine, erectile dysfunction medication, and PrEP) within the same six month period, we were unable to determine to what extent they were being used on the same occasion. To examine this in detail requires the collection of event level data. In our study, we had limited data on adherence to PrEP or modes of use. Future studies should consider differences between daily and intermittent PrEP use in relation to the introduction of new harm reduction strategies to the practice of chemsex. Also, future studies should

consider the reasons why men who are using 'MV only' do not use PrEP and to what extent they utilise other harm reduction strategies.

Flux is the first Australian cohort study of GBM to specifically examine drug use in detail. This large, community-based national sample is geographically dispersed and includes men of all ages, including both those that are engaged and not engaged with gay community life. Our online methodology potentially reduces social desirability bias in reporting illegal or stigmatised behaviours (Davis, Couper, Janz, Caldwell, & Resnicow, 2009; De Vaus, 2013; Engel & Schutt, 2012).

6 Conclusion

Some men have begun to use PrEP to mitigate against the risk of HIV infection through what would otherwise be considered high HIV risk behaviours in the context of intensive sex partying networks. The introduction of PrEP can complement drugs used for chemsex. Gay community peer norms and social connections play a strong role in how drug use is enacted among GBM, making gay community networks a key context in which to promote the uptake of PrEP as an addition to their drug use repertoire, particularly among those at-risk men who participate in chemsex subcultures. Health promotion initiatives can help to normalise PrEP among these men and to develop tools for peer-based support for harm reduction. However, some men who are not connected to these networks also engage in the same high risk behaviours. More information is required about these less socially connected men to enable the development of appropriate harm reduction interventions.

Conflict of interest statement

No potential conflicts of interest were reported by the authors.

Author agreement/declaration

All authors certify that they have seen and approved the final version of the manuscript being submitted. All authors warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

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6.1.4   Chapter six summary

This chapter demonstrates a change in harm reduction behaviour. The prevalence of PrEP use increased dramatically between 2014 and 2017. This increasing coincided with the roll-out of Australian PrEP implementation trials in various jurisdictions and mirrors the increase in prevalence of PrEP use found in Australian behavioural survaillance.[28]

Between 2014 and 2017, prevalence of erectile dysfunction medication and methamphetamine use without concurrent PrEP use significantly decreased overtime, while concurrent use of erectile dysfunction medication, methamphetamine, and PrEP increased substantially. By 2017, it appears that many gay and bisexual men who had used erectile dysfunction medication and methamphetamine prior to the availability of PrEP had since started incorporating PrEP to mitigate against the risks of HIV infection. This suggest that new harm reductions strategies are being adopted among men who engage in chemsex. However, while these results are promising, many gay and bisexual men who were engaging in chemsex continued to report sexual behaviours that placed them at risk of HIV, without the benefit of protection from PrEP. Although they were engaging in high-risk behaviours less frequently, they still remain at risk of HIV.

Chapter Seven

The changing HIV landscape

7.1 The current state of HIV in chemsex

7.1.1 Publication details

7.1.2 Thesis aims related to this chapter

Thesis aim 4: Measure the incidence of PrEP uptake among gay and bisexual men, and describe uptake and non-uptake of PrEP among men who engage in chemsex.

Thesis aim 5: Identify factors associated with use of PrEP as a harm reduction strategy.

7.1.3   Chapter seven in context

Biomedical HIV prevention, in particular, PrEP in HIV-negative men and TasP in HIV-positive men, has the potential to change the associations between use of illicit drugs, condomless anal intercourse with casual partners, and the risk of HIV transmission. With PrEP becoming increasingly available in Australia and with most Australian HIV-positive men having achieved undetectable viral load,[25] there is an increasing proportion of gay and bisexual men who are biomedically protected from HIV. Nonetheless, as identified in the previous chapter, and demonstrated by other community samples,[28] there were approximately one in five HIV-negative men who continued to engage in condomless anal intercourse with casual partners, without the protection of either PrEP or, at least knowingly, TasP.

To date, use of methamphetamine has consistently been linked to HIV infection.[1,24,29] Also, methamphetamine is the only drug whose use has been classified as an eligibility criterion for PrEP access in Australia.[21,22] At the time of this analysis, previous associations between use of methamphetamine and condomless anal intercourse with casual partners had not been tested in the context of biomedical prevention. It is unclear whether men who use methamphetamine are more likely to engage in condomless anal intercourse with casual partners without the protection of PrEP or TasP than other gay and bisexual men who do not use methamphetamine, and, therefore, whether they still remain at increased risk of HIV infection.

To determine whether biomedical prevention has altered what is widely understood about the HIV risks associated with chemsex, in the next chapter, I am among the first internationally to investigate the prevalence, contexts, and motivations for

methamphetamine use, in relation to HIV sexual risk behaviours in the context of HIV

biomedical prevention.

Biomedical HIV protection among gay and bisexual men who use crystal methamphetamine

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Abstract

Background

Use of crystal methamphetamine (crystal) to enhance sexual pleasure among gay and bisexual men (GBM) has been associated with condomless anal intercourse with casual partners (CLAIC) and subsequent HIV infection. As biomedical HIV prevention, such pre-exposure prophylaxis and anti-retroviral therapy (ART) to achieve an undetectable viral load (UVL), changes understandings of 'safe sex', crystal use and its associations with HIV infection may also change. We investigate the relationship between crystal use and HIV sexual risk behaviours, specifically in the context of HIV biomedical prevention.

Methods

Flux is a national, prospective observational study of licit and illicit drug use among Australian GBM. In 2018, 1367 GBM provided details about crystal use and HIV prevention strategies, including condom use, PrEP, and ART. Binary logistic regression was used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI).

Results

Median age was 35 years. One in eight (12.3%) reported crystal use in the previous six months. Use of crystal was independently associated with greater social engagement with gay men and having more sexual partners. Crystal use was also independently associated with use of PrEP and ART to achieve an UVL among GBM who engaged in CLAIC.

Conclusions

Although GBM who used crystal were more likely to have engaged in CLAIC, they were also more likely to use biomedical HIV prevention which mitigates against the

risks of HIV infection. In settings where crystal use among GBM is not uncommon, harm-reduction interventions need to consider biomedical prevention for HIV.

1. Introduction

Use of crystal methamphetamine (crystal) to enhance sexual pleasure among gay and bisexual men (GBM) has been strongly associated with condomless anal intercourse with casual partners (CLAIC) and subsequent HIV infection (Jin et al., 2009; Piyaraj et al., 2018; Plankey et al., 2007; Prestage et al., 2009). In Australia, CLAIC has been identified as a key predictor for HIV infection (Jin et al., 2009). Use of antiretrovirals (ARV) as biomedical HIV prevention strategies, specifically pre-exposure prophylaxis (PrEP) (Grant et al., 2010; McCormack et al., 2016; Molina et al., 2015) and anti-retroviral therapy (ART) to achieve an undetectable viral load (UVL) (Bavinton et al., 2018; Cohen et al., 2011; Rodger et al., 2016; Rodger et al., 2018) have the potential to change the associations between use of crystal and subsequent HIV infection.

PrEP is a highly effective biomedical prevention strategy for HIV-negative individuals (Grant et al., 2010; McCormack et al., 2016; Molina et al., 2015). Among HIV-positive individuals, having an UVL virtually eliminates the possibility of HIV transmission during condomless anal intercourse (Bavinton et al., 2018; Cohen et al., 2011; Rodger et al., 2016; Rodger et al., 2018). PrEP has been approved for use in Australia since 2016 (NPS MedicineWise, 2018) and most Australian HIV-positive men have an UVL (Keen et al., 2018), resulting in an increasing proportion of GBM who are 'biomedically protected'. Nonetheless, there remains about one in five men who continue to engage in CLAIC without the protection of either PrEP or UVL ('biomedically unprotected CLAIC') (Holt et al., 2018). Although they are different methods of preventing HIV transmission, both PrEP and UVL rely on the use of ARVs for this purpose. We have presented the data for these two methods of HIV prevention separately but also refer to them collectively as biomedical prevention (Lea et al., 2017).

GBM have consistently been found to use most illicit drugs, including crystal, at higher rates than other men (Roxburgh et al., 2016). In Australia, crystal use has increased over time among GBM, although in recent years it remained steady (Broady et al., 2018; Lee et al., 2018; Lee, et al., 2018; Lee et al., 2018). Earlier work in the United States and the United Kingdom suggests that GBM are often motivated to use crystal for sexual purposes (Halkitis et al., 2005; Semple et al., 2002; Weatherburn et al., 2017). Crystal is a key drug used to enhance sexual pleasure (colloquially referred to as 'chemsex' or 'party-n-play'). Chemsex is the intentional use of illicit drugs (typically stimulants) to facilitate and enhance sex (Bourne et al., 2015; Stuart., 2019). Compared to GBM who do not use crystal, those who use crystal are likely to engage in more HIV sexual risk behaviours: They have a greater number of sexual partners, are more likely to engage in group sex (sexual behaviours involving more than two men), and are more likely to engage in CLAIC (Lea et al., 2016; Prestage et al., 2007; Saxton et al., 2018; Vosburgh et al., 2012). As biomedical HIV prevention is changing what is considered HIV sexual risk behaviours for HIV transmission (Hammoud et al., 2018; Jin et al., 2015), patterns of crystal use and their associations with HIV risk may have since changed.

Despite previous findings of a strong independent association between use of crystal and CLAIC, event-level data suggest that drug use may be as common on occasions of condom use as it is on occasions of non-condom use (Melendez-Torres et al., 2016; Prestage et al., 2009; Prestage et al., 2005). However, previous associations between use of crystal and engaging in HIV sexual risk behaviours have not been tested in the context of biomedical HIV prevention. At present, it is unclear whether men who use crystal are more likely to engage in HIV sexual risk behaviours without the protection of PrEP or UVL when compared to GBM who do not use crystal.

The links between crystal use and HIV sexual risk behaviours has previously been established. However, the relationship between crystal use and HIV sexual risk behaviours in the context of HIV biomedical prevention have not been explored. In this paper, we investigate the relationship between crystal use and HIV sexual risk behaviours, specifically in the context of HIV biomedical prevention.

2. Methods

The *Following Lives Undergoing Change* (Flux) Study is a national, online, prospective observational study among Australian GBM with a focus on licit and illicit drug use. The study protocol has been described in greater detail elsewhere (Hammoud et al., 2017). In brief, participants were recruited between 2014 and July 2018 through gay community websites and online media, Facebook, mobile phone applications, and gay sexual networking websites. Men were eligible to participate in the study if they were at least 16 years and six months of age, identified as gay or bisexual or had sex with a man in the last 12 months, and lived in Australia. At enrolment, online informed consent was obtained from all participants. No compensation was offered for participation in this study. Ethical approval was provided by the Human Research Ethics Committee of UNSW Sydney.

2.1 Measures

Baseline and six-monthly follow-up questionnaires were completed online using computer-assisted self-interviewing software (Hammoud et al., 2017). Demographic and characteristic items included country of birth, ethnicity, state of residence, education, employment status, sexual identity.

Participants self-reported their recent (previous six months) HIV testing history. HIV serostatus was reported as either HIV-positive, HIV-negative, or unknown. HIV-positive men indicated whether they were on ART and the results were for their last viral load test. HIV-negative and unknown status men indicated whether they had used PrEP in the previous six months, and whether they were still using PrEP at the time of their survey.

Men described their lifetime and recent (previous six months) use of licit and illicit drugs, including crystal, as well as the method and frequency of use. Frequency of use was categorized as: never used; have used but not in the previous six months; once or twice, or at least monthly, in the previous 6 months. Men who reported recent crystal use were also asked about their reasons for use, and whether they had used crystal specifically to enhance sexual pleasure (never, once, more than once). Sexual behaviours in the previous 6 months were reported for three separate partner types: Boyfriends (described as a regular partner with whom one has an ongoing, usually romantic, relationship), 'fuckbuddies' (regular partners with whom one is not in a committed relationship), and casual partners (all other non-regular partners) (Bavinton et al., 2016). We estimated the proportion of men who engaged in condomless anal intercourse with all partner types while biomedically protected or biomedically unprotected during condomless anal intercourse. Men also reported whether they engaged in group sex.

To measure social connectivity in relation to drug and sexual behaviours, social engagement with gay men was assessed using a scale with two items (proportion of friends who are gay men, and amount of free time spent with gay male friends), where higher scores indicated greater social engagement with gay men (Kippax et al., 1998).

The generalized anxiety disorder assessment (GAD7), a seven-item self-report measure that assesses symptoms of anxiety (Spitzer et al., 2006), the patient health questionnaire (PHQ9), a nine-item self-report measure that assesses symptoms of depression (Kroenke et al., 2001), and the Rosenberg self-esteem scale (RSES), a ten-item self-report measure that measures positive and negative feelings about oneself (Robins et al., 2001), were included to measure psychological wellbeing. The Kalichman measure of sexual sensation-seeking (SSSS), was included to measure the propensity to seek out novel or risky sex (Kalichman and Rompa, 1995).

2.2 Analysis

Data were analyzed with SPSS™ version 25 software (IBM Corp, Armonk, NY, USA). Descriptive statistics were used to categorise the demographic and other characteristics of men in this sample according to the frequency of their crystal use. Associations between categorical variables were examined using chi-squared tests; t-tests were used for continuous variables.

In univariate analyses, we assessed age, HIV-status, employment and educational status, social engagement with gay men, sexual and drug using behaviours, including the SSSS, and measures of psychological wellbeing, such as the GAD7, PHQ9, and RSES. We used a Type I error rate of 5% for these analyses.

Binary logistic backward stepwise multiple regression analysis was used first to compare GBM who did not use crystal with those that did use crystal in the previous six months, and subsequently, to compare men who used crystal once or twice in the previous six months with those who used crystal monthly or more often, controlling for

confounding factors and presented as adjusted odds ratios (aOR:) and 95% confidence intervals (CI). Associations with a p-value of <0.05 were retained in the final model.

3. Results

3.1 Sample characteristics

In 2018, 1643 GBM responded to the survey, 276 (16.8%) of whom had been recruited through Australian PrEP implementation trials and were therefore excluded. Each participants' most recent response from 2018 was used in analysis. Compared to the 1367 men included here, the 276 men excluded from this analysis were older (p<0.001) and more likely to use crystal (p=0.001) but were otherwise similar. Higher rates of crystal use among GBM enrolled in PrEP trials may be an artefact of methamphetamine use being a behavioural eligibility criterion for PrEP access (Vaccher et al., 2017).

The median age of the 1367 men included here was 35.0 years (range 16-81). Most (77.7%) were of Anglo-Celtic background, and the majority (69.1%) were university-educated (Table 1). Over two-thirds were in full-time (63.0%) or part-time (13.2%) employment; 23.8% were not in the workforce (e.g., students, pension, unemployed, retired).

Participants predominantly identified as gay (90.7%) or bisexual (6.4%). Most (88.1%) reported sex with at least one man in the previous six months. Half (48.8%) indicated they were in a regular relationship (boyfriend) with another man at the time of survey completion. One in three (30.0%) reported sex with a 'fuckbuddy,' and 49.6% with casual partners in the previous six months. About 1 in 3 (31.8%) reported engaging in group sex. One-third (34.9%) of men reported that most of their friends were gay and 53.8% spent most of their free time with gay friends.

Most men (67.3%) had ever been tested for HIV, with 7.9% reporting they had tested HIV-positive. Among HIV-positive men, 96.3% reported ART, of which 94.2% reported an undetectable viral load. Among HIV-negative or unknown men, 35.0% reported PrEP use in the previous six months, and continued use at the time of their survey.

3.2 Crystal use

Most men (74.6%) had no lifetime history of crystal use. One in eight men (13.0%) had a prior history of crystal use, and another 12.3% had recently (previous six months) used crystal. Among the 169 men who had recently used crystal, most (59.8%) had done so once or twice in the previous six months; 40.2% had done so at least monthly or more often.

3.3 Modes and contexts of crystal use

Among men who had used crystal in the previous six months, the most common route of administration was smoking (72.8%). Other methods included injecting (40.2%), 'shafting' (rectal administration; 11.8%), swallowing (9.5%), and snorting (5.3%). Route of administration reported were not mutually exclusive. More frequent users were more likely to inject. While 26.1% of men who used crystal less often than monthly injected crystal, this proportion increased to 57.4% among those who used it at least monthly or more often (p<0.001).

Among men who had used crystal in the previous six months, most (85.2%) reported using crystal specifically to enhance sexual pleasure. Many cited reasons for use that were explicitly sexual: most said they used crystal in order to engage in chemsex (63.1%), to have 'better sex' (67.5%), and to have 'fun' (49.1%).

Men who had a history of crystal use, and men who used crystal more recently and more frequently, were older than those who had never used crystal (Table 1). About one-third (27.8%) of GBM who used crystal at least monthly or more often were HIV-positive. Men who used crystal in the previous six months scored higher on the measure of sexual sensation-seeking (Table 1). There were no statistical differences observed on measures of depression, anxiety, or self-esteem when comparing men who used crystal and those who did not. Men who used crystal were more socially engaged with gay men in general. Among men who used crystal at least monthly or more often, they also had greater social engagement with gay men who used crystal compared to men use used crystal once or twice in the previous six months.

Table 1: Characteristics of the sample stratified according to use of crystal (N=1367)

	Never used crystal	Used crystal greater than 6 months ago	Used crystal less than monthly in the previous 6 months	Used crystal at least monthly in the previous 6 months
n	**1020**	**178**	**101**	**68**
%	**74.6**	**13.0**	**7.4**	**4.9**
Age (mean; SD)*	36.0 (14.1)	40.2 (10.9)	40.1 (12.0)	41.1 (10.5)
16-20	108	2	3	1
	10.6	1.1	3.0	1.5
21-30	354	34	24	11
	34.7	19.1	24.0	16.4
31-40	211	61	27	22
	20.7	34.3	27.0	32.8
41-50	149	48	21	21
	14.6	27.0	21.0	31.3
>51	198	33	25	12
	19.4	18.5	25.0	17.9
Country of birth				
Australia	811	136	69	52
	79.5	76.4	68.3	76.5
Oceania	30	12	8	1
	2.9	6.7	7.9	1.5
Asia	42	2	8	5
	4.1	1.1	7.9	7.4
North America	16	6	1	0
	1.6	3.4	1.0	0.0
South and central American countries	13	1	1	1
	1.3	0.6	1.0	1.5

Europe	75	18	10	7
	7.4	10.1	9.9	10.3
Middle East	2	1	0	0
	0.2	0.6	0.0	0.0
Africa	9	0	0	1
	0.9	0.0	0.0	1.5
Did not answer	22	2	4	1
	2.2	1.1	4.0	1.5
Education				
Less than university levels	309	56	32	25
	30.3	31.5	31.7	36.8
University levels	711	122	69	43
	69.7	68.5	68.3	63.2
Employment status **				
Full time	629	125	67	40
	61.7	70.2	66.3	58.8
Part time	132	20	15	13
	12.9	11.2	14.9	19.1
Not in workforce	250	28	18	13
	24.5	15.7	17.8	19.1
Did not answer	9	5	1	2
	0.9	2.8	1.0	2.9
HIV testing***				
Never/not recently tested for HIV	386	39	16	6
	37.8	21.9	15.8	8.8
Recently tested for HIV	634	139	85	62
	62.2	78.1	84.2	91.2
HIV Status***				
HIV-negative	594	114	59	40
	58.2	64.0	58.4	58.8
HIV-positive	37	24	26	21
	3.6	13.5	25.7	30.9
Unknown/untested	389	40	16	7
	38.1	22.5	15.8	10.3
Mean (SD)				
Gay social engagement ***	3.5 (1.6)	4.0 (1.6)	4.4 (1.5)	4.1 (1.6)
Gay social engagement with men who use crystal ***	0.3 (0.7)	0.9 (1.1)	1.6 (1.2)	3.0 (1.9)
Patient Health Questionnaire (PHQ9) *	6.3 (6.0)	6.2 (5.9)	6.3 (5.6)	8.4 (6.6)
General Anxiety Disorder (GAD7)	4.9 (5.1)	4.8 (4.9)	4.6 (4.8)	6.1 (5.9)
Sexual sensation seeking scale ***	29.8 (6.2)	31.2 (6.0)	33.1 (5.3)	33.3 (5.5)
Rosenberg self esteem	20.3 (6.4)	20.6 (5.9)	20.3 (6.3)	19.0 (6.7)

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Compared to men who had no history of crystal use, those who had recent and more frequent crystal use reported having more sex partners ($p < 0.001$) and group sex ($p < 0.001$) (Table 2). They were also older and more likely to report biomedically protected condomless anal intercourse with boyfriends ($p < 0.001$), fuckbuddies ($p < 0.001$) and casual partners ($p < 0.001$).

Table 2: Sexual behaviours and use of other drugs in previous 6 months according to use of crystal (N=1367)

	Never used crystal	Used crystal greater than 6 months ago	Used crystal less than monthly in the previous 6 months	Used crystal at least monthly in the previous 6 months
n	**1020**	**178**	**101**	**68**
%	**74.6**	**13.0**	**7.4**	**4.9**
Number of sex partners ***				
Mean (SD)	14.7 (44.4)	21.5 (38.5)	35.3 (71.1)	50.9 (93.5)
None	126	17	3	3
	12.4	9.6	3.0	4.4
Up to 10	549	79	43	17
	53.8	44.4	42.6	25.0
Over 10	333	82	54	47
	32.6	46.1	53.5	69.1
Did not answer	12	0	1	1
	1.2	0.0	1.0	1.5
Sex with boyfriend ***				
No boyfriend	514	85	57	39
	50.4	47.8	56.4	57.4
No anal intercourse	44	9	0	1
	4.3	5.1	0.0	1.5
Consistent condom use	50	3	3	1
	4.9	1.7	3.0	1.5
HIV positive TasP protected condomless anal intercourse	9	6	8	7
	0.9	3.4	7.9	10.3
HIV negative PrEP protected condomless anal intercourse	133	33	22	15
	13.0	18.5	21.8	22.1
HIV positive not on treatment condomless anal intercourse	0	1	0	1
	0.0	0.6	0.0	1.5
HIV negative not on PrEP condomless anal intercourse	267	39	10	4
	26.2	21.9	9.9	5.9
Did not answer	3	2	1	0
	0.3	1.1	1.0	0.0
Sex with fuckbuddies ***				
No fuckbuddy	733	122	60	38
	71.9	68.5	59.4	55.9
No anal intercourse	23	3	1	0
	2.3	1.7	1.0	0.0
Consistent condom use	42	2	2	1
	4.1	1.1	2.0	1.5
HIV positive TasP protected condomless anal intercourse	8	7	11	12
	0.8	3.9	10.9	17.6
HIV negative PrEP protected condomless anal intercourse	137	33	24	11
	13.4	18.5	23.8	16.2
HIV positive not on treatment condomless anal intercourse	1	0	0	0
	0.1	0.0	0.0	0.0

HIV negative not on PrEP condomless anal intercourse	72	11	3	6
	7.1	6.2	3.0	8.8
Did not answer	4	0	0	0
	0.4	0.0	0.0	0.0
Sex with casual partners ***				
No casual partners	533	84	30	27
	52.3	47.2	29.7	39.7
No anal intercourse	64	8	3	1
	6.3	4.5	3.0	1.5
Consistent condom use	116	8	5	3
	11.4	4.5	5.0	4.4
HIV positive TasP protected condomless anal intercourse	11	9	18	15
	1.1	5.1	17.8	22.1
HIV negative PrEP protected condomless anal intercourse	184	47	36	16
	18.0	26.4	35.6	23.5
HIV positive not on treatment condomless anal intercourse	1	1	0	1
	0.1	0.6	0.0	1.5
HIV negative not on PrEP condomless anal intercourse	101	17	8	5
	9.9	9.6	7.9	7.4
Did not answer	10	4	1	0
	1.0	2.2	1.0	0.0
Group sex ***				
No sex partners	134	16	4	4
	13.1	9.0	4.0	5.9
No group sex	715	115	64	30
	70.1	64.6	63.4	44.1
Any group sex	171	47	33	34
	16.8	26.4	32.7	50.0
Drug using behaviours ***				
Never	960	130	19	6
	94.1	73.0	18.8	8.8
Used drugs to enhance sex once	32	17	24	3
	3.1	9.6	23.8	4.4
Used drugs to enhance sex more than once	28	31	58	59
	2.7	17.4	57.4	86.8

*   p<0.05
**   p<0.01
***   p<0.001

In multivariate analysis, use of crystal in the previous six months was independently associated with greater social engagement with gay men (aOR: 1.24; 95% CI: 1.10-1.39), and having more sexual partners (aOR: 1.00; 95% CI: 1.00-1.01) (Table 3). Crystal use in the previous six months was also independently associated with biomedically protected CLAIC among HIV positive GBM (aOR: 14.10; 95% CI: 7.50-

26.54) and biomedically protected CLAIC among HIV negative GBM (aOR: 1.80; 95% CI: 1.17-2.76).

In multivariate analysis, compared to men who used crystal once or twice in the previous six months, men who used crystal at least monthly or more often had greater social engagement with other gay men who use crystal (aOR: 1.80; 95% CI: 1.41-2.31) and higher scores on measures of depression (aOR: 1.07; 95% CI: 1.01-1.13).

Table 3: Associations with crystal use

| | No recent crystal use vs. any crystal use in the previous 6 months n=1367 | | | | | | | | Crystal used once/twice in the previous six months vs. at least monthly use of crystal n=169 | | | | | | | |
| | Univariate analysis | | | | Multivariate analysis | | | | Univariate analysis | | | | Multivariate analysis | | | |
	OR	Upper	Lower	p	aOR	Upper	Lower	p	OR	Upper	Lower	p	aOR	Upper	Lower	p
Characteristics																
Age	1.02	1.01	1.03	0.001					1.01	0.98	1.04	0.585				
Employment status																
Full time	1								1							
Part time	1.30	0.83	2.04	0.257					1.45	0.63	3.36	0.384				
Not in workforce	0.79	0.51	1.20	0.264					1.21	0.54	2.73	0.647				
HIV-status																
HIV-negative	1								1							
HIV-positive	5.51	3.57	8.51	<0.001					1.19	0.59	2.40	0.625				
Unknown/untested	0.38	0.24	0.61	<0.001					0.65	0.24	1.71	0.378				
Gay social engagement with gay men	1.33	1.19	1.47	<0.001	1.24	1.10	1.39	.000	0.90	0.74	1.10	0.310				
Gay social engagement with gay men who use crystal	3.08	2.63	3.61	<0.001					1.79	1.42	2.25	<0.001	1.80	1.41	2.31	<0.001
Number of sexual partners	1.01	1.00	1.01	<0.001	1.00	1.00	1.01	0.008	1.00	1.00	1.01	0.224				
Sexual behaviours with boyfriend																
No boyfriend	1								1							
No anal intercourse	0.12	0.02	0.86	0.035												
Consistent condom use	0.47	0.17	1.33	0.155					0.49	0.05	4.86	0.540				
HIV positive TasP protected condomless anal intercourse	6.24	2.96	13.18	<0.001					1.28	0.43	3.82	0.659				
HIV negative PrEP protected condomless anal intercourse	1.39	0.92	2.11	0.121					1.00	0.46	2.16	0.993				
HIV positive not on treatment condomless	6.24	0.39	100.59	0.197												

	OR	LCI	UCI	p	OR	LCI	UCI	p	OR	LCI	UCI	p
anal intercourse												
HIV negative not on PrEP condomless anal intercourse	0.29	0.16	0.51	<0.001					0.58	0.17	2.00	0.392
Sexual behaviours with fuckbuddies												
No fuckbuddies	1								1			
No anal intercourse	0.34	0.05	2.50	0.287								
Consistent condom use	0.59	0.18	1.95	0.391								
HIV positive TasP protected condomless anal intercourse	13.38	6.76	26.49	<0.001					0.79	0.07	9.01	0.849
HIV negative PrEP protected condomless anal intercourse	1.80	1.18	2.73	0.006					1.72	0.69	4.29	0.243
HIV positive not on treatment condomless anal intercourse	-	-	-	-					0.72	0.32	1.65	0.440
HIV negative not on PrEP condomless anal intercourse	0.95	0.46	1.94	0.880					3.16	0.75	13.39	0.119
Sexual behaviours with casual partners												
No casual partners	1								1			
No anal intercourse	0.60	0.21	1.71	0.339					0.37	0.04	3.78	0.402
Consistent condom use	0.70	0.33	1.50	0.357					0.67	0.15	3.06	0.602
HIV positive TasP protected condomless anal intercourse	17.86	9.63	33.14	<0.001	14.10	7.50	26.54	.000	0.93	0.39	2.19	0.861
HIV negative PrEP protected condomless anal intercourse	2.44	1.63	3.65	<0.001	1.80	1.17	2.76	0.007	0.49	0.23	1.08	0.078
HIV positive not on treatment condomless anal intercourse	5.41	0.48	60.61	0.171								
HIV negative not on PrEP condomless anal intercourse	1.19	0.63	2.25	0.586					0.69	0.20	2.38	0.562

Group sex												
No sex partners	1					1						
No group sex	2.12	1.01	4.46	0.047		0.47	0.11	2.00	0.306			
Any group sex	5.76	2.69	12.35	<0.001		1.03	0.24	4.46	0.968			
Sexual sensation seeking scale	1.10	1.07	1.13	<0.001		1.01	0.95	1.07	0.745			
PHQ9	1.02	1.00	1.05	0.104		1.06	1.01	1.12	0.026	1.07	1.01	1.13	0.025

4. Discussion

In this sample, crystal was primarily used to enhance sexual pleasure and was associated with biomedically protected CLAIC. Prior to the introduction of biomedical HIV prevention strategies, GBM who used crystal were more likely to engage in biomedically unprotected CLAIC, which was strongly associated with subsequent HIV infection (Cochran et al., 2004; Prestage et al., 2009). This analysis, which accounted for the use of PrEP and UVL, found that although GBM who used crystal were more likely to have engaged in CLAIC, they were also more likely to use biomedical prevention which mitigates against the risks of HIV infection. Roux et al. (2018) found that among GBM using PrEP those who engaged in chemsex were also more likely to use PrEP correctly. Among men who engage in biomedically protected CLAIC, crystal use may no longer be a reliable indicator of those at highest risk of HIV infection.

Crystal use was associated with being more sexually active, as well as with seeking novel or risky sex as measured by the sexual sensation-seeking scale. Many crystal users cited enjoyment and sexual pleasure as reasons for use, with the majority using it to enhance sexual experiences. For many, crystal was used purposefully to aid to their ability to enjoy sexual experiences. From this perspective, their crystal use might be described as 'functional' insofar as it enhanced their ability to perform (better) within chemsex networks. PrEP and UVL offer a harm reduction opportunity that may be usefully deployed by men who engage in chemsex (Bavinton et al., 2018; Keen et al., 2018; Murphy, 2015; Rodger et al., 2016; Rodger et al., 2018).

PrEP and UVL offer practical benefits over condom-based HIV protection, specifically among GBM who engage in chemsex, in that they are taken orally, and need not be

linked to individual risk events, specifically while using crystal and other drugs. These findings indicate that while men who used crystal were more likely to be engaging in HIV sexual risk behaviours such as CLAIC, they were also more likely to do so with the protection of PrEP or UVL compared to men who did not use crystal. Both HIV-positive and HIV-negative GBM used biomedical HIV prevention strategies without impeding their ability to engage in the types of sex they desired. There was, however, a proportion of men in this sample who continued to engage in biomedically unprotected CLAI. The proportion of GBM engaging in CLAIC has generally been increasing over time (Holt et al., 2018).

Sexual practices among GBM are influenced by shared understandings of HIV risk and gay community norms, particularly those regarding 'safe sex' (Kippax et al., 1993; Kippax and Race, 2003). Aspects of drug-using behaviours among GBM, particularly in relation to harm reduction, have similarly reflected normative values within specific gay community subcultures (Southgate and Hopwood, 2001). This appears to be equally true among GBM in this sample. Gay community peer norms and social connections play a strong role in how drug use occurs among GBM, making gay community networks a key context in which to promote the uptake of PrEP or greater understanding that an individual with an UVL does not transmit HIV. This particularly applies to those at-risk men who participate in chemsex subcultures, where harm reduction messaging can be incorporated alongside the use of PrEP and UVL. In these settings, harm-reduction interventions need to be carefully nuanced to effectively guide the integration of biomedical prevention.

Overall, men who used crystal in this sample tended to socialize with friends who also used crystal, were strongly embedded in gay community networks, and tended to use

crystal explicitly to enhance and extend their sexual experiences, often in the context of chemsex. HIV-positivity has previously been found to be associated with gay social engagement (Zablotska et al., 2012). This was also true of this sample, where crystal users were also more likely to have tested HIV-positive. Overall, crystal use was associated with greater social engagement with gay men, and particularly with friends who also used crystal.

Social connectivity is inevitably linked to chemsex behaviours (Isaiah Green and Halkitis., 2006). These data suggest an addition influence to sexual practices and specific forms of drug use. Gay community-based sexual subcultures can influence the use of risk-reduction strategies, as these data indicate, including biomedical prevention.

There was no evidence of an association between crystal use and either depression, anxiety, or lowered self-esteem among recent crystal users compared to non-users. However, among GBM who use crystal more frequently, they scored higher on measures of depression compared to GBM who used crystal infrequently. Previous results only found an association between dependent crystal use and anxiety and depression (Prestage et al., 2018). Poorer mental health is specifically associated with frequent (or dependent) use rather than infrequent use. Peer-support in general, and greater social engagement with gay men, have been found to counter the negative mental health effects of homophobia and stigma (Mao et al., 2009; McLaren et al., 2008). Our data suggest social connectedness, specifically gay community connectedness is, separately, associated with both the practice of chemsex and with better mental health. Therefore, men who engage in chemsex may be protected from some of its potential negative outcomes by the coincidental occurrence of greater gay

community connections. It may be that the greater gay social engagement found among recent crystal users in this sample mitigated against depression and anxiety.

4.1 Limitations

This manuscript focuses specifically on biomedical HIV prevention. Chemsex still calls for broader harm reduction strategies. Men who engage in chemsex are at greater risk of other STIs (Prestage et al., 2009). Further consideration into STI among chemsex networks is needed. Daily adherence to PrEP was not reported. However, among Australian GBM clinical and community level adherence is greater than 90.0% (Vaccher et al., 2019).

This cross-sectional analysis describes retrospective accounts of behaviours and motivations. We were, therefore, unable to describe causal, or even temporal, relationships between crystal use and motivations for using biomedical HIV prevention strategies. Further longitudinal research is therefore needed, including future analyses of the longitudinal data being collected within the Flux study.

Although the characteristics and behaviours of participants were similar to other samples of Australian GBM (Holt et al., 2017; Roxburgh et al., 2016), this was a voluntary, online convenience sample and may not be representative of all homosexually active men in Australia. Extrapolating these findings to other contexts may be limited by differences between Australia and other locations. Nonetheless, GBM who used crystal in this sample were more likely to indicate that they used drugs to enhance sex, and many of these men described the specific ways that crystal enhanced their sexual encounters.

5. Conclusions

Results indicate that Australian GBM commonly used crystal in the context of sex, as a tool to functionally enhance sexual experiences, predominantly within gay community networks in which crystal use is prevalent. They also show that among men who use crystal, particularly in the context of chemsex, PrEP and UVL are also often used to mitigate against the risk of HIV infection. Consequently, based on these data, men who used crystal were probably less likely to have undiagnosed HIV infection compared to men who did not use crystal.

Australian GBM who use crystal otherwise did not appear to differ from their peers who do not use crystal on several indicators of risk. Although chemsex and use of crystal has been associated with some physiological risks and increased likelihood of STIs (Bourne et al., 2015; Girometti et al., 2017; Sewell et al., 2017), use of crystal by GBM may nonetheless be perceived as 'functional' in some circumstances. Harm-reduction interventions for GBM are a key priority for sexual health interventions but need to be carefully nuanced and targeted. They should acknowledge both the functional use of some drugs within specific gay party subcultures and the positive impact on mental health that being supported in one's sexuality can have, while simultaneously addressing the risk of problematic drug use. Further research is needed to examine the relationship between dependent or problematic drug use HIV risks in this population.

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7.1.4   Chapter seven summary

In this sample, most gay and bisexual men did not use crystal methamphetamine in 2018. Gay and bisexual men who used crystal methamphetamine also often used PrEP and/or TasP to mitigate against the risk of HIV infection. For most men who used crystal methamphetamine and who engaged in condomless anal intercourse with casual partners, their condomless anal intercourse was biomedically protected, but this was significantly less true of men who did not use crystal methamphetamine but did engage in condomless anal intercourse with casual partners.

This chapter demonstrates that gay and bisexual men who use crystal methamphetamine for chemsex, and who were previously considered at high risk of HIV infection, are now very likely to have commenced using biomedical prevention. Nonetheless, a small proportion of men who engage in chemsex have not adopted biomedical HIV harm reduction strategies to minimise the possibility of HIV transmission during condomless anal intercourse. Among men who did not use crystal methamphetamine, an even larger proportion of their condomless anal intercourse with casual partners remains biomedically unprotected.

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Chapter Eight

Discussion

A potential for change

8.1 Chapter overview

In this chapter, I describe the outcomes of my PhD research in a series of sections. Following this section, in **section 2**, I address the aims of my PhD research. I highlight the interconnectedness of several themes that emerged through a collective interpretation of the results. In **section 3**, I address the objective of my PhD research in the context of current HIV epidemiological trends in Australia, and in **section 4**, I describe key implications that emerged through the results provided. I close my PhD thesis with **section 5,** where I provide my concluding remarks.

A state of flux

8.2   Addressing the aims

I started my PhD research investigating the reasons why gay and bisexual men carry a disproportionate burden of HIV and drug use in Australia. I began this thesis by reviewing the epidemiology literature on HIV and drug use (**chapter 1**, **sections 2** and **3**), focusing specifically on gay and bisexual men to gain a better understanding. Decades of earlier research showed similarities and suggested a common link between HIV drug use among gay and bisexual men. In **chapter 1**, **section 4** and **5**, I explored the contexts that place gay and bisexual men at increased risk of HIV infection and the contexts of drug use in order to understand what cofactors exacerbate HIV risk. Based on this review, the literature appeared to indicate that a higher number of sexual partners, being more socially engaged with other gay men, and adverse mental health were all linked with HIV risk and drug use. The commonality between these disparate factors was chemsex, as engaging in chemsex was associated with condomless anal intercourse with casual partners and subsequent HIV infection. While this was not new knowledge, gay and bisexual men who engage in chemsex continued to remain at high risk of HIV infection.

In **chapter 1**, **section 6**, I reviewed the literature on HIV prevention strategies specific to gay and bisexual men who use drugs to understand why the strategies available prior

to PrEP were not reducing the number of new HIV cases in this population. If previous literature is correct in suggesting that the explanation for this link is that drug use impairs risk judgement, then there was an inherent limitation in the HIV prevention strategies available at the time. If drug use impairs risk judgement, can someone assess their HIV risk when under the influence of drugs? The HIV prevention strategies prior to PrEP were mostly behavioural, meaning in this case a decision to wear a condom correctly, knowledge of a sexual partner's HIV status, and sexual positioning, each of which would need to override the pleasure-seeking behaviours of uninhibited sexual encounters.

At the inception of this PhD research in 2014, PrEP was starting to become more widely available. Several clinical studies demonstrated PrEP to be highly effective among gay and bisexual men. However, this raised two questions. Would PrEP be an efficacious biomedical HIV prevention strategy outside clinical and implementation studies, and what would this mean for gay and bisexual men who engage in chemsex? These two questions formed the basic objective of my PhD research: To what extent to gay and bisexual men who engage in chemsex remain at risk of HIV infection in the context of PrEP?

I set up a large, prospective observational study of licit and illicit drug use among gay and bisexual men in Australia to address my overarching PhD research objective. Men with varying degrees of drug use and social connectivity were recruited to describe the current state of HIV and drug use in Australia among gay and bisexual men (**thesis aim 1**). With limited funds and minimal direct labour costs, I designed, developed, and implemented a cohort management system, as described in **chapter 2**, to automate the

systematic data collection of sensitive information relating to drug use and sexual behaviours among a sample of gay and bisexual men.

8.3 Characteristics of gay and bisexual men who engage in chemsex

Many men in this sample had never used licit or illicit drugs (**chapters 2**, **3**, **4**, and **7**). Among those that reported a history of illicit drug use, less than half reported any use in the previous six months (**chapters 2**, **4** and **7**). A minority of men reported at least monthly use or more often. The prevalence of drug use found in this sample is similar to what has been found in other samples of gay and bisexual men in Australia.[1-5] Compared to men who reported no recent drug use, those that used drugs in the previous six months were more likely to ascribe their use of drugs to their engagement in chemsex (**chapters 2**, **3**, and **7**).

The majority of participants identified as gay, with some identifying as bisexual, and a very small number of men with other diverse sexual identities. Compared to men who reported no recent drug use, men who used drugs in the previous six months were also more socially engaged with other gay men. For the most part, there were no differences observed in anxiety or depression scores between men who used drugs and those that did not. Gay and bisexual men who reported recent drug use were older compared to men who reported no drug use. This was also true among gay and bisexual men who reported the use of PrEP.

Gay and bisexual men who reported recent drug use were more likely to report engaging in behaviours that may represent potential HIV risk. These include condomless anal intercourse with casual partners, group sex, and a greater number of sexual partners. As

identified in **chapter 1**, **section 4**, the characteristics described above exacerbate the risk of HIV. In the sections that follow, I discuss the implications of these behaviours to determine the extent to which gay and bisexual men who engage in chemsex remain at risk in the context of PrEP.

8.4 Baseline prevalence of licit and illicit drug use

Addressing **thesis aim 1**, baseline prevalence of licit and illicit drug use was reported in **chapter 2**. Lifetime and recent use of licit and illicit drugs in this sample was similar to what has been found in other samples of gay and bisexual men.[1-6] Prevalence of licit and illicit drug use in this sample remains higher than in the general Australian adult male population (**chapter 1**, **section 1.9**).[7,8] Use of key chemsex drugs in this sample was also high: 12.0% reported crystal methamphetamine use, 6.9% reported gamma-hydroxybutyrate use, and 15.7% reported erectile dysfunction medication use in the previous six months. Concurrent use of crystal methamphetamine and erectile dysfunction medications was also high.

To determine the extent to which gay and bisexual men who engaged in chemsex remained at risk of HIV in the context of PrEP, I first needed to determine which drugs gay and bisexual men were using to engage in chemsex, and whether their behaviours represented potential HIV risk.

Prestage et al. (2009) identified that the use of erectile dysfunction medications, either on their own or concurrently with methamphetamine, substantially increased the likelihood of HIV seroconversion (Table 1.2). However, methamphetamine was the only drug that deemed people eligible for PrEP in the *Australian PrEP Guidelines*

(discussed in greater detail in **section 4** of this chapter). Licit drug use, specifically recreational use of erectile dysfunction medications, has received little attention in research on chemsex to date, and is rarely acknowledged as a chemsex drug. Analysis of the role erectile dysfunction medications may play in modulating HIV risk is discussed in **chapter 3**. Furthermore, the guidelines were based on data that were collected up until 2007, so not all relevant or commonly used drugs had been considered for analysis. With the prevalence of gamma-hydroxybutyrate use increasing among gay and bisexual men in Australia from 2009,[1-5,10] this raised the question as to whether drugs other than methamphetamine should also be considered in the *Australian PrEP Guidelines.* This question subsequently informed **chapter 4**.

Among men in this sample described in **chapter 3**, many who did not otherwise appear to have indicators of erectile dysfunction ascribed their use of erectile dysfunction medications to reasons such as: 'maintain an erection for longer' (61.0%), 'make it easier to get hard' (53.1%), and 'counter the effects of other drugs' (40.6%). In a separate multivariate analysis, I investigated the concurrent use of erectile dysfunction medications with key chemsex drugs to further establish the context in which they were used (**thesis aim 2**). Results from this analysis showed a strong independent association of erectile dysfunction medication use with amyl nitrites, gamma-hydroxybutyrate, and crystal methamphetamine (**chapter 2**). Compared to men who did not use erectile dysfunction medications, gay and bisexual men who used erectile dysfunction medications were more likely to also use key chemsex drugs, suggesting erectile dysfunction medications are often used in the context of chemsex (**thesis aim 2**).

Similarly, reasons for gamma-hydroxybutyrate use were explicitly ascribed to enhancing sexual pleasure, with 29.1% ascribing its use for sexual arousal and pleasure,

particularly during sex partying in the previous six months (**chapter 3**). Many men who used gamma-hydroxybutyrate in the previous six months reported positive outcomes of their drug use, such as developing closer connections and meeting new friends. Among men who had used crystal methamphetamine in the previous six months, most (85.2%) reported its use specifically to enhance sexual pleasure (**chapter 7**). Many cited reasons for use that were explicitly sexual: most said they used crystal methamphetamine in order to engage in chemsex (63.1%), to have 'better sex' (67.5%), and to have 'fun' (49.1%). Erectile dysfunction medications (**chapter 3**), gamma-hydroxybutyrate (**chapter 4**), and methamphetamine-type drugs (**chapters 5** and **7**) appear to be primarily used in this sample in the context of chemsex (**thesis aim 2**).

Chapters 3 through **7** demonstrate that drug use was associated with being more sexually active, as well as with seeking novel or adventurous sex. It would appear that for many men, licit and illicit drugs were used purposefully to aid their ability to enjoy sexual experiences. From this perspective, their drug use might be described as 'functional' in some circumstances insofar as it enhanced their ability to perform (better) within chemsex networks. This claim is by the absence of any differences on measures of anxiety and depression among men who used drugs in the previous six months, compared to men who reported no drug use (**chapters 3**, **4**, **6**, and **7**). Compared to men who reported using drugs in the previous six months, those that used drugs monthly or more often, particularly crystal methamphetamine, were more likely to report higher rates of depression. In a separate analysis of this sample **Appendix 1**, the prevalence of anxiety and depression among the entire sample was high, albeit similar to previously reported rates among gay and bisexual men in comparison to the general Australian population.[11-13] Although anxiety and depression were not generally associated with drug use or sexual behaviours, men with indicators of problematic drug

use (such as more frequent use, and specifically, dependent methamphetamine use), were more likely to report anxiety and depression. Conversely, use of erectile dysfunction medications were associated with decreased anxiety and depression, and higher self-esteem. This suggests that the relationship between drug use and mental health among gay and bisexual men is complex, and that different drugs and different levels of use may be associated with different mental health outcomes.

Peer-support in general has been found to counter the negative mental health effects of homophobia and stigma.[12-15] The data presented here suggest that social connectedness, specifically gay community connectedness, is separately associated with both the practice of chemsex and with better mental health. Therefore, men who engage in chemsex may be protected from some of its potential negative outcomes by the coincidental occurrence of greater gay community connections. It may be that the greater gay social engagement found among men who engage in chemsex in this sample mitigated against depression and anxiety.

These results suggest that the relationship between drug use and HIV risk among gay and bisexual men is complex. Distinguishing between perceptions of "safe" and "risky" sexual behaviours and HIV is an evolving issue.[16] Rather than being viewed as increases in risk-taking behaviour, drug use, particularly among chemsex networks, needs to be understood in the context of changing definitions of "safe sex" which also likely reflect changes in gay community "safe sex culture" (discussed in greater detail in **section 3**).[17-19]

8.5 Extent to which engaging in chemsex may represent potential HIV risk

Throughout this thesis, I explored the extent to which gay and bisexual men who engage in chemsex also engage in behaviours that may represent potential HIV risk (**thesis aim 3**). The results presented in **chapters 3** to**7** suggest that gay and bisexual men who use drugs in the context of chemsex are also engaging in behaviours that have typically represented potential HIV risk in the past. Similarities emerged when comparing the factors associated with each drug as presented in **chapters 3** through **7**, as shown in Table 8.1. In **chapters 3**, **4**, and **7**, compared to men who reported no drug use, men who used drugs were more likely to engage in behaviours that have typically represented potential HIV risk. These behaviours mirror those in other samples of gay and bisexual men in Australia,[20] and internationally.[21-27] As demonstrated in the literature review in **chapter 1**, these behaviours exacerbate the likelihood of HIV infection among gay and bisexual men.

Table 8.1 Comparison of univariate associations and drug use in the previous six months between chapters provided in thesis PhD thesis

| | Erectile Dysfunction Medications | | | | Gamma-hydroxybutyrate | | | | PrEP initiation | | | | Nonuse of PrEP | | | | PrEP in chemsex networks | | | | Crystal methamphetamine and PrEP | | | |
| | Chapter 3 | | | | Chapter 4 | | | | Chapter 5 | | | | Chapter 5 | | | | Chapter 6 | | | | Chapter 7 | | | |
	OR	Lower	Upper	p	OR	Lower	Upper	p	OR	Lower	Upper	p	OR	Lower	Upper	p	OR	Lower	Upper	p	OR	Lower	Upper	p
GSE	1.46	1.37	1.57	<0.001	2.31	2.11	2.53	<0.001	3.74	1.57	8.92	<0.001	0.71	0.63	0.81	<0.001	1.60	1.272	2.0	<0.01	1.33	1.19	1.47	<0.001
PHQ9	0.67	0.41	1.10	0.113	0.74	0.43	1.27	0.270	†	†	†	†	†	†	†	†	†	†	†	†	1.02	1.00	1.05	0.104
GAD7	0.63	0.40	0.99	0.048	0.52	0.27	1.00	0.05	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†
Meth	7.64	5.82	10.04	<0.001	†	†	†	†	2.54	1.90	3.40	<0.001	1.12	0.76	1.63	<0.001	†	†	†	†	†	†	†	†
Chemsex	†	†	†	†	3.96	3.05	5.53	<0.001	2.89	2.10	3.94	<0.001	0.48	0.30	0.78	0.003	†	†	†	†	†	†	†	†
Group sex	3.85	3.11	4.75	<0.001	3.96	3.05	5.53	<0.001	3.24	2.45	4.29	<0.001	0.35	0.24	0.51	<0.001	3.81	1.89	7.72	<0.01	5.76	2.69	12.35	<0.001
Sex partner	3.39	2.74	4.19	<0.001	1.01	1.01	1.02	<0.001	5.34	2.31	12.34	<0.001	0.09	0.03	0.26	<0.001	3.81	1.89	7.72	<0.01	1.01	1.00	1.01	<0.001
CLAIC	2.89	2.34	3.57	<0.001	10.06	6.41	15.81	<0.001	11.95	7.06	20.20	<0.001	0.15	0.087	0.2	<0.001	14.91	4.49	49.53	<0.01	2.44	1.63	3.65	<0.001

GSE: Gay social engagement scale measure of social connectivity; PHQ9: Patient Health Questionnaire 9-item measure of depression; GAD7 Generalized Anxiety Disorder 7-item measure of generalised anxiety; Meth: Use of methamphetamine-type drugs; Chemsex: drugs used to enhance sexual pleasure; CLAIC: Any condomless anal intercourse with casual partners.

† Not measured

The results presented in **chapters 3** and **4** highlight a potential gap in the *Australian PrEP Guidelines,* identifying that gay and bisexual men who use drugs other than methamphetamine to engage in chemsex are also engaging in behaviours that place them at high risk of HIV. The data presented in **chapters 3** and **4**, from a time when PrEP was not widely available in Australia, suggest that gay and bisexual men who engage in chemsex were at high-risk of HIV infection. These findings challenge aspects of coverage based on the *Australian PrEP Guidelines*, and as such, informed the arguments made and perspectives offered in **chapter 5** (discussed in more detail in **chapter 8**, **section 4**).

8.6 Incidence of PrEP update and factors associated with use and nonuse of PrEP

To determine whether gay and bisexual men who engage in behaviours corresponding to the *Australian PrEP Guidelines* initiate PrEP, in **chapter 5** I explored the incidence of PrEP use among HIV-negative men and presented factors associated with the use and non-use of PrEP (**thesis aim 4**). More specifically, I explored whether gay and bisexual men who engaged in chemsex subsequently initiated PrEP (**thesis aim 4**) as an HIV prevention strategy (discussed in relation to **thesis aim 5**). At the time of this data collection in 2018, access to PrEP in Australia was mostly through implementation trials. To access PrEP, gay and bisexual men needed to have met the eligibility criteria through self-reported behaviours and so may have been motivated to report such behaviours (Table 1.3).[28,29] With that, it is possible that their responses may have overstated their risk behaviours to qualify for entry to the trials. My research project was not a PrEP trial, nor was knowledge of or access to PrEP a requirement for joining the study. Participants simply reported their sexual and drug using behaviours during

their participation in the study. For those not using PrEP at baseline, their behaviours before initiating PrEP were reported without any particular expectations about subsequent circumstances. Participants who were accessing PrEP through implementation trials were excluded from this particular analysis to remove potential biases. Behaviours corresponding to the *Australian PrEP Guidelines* were used to determine each participants' eligibility to access PrEP. Gay and bisexual men who met these criteria were herein referred to as 'PrEP-eligible.' To measure incidence of PrEP uptake (**thesis aim 4**), behaviours reported at the individual level in previous rounds were compared with PrEP uptake in subsequent rounds (**thesis aim 1**) in order to determine whether gay and bisexual men who were at high-risk of HIV infection initiated PrEP (**thesis aim 4**).

Among gay and bisexual men who previously reported high-risk HIV behaviours, particularly among those who reported behaviours that corresponded to the *Australian PrEP Guidelines*, there was a rapid uptake of PrEP (**thesis aim 4**). The rapid rate of PrEP initiation in this sample mirrors the increasing prevalence of PrEP use among gay and bisexual men found in Australian behavioural surveillance (Figure 8.1).[30] Factors predicting subsequent PrEP initiation included methamphetamine use, engaging in chemsex, receptive condomless anal intercourse with casual partners, condomless anal intercourse with regular partners who had a detectable HIV viral load or were not on treatment, having a greater number of sexual partners, and engaging in group sex. These factors were similar to those associated with use of erectile dysfunction medications in **chapter 3,** use of gamma-hydroxybutyrate in **chapter 4**, and use of crystal

methamphetamine in **chapter 7** (Table 8.1). Men who initiated PrEP were also more socially engaged with other gay men compared to men who did not initiate PrEP.

Figure 8.1   Sex practices with casual male partners in the previous six months, 2013 – 2017
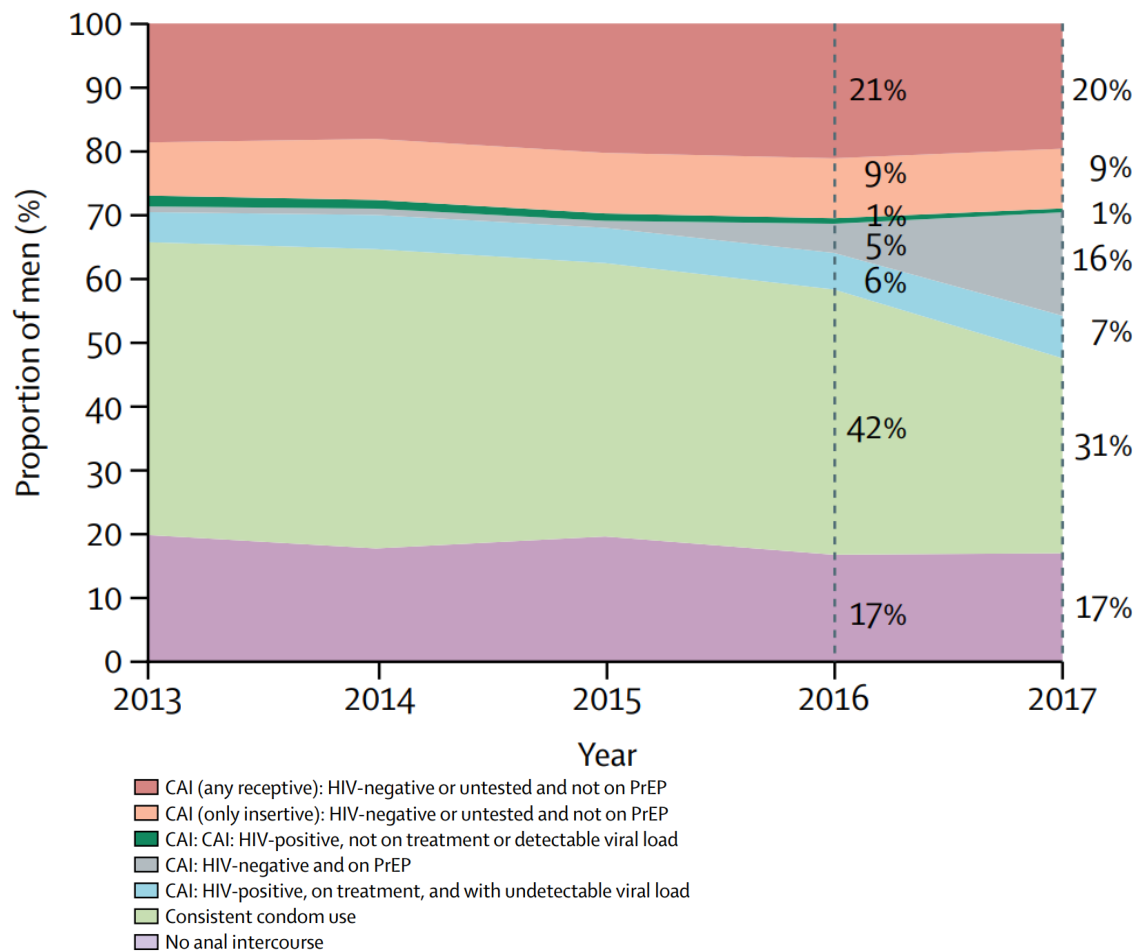
CAI: Condomless anal intercourse; PrEP: HIV pre-exposure prophylaxis.

Source: Holt M, Lea T, Mao L, Kolstee J, Zablotska I, Duck T, Allan B, West M, Lee E, Hull P. Community-level changes in condom use and uptake of HIV pre-exposure prophylaxis by gay and bisexual men in Melbourne and Sydney, Australia: results of repeated behavioural surveillance in 2013–17. The Lancet HIV 2018; 5(8): e448-e56.[30]

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In **chapter 1**, **section 1.27**, I described two projected scenarios in HIV prevention anticipating the effects of PrEP use (Figure 1.8). The first scenario depicted the ideal situation, with the prevalence of PrEP use reducing the proportion of men engaging in

condomless anal intercourse with casual partners. The second scenario depicted the increase in PrEP use reducing the proportion of men who engage in consistent condom-protected anal intercourse with casual partners. In 2017, it appears that the less ideal scenario has transpired (Figure 8.1).[30] The increased proportion of gay and bisexual men who use PrEP has reduced the proportion of gay and bisexual men who reported consistent condom-protected anal intercourse.

To explore why PrEP-eligible men were not using PrEP, I conducted a further analysis restricting the sample to gay and bisexual men who met the criteria for PrEP eligibility to compare the differences between PrEP uptake and non-uptake among eligible men. No differences were observed for the use of methamphetamine among those that initiated PrEP and those that did not. That is, methamphetamine use alone did not differ between PrEP-eligible men who subsequently initiated PrEP compared to their PrEP-eligible counterparts who did not initiate PrEP during study follow-up (**thesis aim 3** and **4**). On the other hand, men who were less likely to use any illicit drugs for the purpose of chemsex were also less likely to initiate PrEP (**thesis aims 4** and **5**). It would appear that men who were engaging in chemsex, regardless of the drug(s) they use, have introduced PrEP to their drug-use regimen to mitigate against the risk of HIV in what would otherwise be considered a high HIV risk environment. PrEP-eligible men who did not access PrEP were also engaging in other behaviours that could pose a potential risk of HIV compared to non-eligible men (**thesis aim 3**). These included receptive condomless anal intercourse, a greater number of sexual partners, and group sex, similar to what was found in **chapters 3**, **4**, and **7** (Table 8.1). Although PrEP-eligible men who were not using PrEP were engaging in the same high-risk HIV behaviours, they appeared to be doing so less frequently than their PrEP-using eligible counterparts who

were using PrEP (**thesis aims 3**, **4**, and **5**). Furthermore, PrEP-eligible men who were not using PrEP were less socially engaged with other gay men.

Men who initiated PrEP became more sexually active, and also became more likely to engage in riskier sexual behaviours upon PrEP initiation (**Appendix 2**).[31] However, proportions of methamphetamine use before and after PrEP uptake remained stable. So, it would appear that gay and bisexual men began using PrEP primarily to enable their sexual behaviours, not for reasons related to their use of chemsex drugs.

Prestage et al. (2009) identified the concurrent use of erectile dysfunction medications and methamphetamine to be a strong predictor of subsequent HIV infection. I built on my PhD supervisors' work to explore whether gay and bisexual men who concurrently use erectile dysfunction medications and methamphetamine are using PrEP (**thesis aim 4**) to mitigate against the risks of HIV infection (**thesis aim 5**), which then informed **chapter 6**.

8.7 PrEP as a harm reduction strategy among gay and bisexual men who engage in chemsex

The results presented in **chapter 6** show prevalence of PrEP use substantially increased from 1.0% in 2014 to 27.6% in 2017. The prevalence of concurrent use of erectile dysfunction medications and methamphetamine without the use of PrEP had decreased from 4.5% in 2014 to 3.1% in 2017. Simultaneously, the prevalence of concurrent use of erectile dysfunction medications and methamphetamine alongside the use of PrEP had increased during the same period (1.9% to 6.0%) (Figure 6.1) (**thesis aim 5**). Compared to men who concurrently used erectile dysfunction medications and methamphetamine without using PrEP, those that used all three drugs were more likely

to engage in sexual behaviours that would have represented HIV risk were biomedically protected. Similar to the findings reported in **chapters 3**, **4**, **5**, and **7** (Table 8.1), those who were using all three drugs were more likely to report using illicit drugs to engage in chemsex, receptive condomless anal intercourse with casual partners, a greater number of sexual partners, and group sex. They were also more likely to be socially engaged with other gay men. It would appear that prior to 2017, gay and bisexual men who concurrently used erectile dysfunction medications and methamphetamine before the widespread availability of PrEP were engaging in behaviours that represented a potential HIV risk (**thesis aim 3**). However, many of these men have since started to use PrEP to mitigate against the risk of HIV infection (**thesis aim 5**). This would suggest that PrEP may be a suitable harm reduction strategy for gay and bisexual men who use any drug during chemsex.[32] Comparing the findings from Prestage et al. (2009) to the sample used in my PhD research, we can see that a subculture of men who were once at highest risk of HIV, are now using PrEP to reduce, or remove the risk of HIV infection. When using PrEP as a biomedical HIV prevention strategy, it was also unlikely to impede men's ability to engage in the type of sex they desired.

Although these results are promising, there remains a proportion of men who concurrently use erectile dysfunction medications and methamphetamine and also report engaging in high-risk sexual behaviours (**thesis aim 3**), but do not appear to use any biomedical HIV prevention strategy. The proportion of men who appear not to be using any biomedical HIV prevention strategy is similar to proportions found in behavioural surveillance data from Australian gay and bisexual men,[30] and internationally.[33] Based on these results, I determined that PrEP appears to have substantial coverage among gay and bisexual men who use methamphetamine, which corresponds to the *Australian PrEP Guidelines*. However, there is also a proportion of men who are engaging in

chemsex (**chapters 3** through **7**) but are not accessing PrEP, even among those using methamphetamine.

By December 2017, it was estimated that 31,502 gay and bisexual men were eligible to access PrEP in Australia.[34] Among those, 28% were eligible to access PrEP.[35] In April 2018, PrEP received public subsidy in Australia.

The associations between use of methamphetamine, HIV sexual risk behaviours, and subsequent HIV infection have previously been reported in Australian research,[9,11,36] and in research in other similar countries.[24,27,37-40] The analysis conducted in **chapter 7** used data collected in 2018. At the time of writing, the relationship between crystal use and HIV sexual risk behaviours in the context of PrEP had not been explored. To determine the extent to which men who use crystal methamphetamine remain at risk of HIV in the context of PrEP, I explored behaviours that represent potential HIV risks among gay and bisexual men who use crystal methamphetamine (**thesis aim 3**), to identify factors associated with PrEP use as a harm reduction strategy (**thesis aim 5**).

Unsurprisingly, crystal methamphetamine was primarily used in the context of chemsex (**thesis aim 2**) and was associated with engaging in behaviours that represent HIV risks (**thesis aim 3**), similar to what was found in **chapters 3** through **6** (Table 8.1). However, in this analysis, gay and bisexual men who were using crystal methamphetamine to engage in chemsex were also very likely to be using PrEP to mitigate against the risks of HIV (**thesis aim 5**). Similarly, among gay and bisexual men living with HIV, those who used crystal methamphetamine and engaged in condomless anal intercourse with casual partners were more likely to be biomedically protected (**chapter 7**). These data confirm that crystal methamphetamine use may no longer be a reliable indicator of those at high risk of HIV infection.

PrEP disrupts the association between chemsex and HIV

8.8   Changing the trajectory of HIV epidemiological trends

Between 2014 and 2019, there has been a 23% decline in new HIV infections in Australia.[41-43] The represents the lowest number of new HIV notifications since 2001, with the decline most substantial among gay and bisexual men (Figure 8.2). This corresponds with increasing use of PrEP and TasP among Australian gay and bisexual men.[44] This decrease in the number of new HIV infections in Australia has also been reported in the United Kingdom.[45] Public Health England reported a 28% decrease in new HIV notifications since 2000, attributing the decline to a nationwide HIV prevention campaign, which included the use of PrEP and TasP. Similar to what has been found in **chapter 1**, **section 1.27**,[17,46-52] it appears that increases in PrEP use has corresponded with a decline in incidence of HIV among gay and bisexual men in Australia.

Figure 8.2   HIV notifications in Australia by exposure category, 2014 – 2018
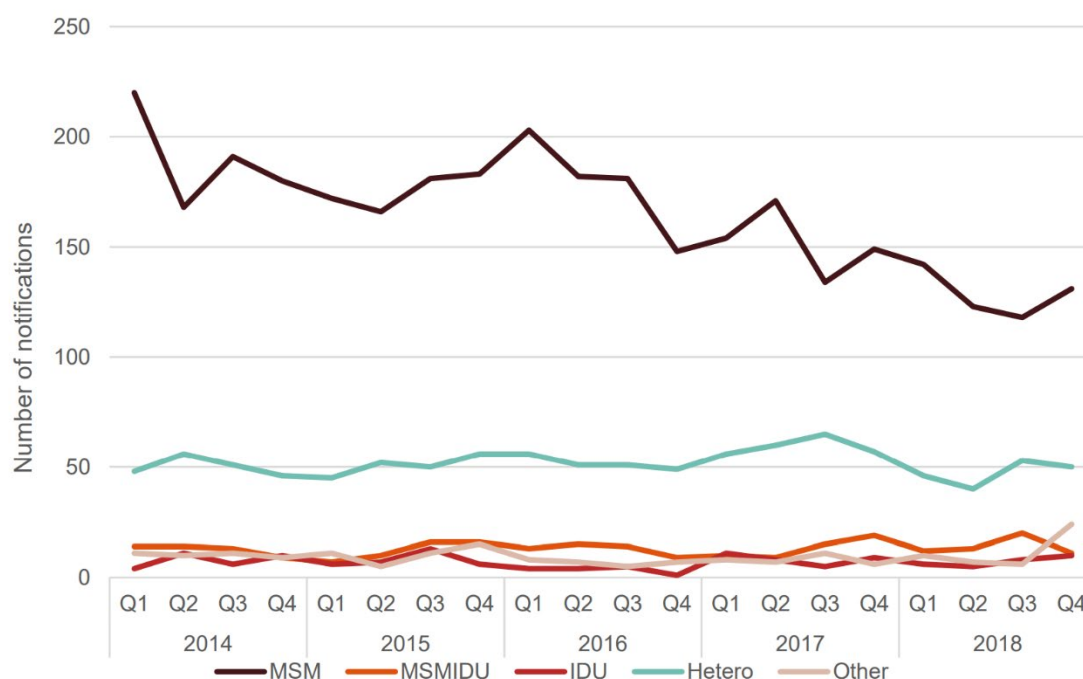
Q: Quarter; MSM: men who have sex with men; MSMIDU: men who have sex with men and injecting drug users; IDU: injecting drug users; Hetero: heterosexual men and women; Other;

Source: Kirby Institute National HIV notifications Q1 2014 – Q4 2018. Sydney: Kirby Institute, UNSW Sydney 2019.[53]

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PrEP offers a harm reduction opportunity that can be usefully deployed by men who engage in a range of HIV-risk behaviours, including chemsex.[54] Before the introduction of PrEP, gay and bisexual men who engaging in chemsex were more likely to engage in condomless anal intercourse with casual partners, which was strongly associated with subsequent HIV infection.[9] However, in this sample, the use of chemsex drugs was also highly associated with concurrent use of biomedical HIV prevention, and particularly with use of PrEP. This suggests that PrEP may have significant implications on our understanding of the risk profile of gay and bisexual men who engage in chemsex. Incorporating PrEP into sexual and drug use practices offers a highly effective harm reduction strategy for gay and bisexual men who engage in chemsex. The initiation of

PrEP by gay and bisexual men who engage in chemsex will certainly reduce their risk of HIV infection. PrEP offers a way for these men to feel less constrained in acting on their sexual desires, without the accompanying risk of HIV infection (**chapter 6**).

Coinciding with the rapid uptake of PrEP in Australia, gay and bisexual men have become much less consistent with their condom use.[30] In this sample, gay and bisexual men who initiated PrEP tended to continue using PrEP thereafter (**Appendix 2**). They also reported higher rates of receptive condomless anal intercourse and group sex, and a higher number of sexual partners both at the time of PrEP initiation and in the six-month period thereafter. This suggests more than a transient change in their behaviour is happening in response to the use of PrEP. Based on the results I have presented in my thesis and the recent decline in HIV notifications, gay and bisexual men who engage in chemsex while using PrEP at such high and seemingly increasing rates are at little to no risk of HIV.

8.9   PrEP in chemsex networks

Previous event-level data had found that among gay and bisexual men who engage in condomless anal intercourse, drug use did not distinguish between occasions when they used condoms and occasions when they did not use condoms.[9,55,56] Although data presented in this thesis indicate that drug use is associated with engaging in HIV risk behaviours, they do not necessarily indicate that drug use in itself leads to these sexual behaviours. Other factors that have been identified as affecting the relationships between sexual risk behaviour and HIV, such as being younger in age.[26]

PrEP offers practical benefits over condom-based HIV prevention, particularly among gay and bisexual men who engage in chemsex as PrEP is taken orally and need not be

linked to individual risk events while using drugs during chemsex. These findings indicate that while men engaging in chemsex were more likely to be engaging in condomless anal intercourse with casual partners, they were also significantly more likely to do so with protection from PrEP, compared to men who did not use drugs (**chapter 7**). This suggests that PrEP use has been key to changing the HIV epidemiological trends among gay and bisexual men in Australia (Figure 8.3).

Figure 8.3   HIV notifications diagnoses by year in men who have sex with men, by percentage of high-risk men on PrEP, and percentage of HIV-positive men who have sex with men on antiretroviral treatment within 6 weeks of diagnosis
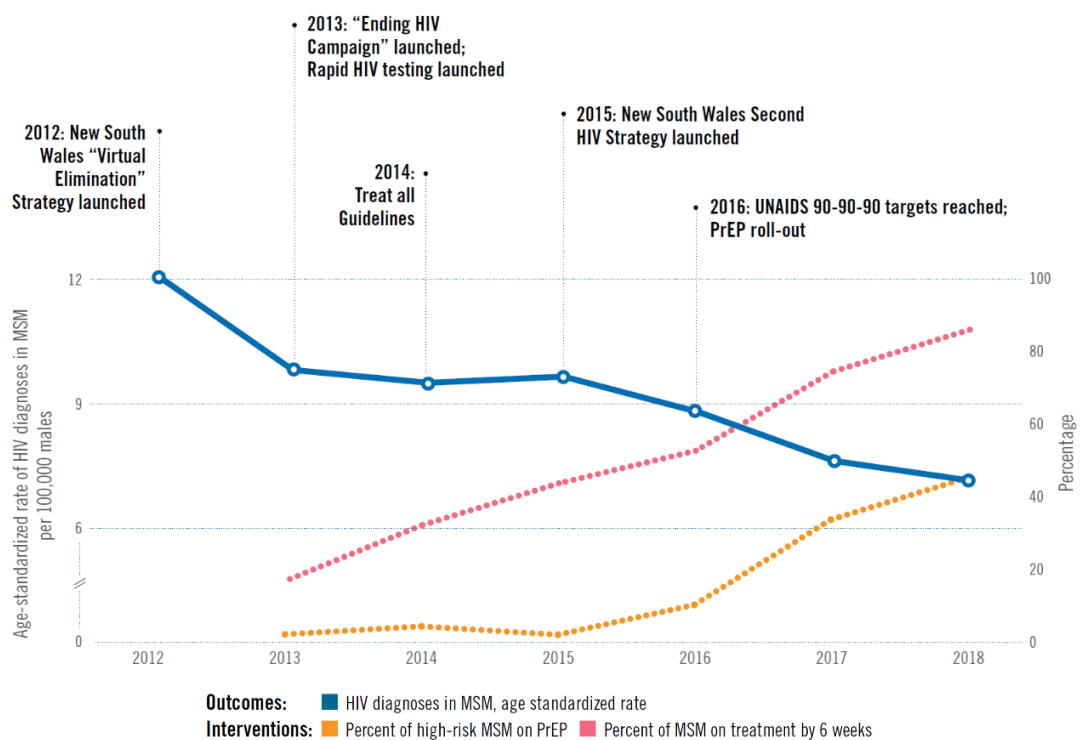
MSM: Men who have sex with men; PrEP: Pre-exposure prophylaxis.

Source: amfAR, AVAC, & Friends of the Global Fight. Translating Progress into Success to End the AIDS Epidemic. 2019.[44]

Permission obtained from the Kirby Institute, UNSW Sydney © 2019

8.10 Subcultural affiliation and its influence on risk and harm reduction

Associations between drug use and HIV risk behaviours have long been established.[40,57,58] Results presented in my PhD research mirror those finding (**chapters 3** through **7**), identifying links between high-risk behaviours and the use of other drugs throughout the HIV epidemic, such as amyl nitrite.[59,60] These similarities raise questions as to whether issues concerning drug-related HIV risk among gay and bisexual men may not be about the type of drug used so much as about the (sexual) networks in which drugs are used?

Demonstrated in **chapters 3** and **4**, men who were more socially engaged with other gay men were more likely to use licit and illicit drugs to engage in chemsex, which was associated with indicators of HIV risk including condomless anal intercourse with casual partners. However, in **chapters 5** through **7**, men who were more socially engaged with other gay men and were using licit and illicit drugs to engage in chemsex were shown to also be more likely to use PrEP to mitigate against the risks of HIV (**thesis aim 5**). More significantly, among men who engaged in chemsex, most of their condomless anal intercourse was biomedically protected, especially when compared to men who did not engage in chemsex (**chapter 7**).

Gay social engagement appears to indicate contradictory outcomes. That is, when examining HIV risk behaviour, gay social engagement indicates greater risk.[22,61-63] Conversely, when examining knowledge and application of HIV risk reduction strategies, gay social engagement indicates greater access to detailed knowledge about, and often better application of these strategies.[17,64-70] This was also evident in the results

presented in my PhD research. Gay and bisexual men who were more socially engaged with other gay men were also more likely to engage in HIV risk behaviours (**chapters 3** and **4**). Moreover, gay and bisexual men who were more socially engaged with other gay men were also more likely to use PrEP as a harm reduction strategy (**chapters 5** through **7**). These contrasting outcomes may be two sides of the same coin: gay social engagement may have always been indicative of a complex tension between pleasure-seeking and risk reduction. This is particularly evident among gay community-connected gay and bisexual men, where greater knowledge and experience accompany increased gay social engagement.

These findings raise questions as to whether the original interpretation of the effect of gay social engagement may have been imprecise. Perhaps gay social engagement during the early HIV epidemic may not have been solely indicating knowledge of safe sex, such as condom use, as described by Kippax et al. (1993) Gay social engagement may have also been indicative of gay men's inclination to be protective of their sexuality. That is, what was being reported was not just that more gay community engaged men were more likely to adopt 'safe sex' practices, but that they were also more likely to engage in anal intercourse with casual partners, and therefore more likely to use condoms. They may have also been more committed to finding ways through the epidemic that still enabled them to act on their sexual desires, while also taking advantage of their knowledge and experience to reduce HIV risk. From this perspective, in the context of PrEP, gay community engaged men are more likely to adopt new harm reduction technologies that enable them to have the sex they want.[71] The use of PrEP may be viewed as a more attractive harm reduction strategy than condoms because it has fewer restrictions on sexual behaviour, at least in consideration of HIV risk. Furthermore PrEP could be more effective than condoms for some men, particularly

those who engage in chemsex, as it does not require correct use at the time of sex, as is the case for using a condom.

Conceivably, engaging in chemsex may have been an indicator of risk throughout the HIV epidemic, and gay social engagement also happens to be highly associated with chemsex. An important aspect of gay social engagement may have always been about gay men seeking ways to continue to enable them to have the sex they desired with as few restrictions as possible, and in ways that protected themselves and their partners from HIV. Condoms were one, if inconsistent, solution. PrEP, however, offers the potential of a more reliable and convenient option for some men, perhaps especially for the purposes of chemsex.

These data reinforce the pivotal role gay community networks have played in HIV risk reduction throughout the epidemic by facilitating access to information and reinforcing social norms.[17,72] The *Diffusion of Innovations* theory suggests that innovations tend to spread more quickly through tightly bonded networks of similar people.[73] Gay community affiliations and social connections offer such an opportunity because they can promote PrEP as a harm reduction strategy, particularly in the context of chemsex networks. These sorts of peer networks can be used to disseminate information and normalise new prevention technologies such as PrEP.

Implications

8.11   Limitations in the Australian PrEP Guidelines

Men in this sample who initiated PrEP usually reported behaviours that corresponded to the *Australian PrEP Guidelines*. However, not all men whose behaviours corresponded to these criteria subsequently initiated PrEP. As discussed in **chapter 1**, **section 1.26.1**, the data used to form the *Australian PrEP Guidelines* were based on the *HIM Study* which collected data between 2001 and 2007, at a time when there was considerably less attention into other drugs such as gamma-hydroxybutyrate.[9] The *HIM Study* also found that use of erectile dysfunction medications, either on their own or concurrently with methamphetamine, substantially increases the likelihood of HIV seroconversion (Table 1.2).[9] Yet, methamphetamine was the only drug criterion in the *Australian PrEP Guidelines*. **Chapters 2** and **3** identify erectile dysfunction medications and gamma-hydroxybutyrate as key drugs used by gay and bisexual men in Australia when engaging in chemsex. This highlights a potential limitation of the *Australian PrEP Guidelines*, in that the data used to form these guidelines may not accurately capture all potential risk practices that are relevant to gay and bisexual men who engage in chemsex. Thus, the guidelines in their current form leave a potential gap in PrEP eligibility among a population at high risk of HIV infection. Erectile dysfunction medications and gamma-hydroxybutyrate, and, indeed, any licit or illicit drug used to enhance sexual pleasure

should be considered alongside methamphetamine in the context of sexual risk behaviour and HIV infection.

Among PrEP-eligible men who did not initiate PrEP, despite having engaged in behaviours which placed them at high risk of HIV, they engaged in these behaviours less frequently and less consistently over time than men who did initiate PrEP, regardless of whether they engaged in chemsex (**Appendix 2**). For some of these men, their decision not to initiate PrEP may be based on a reasonable assessment of their current risk profile. For others, however, it may reflect misconceptions about the level and types of risk required to make the use of PrEP worthwhile.[74,75] Some men's understandings of risk may need to be challenged. However, despite meeting the formal eligibility criteria for PrEP, PrEP-eligible men who did not initiate PrEP were often less socially connected to other gay men. Their perception of their own level of risk compared with other gay men may be due to their relative lack of social connection and this may influence how they make their decisions about the need to use PrEP.

Although the *Australian PrEP Guidelines* determine eligibility based on reported risk behaviours in the previous three months, they do not assess the frequency of these risk behaviours. In some cases, it may be that some men underestimate their level of risk, but it may also be that a single episode of risk behaviour as indicative of eligibility for PrEP may be an overestimation of their level of risk on an ongoing basis. Nonetheless, a one-off event can pose HIV transmission risk that might otherwise be protected by PrEP. Even though some high-risk men were engaging in these behaviours less often or inconsistently, it nonetheless raises concerns about the sensitivity of the *Australian PrEP Guidelines* and their potential accuracy. In 2018, the *Australian PrEP Guidelines* were updated to include recommendations for on-demand PrEP.[29] Evidence suggests

that on-demand PrEP is a highly effective HIV prevention strategy among gay and bisexual men.[76-78] On-demand PrEP could be usefully deployed to gay and bisexual men who engage in high-risk behaviours less frequently but are not currently using any other HIV prevention strategy. However, on-demand PrEP relates specifically to sexual behaviours. It does not directly address the interconnectedness between licit or illicit drug use, sex, or the frequency to engage in chemsex. These findings suggest that use of any licit or illicit drug to engage in chemsex, regardless of frequency, should be included in *Australian PrEP Guidelines*. Moreover, broadening the eligibility criteria to include a wider spectrum of licit and illicit drug use may help to identify more gay and bisexual men at high-risk of HIV and suitable for PrEP.

8.12 Tailoring harm reduction programs to cater for different types of drug use

Many participants reported that they derived clear, if subjective, pleasure and benefits from drug use, particularly regarding sexual enjoyment. Harm reduction interventions for gay and bisexual men are a key priority in sexual health research, but need to be carefully nuanced. Interventions need to acknowledge that some men appear to use drugs functionally, or at least they appear to experience drug use as functional and derive pleasure from use. Interventions should provide men with the tools to ensure that their use does not become problematic. They should acknowledge functional use of some drugs within specific gay party subcultures, while simultaneously addressing the potential risk of problematic drug use. Specifically, there is a need for health promotion initiatives for gay and bisexual men who engage in chemsex to address the potential risk of HIV transmission that accompanies the use of chemsex drugs, including but not restricted to methamphetamine. These initiatives need to acknowledge the emic value of

the drugs within particular sexual cultures, their relation to condomless anal intercourse, and how this might challenge harm minimisation approaches.

Peer norms and social connections play a strong role in how drug use is enacted among gay and bisexual men, making gay community networks a key context in which to promote the uptake of PrEP as an addition to their drug use repertoire, particularly among those who engage in chemsex. In 2017 when the data included in **chapter 6** were collected, most (71.7%) men who reported using PrEP also reported having at least some friends who used it. The strong social support provided by particular gay community sexual networks could mediate individuals' drug use to prevent associated harms through modern HIV prevention technologies.[66-70,79] Peer networks may play an important role in disseminating information and normalising new prevention technologies, in the same way as they appear to play a role in normalising the drug use identified herein.[80,81] In these settings, harm reduction interventions need to be carefully nuanced to guide the integration of PrEP effectively, including on-demand PrEP for gay and bisexual men who engage in HIV risk behaviours less frequently, or among non-adherent men.[82] Indeed, the data reported here suggest that this process is already well underway. In particular, given the strong role of peer norms and social connections within gay drug using networks, harm reduction can utilise these networks to develop interventions that are appropriate to both the perceived and actual needs of individual drug users within them.

Melendez-Torres et al. (2016) suggest health care professions should adapt to changing trends in drug use, and different drugs used, suggesting that the evidence base for their engagement with gay men may be dated.[83] Similarly, Flores-Aranda et al. (2019) suggest that harm reduction interventions that fail to consider the pleasures associated

with engaging in chemsex will likely fail.[84] Their arguments also speak to the broader category of men who have sex with men I raised in **chapter 1**, **section 1.3.2**. Men who have sex with men but do not identify as gay or bisexual may not be connected to gay community networks and therefore have less knowledge or access to resources such as PrEP or drug-related harm reduction strategies. This may place them at high risk of HIV infection. The results I presented in **chapters 3** through **7** demonstrate that greater social engagement with gay men is associated both with elevated drug using behaviours and the adoption of harm reduction strategies. Those who are more connected to gay community networks are more likely to have access to harm reduction strategies and evolving technologies, notably PrEP in this project (**chapters 5** through **7**). Moreover, gay and bisexual men who are more or less socially engaged with gay community may also hold differing perceptions of social norms about or perceived acceptability of drug using behaviours, as well as different understandings of the level of risk required to warrant the use of PrEP.

Section Five

Concluding remarks

PrEP is changing the experience of gay and bisexual men who engage in chemsex and the association it has with HIV, as well as how these experiences are understood. This thesis has provided essential data on sensitive topics about a population where drug use has been represented as being 'problematic'. Demonstrating the interplay between sex, drugs, and HIV, these results highlight how PrEP can complement drug use in chemsex networks. PrEP appears to offer a means for some men who derive pleasure through chemsex to engage in behaviours that otherwise placed them at high risk of HIV. Without PrEP many may have engaged in such behaviours, with all of the attendant risks, even if they may have done so less often or less consistently.

These findings emphasise a need to reinforce the message that the use of any drug, licit or illicit, in a sexual setting, or the frequency of HIV sexual risk behaviour, should involve HIV prevention tools such as PrEP. These findings call for focused HIV harm reduction programs that are contextualised by the reality of some gay and bisexual men's drug use and sexual behaviours, and their connections with gay community networks. The results show that the relationship between drug use and sexual risk behaviour for many gay and bisexual men requires a nuanced approach to drug research that recognises the importance of pleasure as much as risk.

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Appendices

1.1 Mental health among gay and bisexual men who use drugs

1.1.1 Publication details

Prestage G, Hammoud MA, Jin F, Degenhardt L, Bourne A, Maher L. Mental health, drug use and sexual risk behavior among gay and bisexual men. International Journal of Drug Policy 2018; 55: 169-79.

1.1.2 Items related to this thesis

Item 1: Describe factors associated with anxiety and depression among gay and bisexual men who use drugs.

1.1.3 Appendix one in context

Gay and bisexual men have higher rates of anxiety and depression compared to other men.[1-3] Motivations to engage in chemsex are usually ascribed to psychological vulnerabilities,[4-6] and based on an assumed causative link between drug use which can lead to sexual risk behaviours. In a separate analysis of this sample, the prevalence of anxiety and depression was also high. However, anxiety and depression were not generally associated with drug use or sexual behaviours. This was also demonstrated in **chapters 3** through **7**. There were no differences observed on measures of anxiety and depression when comparing men who did not use drugs to those that do (Table 8.1).

Gay and bisexual men with indicators of problematic drug use, and specifically on dependent methamphetamine use, was associated with anxiety and depression. Conversely, erectile dysfunction medications use was associated with decreased anxiety and depression, and higher self-esteem. This suggests that the relationship between drug use and mental health among gay and bisexual men is complex, and that different drugs and different levels of use may be associated with different mental health outcomes. Most men in this sample who used illicit drugs had no indicators of problematic or dependent use and no indicators of poor mental health. These differences may be due to the broad community sample used in my PhD research, whereas other studies are restricted to clinical populations, HIV positive men, or recruited through gay venues frequented by intensive sex partying networks.[4-6] Given the important role of personal

and social connectedness, and of experiences of stigma, social and community norms

undoubtedly influence individual men's experiences, either positively or negatively.[1]

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[1] List of references for citations provided in Appendices chapter contexts are provided on page 308
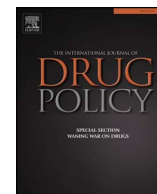
Mental health, drug use and sexual risk behavior among gay and bisexual men

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ABSTRACT

Background: Compared to the general population, among gay and bisexual men (GBM) prevalence rates of anxiety and depression, and of drug use, are high.

Objective: This paper explores the relationship between mental health, sexual risk behavior, and drug use among Australian GBM. We identify factors associated with indicators of poor mental health.

Methods: Between September 2014 and July 2017, 3017 GBM responded to measures of anxiety and depression in an online cohort study of drug use.

Results: Mean age was 35.3 years (SD 12.8). 17.9% screened positive for current moderate-severe anxiety and 28.3% for moderate-severe depression. The majority (52.2%) reported use of illicit drugs in the previous six months, including 11.2% who had used methamphetamine. One third had high (20.4%) or severe (10.6%) risk levels of alcohol consumption, and 18.3% who were current daily smokers. Most illicit drug use in general was not associated with either anxiety or depression, but men who used cannabis were more likely to show evidence of depression (p = 0.005). Among recent methamphetamine users, 28.0% were assessed as dependent: dependent users were more likely to show evidence of both depression and anxiety than were non-dependent users. High or severe risk drinking was associated with depression and daily tobacco use was associated with both anxiety and depression. Depression and anxiety was associated with: less personal support, viewing oneself as 'feminine', and being less socially engaged with gay men. Sexual risk behavior was not associated with either depression or anxiety.

Conclusion: Prevalence of anxiety and depression was high, as was prevalence of licit and illicit drug use. Substance use was associated with anxiety and depression only when the use was considered problematic or dependent. Social isolation and marginalization are strong drivers of poor mental health, even within this population for whom anxiety and depression are common.

Introduction

In recent years, gay and bisexual men (GBM) have been represented as engaging in unrestrained risk-taking through a 'dangerous' mix of drugs and sex (or 'chemsex') exacerbated by psychological vulnerabilities (Stuart, 2016). Concerns around chemsex have usually been based on an assumed causative link between drug use and poor mental health and an assumption that drug taking leads to sexual risk taking.

Compared to other men, GBM report high rates of depression and anxiety (Cochran, Sullivan, & Mays, 2003; King et al., 2008; Meyer, 2003), but there are few data estimating the prevalence of depression

and anxiety among Australian GBM. Where such data exist, they suggest relatively high rates (Lyons, Pitts, & Grierson, 2013; Mao et al., 2009; McLaren, Jude, & McLachlan, 2008). These high prevalences are often ascribed to experiences of homophobia or wider societal stigma (Meyer, 2003), and for this reason peer-support in general, and greater social engagement with gay men tend to counter the negative mental health effects of homophobic stigma (Mao et al., 2009; McLaren et al., 2008).

GBM also report high prevalence of illicit drug use (Cochran, Ackerman, Mays, & Ross, 2004; Conron, Mimiaga, & Landers, 2010; Hickson, Bonell, Weatherburn, & Reid, 2010; Roxburgh, Lea, de Wit, &

Degenhardt, 2016). Illicit drug use, and use of methamphetamine in particular, has been associated with sexual risk behavior and HIV infection among GBM (Halkitis, Green, & Mourgues, 2005; Prestage et al., 2007; Prestage, Grierson, Bradley, Hurley, & Hudson, 2009; Prestage, Jin et al., 2009; Vosburgh, Mansergh, Sullivan, & Purcell, 2012). Drug use and sexual risk behavior are often linked to poor mental health (Halkitis, Fischgrund, & Parsons, 2005; Halkitis, Green et al., 2005; Kurtz, 2005; Rosario, Schrimshaw, & Hunter, 2006).

Few Australian studies have investigated the association between mental health and sexual risk-taking, and there is little evidence for such an association at a population level (Lyons et al., 2013). Despite a strong independent association between illicit drug use and sexual risk behavior, event-level data indicate that GBM may be as likely to use drugs on occasions of condom use as they are on occasions of non-condom use (Prestage et al., 2005; Prestage, Jin et al., 2009). For many GBM, drug use is primarily for the purposes of intensive sex partying, to enhance their sexual experiences, and the association with sexual risk is a foreseeable but not purposeful consequence (Halkitis, Green et al., 2005; Hurley & Prestage, 2009; Weatherburn, Hickson, Reid, Torres-Rueda, & Bourne, 2017). Although the illicit drugs commonly used for these purposes are often referred to as 'club drugs' or 'party drugs' (Halkitis, Green et al., 2005; Halkitis, Palamar, & Mukherjee, 2007), previous Australian research has also highlighted the key role of erectile dysfunction medication (EDM; Prestage, Jin et al., 2009). GBM use these medications to enable more intense sexual function during sex partying, and to counter the effects of other drugs on their ability to achieve and maintain erections (Hammoud et al., 2017). In separate analyses, we have found that during intensive sex partying, GBM commonly use the combination of methamphetamine, HIV pre-exposure prophylaxis (Truvada™), and EDM (particularly Viagra™), or 'MTV' (Hammoud, Vaccher, & Prestage, 2018).

In this paper, we examine whether poorer mental health is associated with greater likelihood to use drugs and engage in sexual risk behavior among GBM. We also investigate how these relationships between mental health, drug use, and sexual risk behavior are affected by wider psychosocial factors known to influence health behaviors and outcomes among GBM, including social support, community engagement, and experiences of stigma.

Methods

The methods of the *Following Lives Undergoing Change (Flux) Study* – an online prospective observational study of Australian GBM – are described in greater detail elsewhere (Hammoud et al., 2017). In brief, participants were recruited between August 2014 and July 2017 via gay community websites and online media, Facebook, mobile phone applications, and gay sexual networking websites. Participants provided informed consent and ethical approval was provided by the Human Research Ethics Committee of UNSW Australia.

Measures

The online baseline questionnaire included: demographic items, questions on sexual identity, HIV testing history and self-reported serostatus. Men were asked about their sexual behavior and condom use in the previous six months with three categories of partner type, regular ('boyfriend') partners, 'fuckbuddies', and casual partners (Bavinton et al., 2016; Down, Ellard, Bavinton, Brown, & Prestage, 2017).

Mental health measures included the generalised anxiety disorder assessment (GAD7) and the patient health questionnaire (PHQ9) to measure anxiety and depression respectively (Kroenke, Spitzer, & Williams, 2001; Spitzer, Kroenke, Williams, & Löwe, 2006). Social connectedness was also measured, including a previously used measure of social engagement with gay men based on two items measuring: proportion of male friends who are gay; and amount of free time spent with gay male friends (Zablotska, Holt, & Prestage, 2012). Measures of

other psychosocial states included a direct question on self-perceived masculinity/femininity and, in 2017, the Rosenberg measure of global self-esteem (Rosenberg, Schooler, Schoenbach, & Rosenberg, 1995).

Men were asked if they had ever used each illicit drug type, and how frequently they had used each drug in the previous six months ('never', 'once or twice', 'at least monthly', 'every week', 'daily'). We used the Alcohol Use Disorders Identification Test (AUDIT-C) alcohol screen to identify active alcohol use disorders (Saunders, Aasland, Babor, De la Fuente, & Grant, 1993). Men with a score of 6–7 were classified as 'high risk' and those with a score of 8 or above as 'severe risk'. Regarding use of tobacco and EDM, men were asked if they had ever used these substances, and how frequently they had done so in the previous six months (less than once a month, monthly, weekly, every second day, and daily).

Men were also asked about whether they were concerned about their drug and whether someone close to them had expressed concern about their drug use. The severity of dependence scale (SDS) is often used to measure psychological dependence on certain drugs (Gossop et al., 1995; Lea, de Wit, & Reynolds, 2014; Topp & Mattick, 1997). It was included here to measure methamphetamine dependence, with a score of 4 indicating dependence in an individual.

Participants and sample

Men who lived in Australia, aged sixteen years and six months or above, were eligible for participation if they were gay- or bisexual-identified or had sex with another man in the previous year. Recruitment into the Flux Study occurred between August 2014 and July 2017. Overall, 3253 completed the minimum data requirements for the online questionnaire. There were 236 men who did not respond to questions on either the GAD7 or PHQ9 measures and were excluded from these analyses, leaving a sample of 3017 men. Compared to the 3017 men included here, the 236 excluded men were younger (Mean = 35.3 vs Mean = 31.6; Odds Ratio (OR) = 1.02; 95%Confidence Interval (CI) = 1.01–1.03; p < .001) and less likely to be university-educated (55.4% vs 43.6%; OR = 0.62; 95%CI = 0.48–0.81; p < 0.001), but were otherwise similar.

Analysis

Data were analyzed with SPSS™ version 23 software. Descriptive statistics were used to describe the demographic and other characteristics of men with evidence of anxiety and depression. For univariate analyses of whether they had evidence of anxiety and, separately, of whether they had evidence of depression, we included: age, education, cultural background, social engagement with gay men, sexual identification, level of personal support, relationship status, HIV status, and sexual risk behavior. Categorical variables were analyzed using Pearson's chi-square test and t-tests were used for continuous variables. We used Type I error of 5% for these analyses. To assess statistical associations with depression or anxiety, we used logistic regression models and presented Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI). Associations with a p-value of less than 0.05 in univariate analyses were included in the multivariate analyses.

Results

Sample characteristics

The mean age of the 3017 men included here was 35.3 years (SD 13.3); median age was 32. Most (71.8%) were of Anglo-Celtic background and the majority (55.4%) was university-educated. Nearly half were in managerial (16.9%) or professional (28.4%) employment. Most men (82.4%) had ever been tested for HIV with 6.7% reporting they were HIV-positive.

Participants predominantly identified with the term 'gay' either

somewhat (28.2%) or strongly (66.6%). Most (89.5%) reported sex with a man in the previous six months, including 64.2% with casual partners. One third (35.1%) reported having engaged in condomless anal intercourse with casual partners in the previous six months. One quarter (25.0%) had engaged in group sex.

About a third (36.2%) indicated they were in a relationship with another man. Over a quarter (29.7%) indicated that most of their friends were gay men and 19.5% spent 'a lot' of time with gay friends. About a third (30.4%) reported being at least 'somewhat' involved in the gay community, and over a third (39.1%) indicated they were very open about their homosexuality and talked freely about it. Many men indicated that they received 'a lot' of support from family (35.8%), gay friends (39.6%), heterosexual friends (44.6%), and work or school colleagues (16.0%).

One quarter (25.6%) reported using EDM in the previous six months. Two thirds (65.9%) had ever used tobacco, including 18.3% who were current daily smokers. One third were either high (20.4%) or severe (10.6%) risk drinkers. Most men (n = 2457; 81.4%) had ever used illicit drugs, including 1689 men (52.2%) who had used them in the previous six months. Prevalence of use of different drug types in the previous six months included: amyl nitrite (34.7%); cocaine (14.0%); ecstasy (17.5%); GHB (8.3%); cannabis (29.5%); methamphetamine (15.0%); and heroin (0.1%). One in seven men (15.5%) reported having used drugs during sex in the previous six months, including 5.7% who indicated having done so on the majority of occasions they had sex.

One in seven of the men who had used illicit drug in the previous six months (14.2%) indicated they were at least 'a little' concerned about their drug use. Also, one in nine men (11.6%) who had recently used illicit drugs indicated that someone close to them was concerned about their drug use. Among the 358 men who had recently used methamphetamine, 28.0% were classified as dependent based on the SDS measure.

In total, 2944 men (97.6%) responded to the items in the GAD7. Over half (57.6%) showed minimal or no evidence of anxiety with a score below 5, and one quarter (24.3%) had evidence of mild anxiety (scores between 5 and 9). Moderate (scores 10–14) and severe (scores above 14) anxiety was evident for 10.5% and 7.5% of men respectively. In total, 2970 men (98.4%) responded to the items in the PHQ9. Just under half (44.1%) showed minimal or no evidence of depression with a score below 5, and one quarter (27.5%) had evidence of mild depression (scores between 5 and 9). Moderate (scores 10 and 14), moderately severe (scores 15–19), and severe (scores above 19) depression was evident for 13.8%, 8.5% and 6.0% of men respectively.

During 2017, 1814 men completed the measure of global self-esteem, with a mean score of 20.10. One in five (19.2%) of those who completed the self-esteem measure scored less than 15, which is categorized as 'low self-esteem'. The majority (57.7%) had a normal self-esteem score (between 15 and 25), and 23.2% were categorized as having high self-esteem (scores above 25).

Also during 2017, these 1814 men were asked about their history of abuse from other people. Half (51.8%) indicated having ever been verbally abused, and 26.0% had ever experienced discrimination. Over a quarter (29.8%) reported having ever been physically assaulted, including 18.3% who said they had ever been sexually assaulted. In the previous six months, 33.8% had been verbally abused, 16.0% had experienced discrimination, 9.2% had been physically assaulted, and 5.8% had been sexually assaulted.

Depression

Those who showed evidence of depression were more likely to be aged 25 years or younger (Table 1). They were also less likely to be: of Anglo-Celtic background (particularly Aboriginal men), or university-educated. Men who had not been tested for HIV, and those who were not in a relationship were more likely to have depression. Men who viewed themselves as feminine were more likely to have depression,

whereas those who viewed themselves as masculine were less likely to experience depression. Men who reported having no sexual partners in the previous six months were more likely to experience depression. Also, those who showed evidence of depression were less likely to have engaged in group sex. Men who always used condoms during anal intercourse with casual partners were less likely to show evidence of depression. Use of drugs during sex was not associated with depression. There was no difference in likelihood of experiencing depression by year of enrollment.

Those who were more socially engaged with gay men were less likely to show evidence of depression (Table 1). Men who received greater support from gay friends were also less likely to have experienced depression.

There were few associations between illicit drug use and depression (Table 1). Men who had used amyl nitrite (p = .017), cocaine (p = .003), and GHB (p = .018) in the previous six months were less likely to show evidence of depression. On the other hand, men who used cannabis were more likely to show evidence of depression (p = .005). Although frequency of use of most drugs was not associated with depression, among men who had recently used cannabis 28.7% of those who had used it less than monthly and 35.5% of those who had used it at least monthly had evidence of depression (p = .019).

Over a third (38.9%) of men who were concerned about their drug use and 28.4% of those who were not concerned about their drug use had evidence of depression (p = .008). Among those for whom someone close had expressed concern about their drug use, 50.8% showed evidence of depression, compared with 24.5% of those to whom no one had expressed such concern (p < .001). Among recent methamphetamine users, 46.2% of those classified as dependent showed evidence of depression, compared with 19.9% of those who were not classified as dependent (p < .001).

Men who had used EDM in the previous six months were less likely to show evidence of depression (Table 1). Men who smoked tobacco daily and those who were classified as high or severe risk drinkers were more likely to have depression.

In multivariate analysis, evidence of depression was associated with Aboriginal background, feeling feminine, and daily tobacco use (Table 1). Not meeting the criteria for depression was associated with older age, full-time employment, being in a relationship, and personal support from gay friends. Consistent condom use with casual partners and recent use of methamphetamine were also independently associated with lack of depression.

Anxiety

Men who had evidence of anxiety were similar in most respects to the men who had evidence of depression (Table 2). As well as having similar sociodemographic characteristics that distinguished them from men without evidence of anxiety, their sexual behavior and gender role expression distinguished between those with and without anxiety in similar ways to what was the case for depression. Gay social engagement and peer support similarly differentiated between those with and without evidence of anxiety.

As with depression, there was little association between illicit drug use and anxiety (Table 2). Although frequency of use of most drugs was not associated with anxiety, among men who had recently used GHB, however, 9.6% of those who had used it less than monthly, and 22.4% of those who had used it at least monthly had evidence of anxiety (p = .008). Daily smokers were more likely to experience anxiety (p < .001). One quarter (25.1%) of men who were at all concerned about their drug use showed evidence of anxiety compared with 14.6% of those who were not concerned about their drug use (p = .002). Also, of men who had someone close to them express concern about their drug use, 34.1% showed evidence of anxiety, compared with 15.0% of those who did not have people express such concern (p < .001). Among recent methamphetamine users, 28.1% of those classified as

Table 1

Characteristics of sample, sexual behavior, and depression (PHQ9). N = 2970.

N (%)	No evidence of depression (< 10) (n = 2128)	Evidence of depression (10 +) (n = 842)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
Age categories						
20 years or less	198 (56.7)	151 (43.3)	1.00		1.00	
21–25 year	337 (63.6)	193 (36.4)	0.75 (0.57–0.99)	0.042	1.14 (0.84–1.54)	0.410
26–35 years	631 (74.2)	219 (25.8)	0.46 (0.35–0.59)	< 0.001	0.88 (0.64–1.20)	0.412
36–50 years	575 (75.5)	187 (24.5)	0.43 (0.33–0.56)	< 0.001	0.87 (0.63–1.21)	0.407
Over 50 years	386 (80.8)	92 (19.2)	0.31 (0.23–0.43)	< 0.001	0.59 (0.41–0.84)	0.003
Not stated	1	0				
Cultural background						
Anglo-celtic	1586 (74.4)	546 (25.6)	1.00		1.00	
Aboriginal or Torres Strait Islander	34 (47.9)	37 (52.1)	3.16 (1.96–5.09)	< 0.001	2.25 (1.37–3.71)	0.001
Other	498 (66.1)	255 (33.9)	1.49 (1.24–1.78)	< 0.001	1.23 (1.01–1.49)	0.035
Not stated	10	4				
Education						
Less than university level	865 (65.5)	456 (34.5)	1.00			
University level	1258 (76.6)	385 (23.4)	0.61 (0.51–0.72)	< 0.001		
Not stated	5	1				
Employment status						
Full-time employed	1322 (79.1)	350 (20.9)	1.00		1.00	
Part-time employed	259 (65.1)	139 (34.9)	2.05 (1.60–2.62)	< 0.001	1.73 (1.34–2.23)	< 0.001
Not in workforce	522 (60.3)	344 (39.7)	2.50 (2.08–3.02)	< 0.001	1.91 (1.55–2.36)	< 0.001
Not stated	25	9				
HIV testing history						
HIV-negative	1668 (74.0)	586 (26.0)	1.00			
HIV-positive	147 (74.6)	50 (25.4)	0.97 (0.69–1.35)	0.850		
Untested	313 (60.3)	206 (39.7)	1.89 (1.54–2.30)	< 0.001		
In relationship with regular partner						
Not in a relationship	1263 (66.7)	631 (33.3)	1.00		1.00	
In a relationship	865 (80.4)	211 (19.6)	0.49 (0.41–0.58)	< 0.001	0.68 (0.57–0.83)	< 0.001
Sexual identity						
Gay	1905 (72.3)	730 (27.7)	1.00			
Bisexual	176 (67.2)	86 (32.8)	1.28 (0.97–1.67)	0.079		
Other	47 (64.4)	26 (35.6)	1.44 (0.89–2.35)	0.139		
Identification as masculine/feminine						
Neither masculine or feminine	846 (69.3)	374 (30.7)	1.00		1.00	
Feminine	98 (53.0)	87 (47.0)	2.01 (1.47–2.75)	< 0.001	1.62 (1.16–2.27)	0.005
Masculine	1090 (76.3)	338 (23.7)	0.70 (0.59–0.83)	< 0.001	0.87 (0.72–1.05)	0.150
Very masculine	91 (68.4)	42 (31.6)	1.04 (0.71–1.54)	0.827	1.32 (0.87–2.00)	0.196
Not stated	3	1				
Study enrolment years						
2014	498 (72.7)	187 (27.3)	1.00			
2015	946 (70.9)	389 (29.1)	1.10 (0.89–1.35)	0.386		
2017	684 (72.0)	266 (28.0)	1.04 (0.83–1.29)	0.755		
Sexual behavior in previous 6 months						
Number of partners						
None	165 (53.4)	144 (46.6)	1.00		1.00	
1–10	1177 (73.8)	418 (26.2)	0.41 (0.32–0.52)	< 0.001	0.61 (0.46–0.81)	0.001
Over 10	786 (73.7)	280 (26.3)	0.41 (0.31–0.53)	< 0.001	0.69 (0.52–0.93)	0.013
Any group sex						
Did not engage in group sex	1562 (70.1)	665 (29.9)	1.00			
Did engage in group sex	566 (76.2)	177 (23.8)	0.74 (0.61–0.89)	0.002		
Sex with casual partners						
No casual partners	730 (68.9)	329 (31.1)	1.00			
No anal intercourse	145 (72.1)	56 (27.9)	0.86 (0.61–1.20)	0.366		
Condom use only	503 (75.5)	163 (24.5)	0.72 (0.58–0.90)	0.003		
Any condomless anal intercourse	750 (71.8)	294 (28.2)	0.87 (0.72–1.05)	0.145		
Drug use						
Illicit drug use in previous six months[a]						
Amyl nitrite	764 (74.2)	266 (25.8)	0.83 (0.70–0.98)	0.032		
Cocaine	323 (77.5)	94 (22.5)	0.71 (0.55–0.90)	0.005		
Ecstasy	385 (73.8)	137 (26.2)	0.92 (0.81–1.05)	0.226		
GHB	188 (77.7)	54 (22.3)	0.71 (0.52–0.97)	0.034		
Heroin[b]	1 (33.3)	2 (66.7)				
LSD	66 (38.0)	31 (32.0)	1.09 (0.86–1.39)	0.456		
Cannabis	601 (68.5)	277 (31.5)	1.27 (1.07–1.51)	0.008		
Methamphetamine	325 (73.2)	119 (26.8)	0.92 (0.73–1.16)	0.472		
Ketamine	93 (73.8)	33 (26.2)	1.21 (0.94–1.55)	0.137		

(continued on next page)

Table 1 (*continued*)

N (%)	No evidence of depression (< 10) (n = 2128)	Evidence of depression (10 +) (n = 842)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
None	1002 (70.4)	422 (29.6)	0.89 (0.76–1.04)	0.136		
Erectile dysfunction medication						
Not used	1550 (69.9)	666 (30.1)**	1.00			
< monthly use	295 (76.6)	90 (23.4)	0.69 (0.53–0.89)	0.004		
At least monthly use	283 (76.7)	86 (23.3)	0.72 (0.55–0.95)	0.019		
Tobacco						
Not used	1389 (74.4)	478 (25.6)	1.00		1.00	
< daily use	393 (70.3)	166 (29.7)	1.29 (1.04–1.60)	0.020	1.07 (0.85–1.34)	0.584
Daily use	345 (63.5)	198 (36.5)	1.56 (1.25–1.95)	< 0.001	1.54 (1.24–1.91)	< 0.001
Not stated	1	0				
Mean scores (SD)						
Alcohol – AUDIT-c	2.08 (0.95)	2.14 (1.03)	1.07 (0.99–1.16)	0.098		
Mean gay social engagement (SD)	3.66 (1.62)	3.28 (1.70)	0.87 (0.83–0.91)	< 0.001		
Mean level of personal support from gay friends (SD)	3.17 (0.91)	2.86 (1.03)	0.72 (0.67–0.79)	< 0.001	0.76 (0.70–0.83)	< 0.001

[a] Items are not mutually exclusive: Could have used multiple drugs.

[b] Numbers too small to interpret.

dependent showed evidence of anxiety, compared with 9.2% of those not classified as dependent (p < .001).

Self-esteem

What distinguished men who had evidence of low self-esteem from those with higher self-esteem was similar in most respects to what distinguished the men who had evidence of either depression or anxiety from those without either of those mental health conditions (Table 3).

Among those to whom someone close had expressed concern about their drug use, 27.9% had lower self-esteem, compared with 17.4% of those to whom no one had expressed such concern (p = .008). Of those, 34.1% had low self-esteem, compared with 15.0% of those who did not have people express such concern (p < .001).

Abuse and discrimination

Men who had experienced discrimination, been verbally abused, or been physically or sexually assaulted were more likely to have evidence of depression than were men who had not had such experiences (Fig. 1). Anxiety and self-esteem were similarly associated with experiences of discrimination, abuse, and assault.

Masculinity, femininity, and sex partying

Men who considered themselves as being masculine were more likely to engage in intensive sex partying behaviors than were men who did not view themselves as masculine (Table 4). They reported having a greater number of sex partners, and were more likely to have engaged in group sex and condomless anal intercourse with casual partners in the previous six months. Men who considered themselves as masculine were also more likely to have recently used amyl nitrite, methamphetamine, and EDM, and they were more socially engaged with gay men.

Discussion

Although prevalence of anxiety and depression was high, poor mental health was generally not associated with either illicit drug use or sexual behavior, despite popular commentary to the contrary (Stuart, 2016). Use of alcohol and particularly, daily tobacco use, was associated with both anxiety and depression, as well as with lower self-esteem. On the other hand, use of EDM was associated with reduced risk of poor mental health outcomes.

Poor mental health tends to reflect social disadvantage, marginalization, and vulnerability in most populations (Wilkinson & Marmot, 2003; World Health Organization, 2014). Factors such as lower education, lack of employment, younger (and older) age, and cultural or ethnic minority status have all been associated with anxiety and depression (World Health Organization, 2014), as well as with low self-esteem (Twenge & Campbell, 2002). This was confirmed in our analysis. Prevalence of depression and anxiety are higher among GBM than they are among other men (Lyons et al., 2013; McLaren et al., 2008). Even so, standard socioeconomic factors that have been found to be associated with poor mental health in the general population, also appear to contribute to poor mental health among GBM. While prevalence of depression and anxiety was high among otherwise relatively advantaged men in our sample, they were even higher among participants with lower socioeconomic status.

We found little association between illicit drug use in general and poor mental health outcomes. Indeed, our data suggest that use of some illicit drugs was associated with better mental health outcomes. In a related analysis, we found no association between injecting drug use and mental health (Bui, Zablotska-Manos, Hammoud, & Maher, 2018). Problematic drug use, and, specifically dependent methamphetamine use, was, however, associated with poor mental health, and daily tobacco use was strongly associated with both depression and anxiety. On the other hand, use of EDM – which GBM tend to use to enhance sexual pleasure, particularly in the context of intensive sex partying – was associated with decreased anxiety and depression, as well as with higher self-esteem. These data indicate that the relationship between drug use and mental health in GBM is neither simple nor direct, and that different levels of use of different types of drugs may be associated with very different mental health outcomes. The majority of men who used illicit drugs were not necessarily dependent users nor was their use always considered problematic, and they mostly appeared to have no greater risk of poor mental health. However, for a minority of men who used drugs, their drug use did appear to be dependent or was considered problematic (either by themselves or by others), and these men also tended to show evidence of poor mental health.

The hypothesis that sexual risk behavior often reflects poor mental health was also not supported by our analyses. Overall, there was no independent association between mental health and sexual risk behavior. Although men who always used condoms for anal intercourse with casual partners tended to report lower anxiety or depression, men who engaged in condomless sex were not at increased risk of either condition. Also, any anal intercourse, regardless of condom use, was

Table 2
Characteristics of sample, sexual behavior, and anxiety (GAD7). N = 2944.

N (%)	No evidence of anxiety disorder (< 10) (n = 2412)	Evidence of anxiety disorder (10+) (n = 532)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
Age categories						
20 years or less	250 (72.5)	95 (27.5)	1.00			
21–25 year	406 (77.8)	116 (22.2)	0.75 (0.55–1.03)	0.075		
26–35 years	690 (81.9)	152 (18.1)	0.58 (0.43–0.78)	< 0.001		
36–50 years	648 (85.2)	113 (14.8)	0.46 (0.34–0.63)	< 0.001		
Over 50 years	417 (88.2)	56 (11.8)	0.35 (0.25–0.51)	< 0.001		
Not stated	1	0				
Cultural background						
Anglo-celtic	1765 (83.4)	351 (16.6)	1.00			
Aboriginal or Torres Strait Islander	52 (72.2)	20 (27.8)	1.93 (1.14–3.28)	0.014		
Other	584 (78.6)	159 (21.4)	1.37 (1.11–1.69)	0.003		
Not stated	11	2				
Education						
Less than university level	1019 (78.2)	284 (21.8)	1.00			
University level	1388 (84.9)	247 (15.1)	0.65 (0.53–0.79)	< 0.001		
Not stated	5	1				
Employment status						
Full-time employed	1439 (86.5)	224 (13.5)	1.00		1.00	
Part-time employed	316 (80.4)	77 (19.6)	1.67 (1.25–2.25)	0.001	1.43 (1.06–1.92)	0.018
Not in workforce	628 (73.5)	226 (26.5)	2.39 (1.93–2.97)	< 0.001	1.97 (1.58–2.45)	< 0.001
Not stated	29	5				
HIV testing history						
HIV-negative	1864 (83.4)	371 (16.6)	1.00			
HIV-positive	166 (83.8)	32 (16.2)	0.97 (0.65–1.44)	0.874		
Untested	380 (74.7)	129 (25.3)	1.71 (1.36–2.14)	< 0.001		
In relationship with regular partner						
Not in a relationship	1493 (79.6)	383 (20.4)	1.00		1.00	
In a relationship	919 (86.0)	149 (14.0)	0.63 (0.51–0.78)	< 0.001	1.27 (1.02–1.58)	0.030
Sexual identity						
Gay	2143 (82.0)	470 (18.0)	1.00			
Bisexual	213 (82.2)	46 (17.8)	0.99 (0.71–1.38)	0.928		
Other	56 (77.8)	16 (22.2)	1.30 (0.74–2.29)	0.358		
Identification as masculine/feminine						
Neither masculine or feminine	958 (79.1)	253 (20.9)	1.00		1.00	
Feminine	126 (68.9)	57 (31.1)	1.86 (1.26–2.75)	0.002	1.54 (1.08–2.19)	0.017
Masculine	1225 (86.5)	191 (13.5)	0.54 (0.42–0.70)	< 0.001	0.67 (0.54–0.83)	< 0.001
Very masculine	100 (76.9)	30 (23.1)	1.14 (0.74–1.75)	0.562	1.25 (0.80–1.96)	0.329
Not stated	3	1				
Study enrolment years						
2014	557 (82.0)	122 (18.0)	1.00			
2015	1087 (82.3)	234 (17.7)	0.98 (0.77–1.25)	0.888		
2017	768 (81.4)	176 (18.6)	1.05 (0.81–1.35)	0.728		
Sexual behavior in previous 6 months						
Number of partners						
None	223 (72.9)	83 (27.1)	1.00			
1–10	1301 (82.3)	279 (17.7)	0.58 (0.43–0.77)	< 0.001		
Over 10	888 (83.9)	170 (16.1)	0.51 (0.38–0.70)	< 0.001		
Any group sex						
Did not engage in group sex	1780 (80.7)	427 (19.3)	1.00			
Did engage in group sex	632 (85.8)	105 (14.2)	0.69 (0.55–0.87)	0.002		
Sex with casual partners						
No casual partners	837 (79.7)	213 (20.3)	1.00			
No anal intercourse	169 (85.4)	29 (14.6)	0.67 (0.44–1.03)	0.067		
Condom use only	553 (83.5)	109 (16.5)	0.78 (0.60–1.00)	0.049		
Any condomless anal intercourse	853 (82.5)	181 (17.5)	0.83 (0.67–1.04)	0.105		
Drug use						
Illicit drug use in previous six months[a]						
Amyl nitrite	852 (83.0)	174 (17.0)	0.89 (0.72–1.08)	0.238		
Cocaine	351 (84.8)	63 (15.2)	0.79 (0.59–1.05)	0.101		
Ecstasy	426 (82.6)	90 (17.4)	0.99 (0.85–1.16)	0.912		
GHB	209 (86.4)	33 (13.6)	0.70 (0.48–1.02)	0.061		
Heroin[b]	1 (25.0)	3 (75.0)				
LSD	80 (84.2)	15 (15.8)	0.97 (0.74–1.28)	0.845		
Cannabis	700 (80.4)	171 (19.6)	1.16 (0.95–1.43)	0.149		
Methamphetamine	381 (85.8)	63 (14.2)	0.71 (0.54–0.95)	0.020	0.70 (0.51–0.94)	0.019
Ketamine	103 (82.4)	22 (17.6)	1.13 (0.84–1.51)	0.429		

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Table 2 (*continued*)

N (%)	No evidence of anxiety disorder (< 10) (n = 2412)	Evidence of anxiety disorder (10 +) (n = 532)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
None	1135 (80.8)	270 (19.2)	0.86 (0.72–1.04)	0.123		
Erectile dysfunction medication						
Not used	1760 (80.5)	425 (19.5)	1.00			
< monthly use	337 (86.2)	54 (13.8)	0.65 (0.48–0.88)	0.006		
At least monthly use	315 (85.6)	53 (14.4)	0.70 (0.50–0.96)	0.029		
Tobacco						
Not used	1563 (84.1)	295 (15.9)	1.00		1.00	
< daily use	445 (80.8)	106 (19.2)	1.32 (1.03–1.70)	0.029	1.19 (0.92–1.54)	0.180
Daily use	403 (75.5)	131 (24.5)	1.64 (1.27–2.13)	< 0.001	1.73 (1.35–2.21)	< 0.001
Not stated	1	0				
Mean scores (SD)						
Alcohol – AUDIT-c	2.08 (0.96)	2.15 (1.04)	1.07 (0.97–1.18)	0.173		
Mean gay social engagement (SD)	3.61 (1.63)	3.29 (1.68)	0.89 (0.84–0.94)	< 0.001		
Mean level of personal support from gay friends (SD)	3.13 (0.93)	2.87 (1.00)	0.76 (0.69–0.83)	< 0.001	0.80 (0.72–0.88)	< 0.001

[a] Items are not mutually exclusive: Could have used multiple drugs.

[b] Numbers too small to interpret.

associated with higher self-esteem. Group sex, which is commonly associated with intensive sex partying and HIV transmission risk (Grov, Rendina, Ventuneac, & Parsons, 2013; Prestage, Jin et al., 2009), was more commonly practiced by men with lower depression and anxiety as well as those with higher self-esteem. Men who were not sexually active tended to score poorly on all three of these measures.

As was the case with other Australian studies (Lyons et al., 2013; Mao et al., 2009; Prestage et al., 2005), we found little association between illicit drug use in general, sexual risk behavior, and poor mental health outcomes. Internationally, however, previous studies have observed such associations (Cochran et al., 2004; Halkitis, Green et al., 2005; Kurtz, 2005). This difference between our, Australian, data and what has been found elsewhere could be due to multiple factors. Ours was a broad community-based sample, whereas some studies have been restricted to clinic populations or HIV-positive men, or they have recruited through intensive sex partying networks or through gay venues. Also, differences between Australia and other countries in the prevalence of use of illicit drugs for particular demographic groups, such as those based on race or ethnicity, may also account for differences in our findings. Some studies present implicit links between drug use and mental health and so the associations between drug use and sexual risk behavior have been attributed to mental health on that basis. It is also possible that there are differing cultural values between Australia and other locations, such that pleasure-seeking behaviors may be less often viewed as pathological among GBM, even when they involve risk.

Poor mental health can be a consequence of sexual repression (Brown, 1984; Rubin, 2002). This also applies to many GBM who have avoided acknowledging their homosexuality or acting on their desires for fear of negative consequences (D'Augelli, 2002; Gonsiorek, 1988; Rosario et al., 2006; Ryan, Huebner, Diaz, & Sanchez, 2009). Similar arguments have been made about men who avoid sexual contact due to fear of HIV (Meyer & Dean, 1998).

High rates of depression and anxiety among GBM are typically ascribed to experiences of stigma and discrimination, and their experiences as members of a marginalized population (McLaren et al., 2008; Ryan et al., 2009). However, poor mental health is not uniform across all groups of GBM. Younger GBM have previously been found to experience depression and anxiety, (and lower self-esteem) at higher rates than their older counterparts (D'Augelli, 2002). Men who remain relatively 'closeted' about their homosexuality or who are more socially isolated, particularly from their GBM peers, or who experience anti-homosexual stigma tend to experience these mental health issues at

higher rates than do openly gay-identified men (Hershberger & D'Augelli, 1995; Mao et al., 2009). Similar differences were found in this sample. In particular, men who were less engaged in gay community life, those who had experienced stigma and discrimination, and men who were less supported by gay friends, all had poorer mental health.

On the mental health measures, men who described themselves as masculine scored better than did men who did not describe themselves as masculine. On the other hand, those who described themselves as feminine were more likely to have experienced both depression and anxiety (as well as low self-esteem). Hegemonic forms of masculinity are generally given greater social value than are forms of femininity, and men who are viewed as more feminine encounter greater levels of stigma and discrimination (Connell, 2005). In some respects, it has been argued that aspects of gay community culture also favor particular forms of masculinity, particularly for sex partners (Connell, 1992; Nardi, 2000). In particular, intensive sex partying subcultures tend to be highly masculine (Dean, 2009; Haig, 2006; McInnes, Bradley, & Prestage, 2009) and masculine men probably fare better in 'party n play' sexual networks. In our sample, masculine-identified men were more sexually active, tended to be more sexually adventurous, were more socially connected to gay men, and were more likely to use drugs associated with intensive sex partying. That they generally have better mental health is therefore perhaps not surprising. Nonetheless, in addition to experiences of discrimination and stigma, and of success and rejection regarding both sexual partnering and gay socializing, it is unclear to what extent individuals' self-perception of themselves as either masculine or feminine plays a role in determining their relative mental health.

With no direct association between mental health and either drug use in general or any of the indicators of sexual risk, our data indicate that social, personal, and community connectedness and experiences of stigma and discrimination are important considerations, as are self-perceptions about masculinity and femininity. If resilience is understood in this context as the capacity to avoid dependent or problematic use of drugs, rather than use of drugs in general, then confronting homophobia, both personally and culturally, appears to be a key component.

Overall, it is perhaps not surprising that GBM who are more sexually active and who actively participate in gay party subcultures might enjoy better mental health than are those who are more socially isolated, and who actively repress aspects of their sexuality. The use of drugs to enhance sexual and partying experiences tends to be peripheral

Table 3

Characteristics of sample, sexual behavior, and global self-esteem. N = 1814.

N (%)	Normal to high self-esteem (15 +) (n = 1467)	Low self-esteem < 15 (n = 347)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
Age categories						
20 years or less	102 (78.5)	28 (21.5)	1.00		1.00	
21–25 year	204 (73.6)	73 (26.4)	0.76 (0.46–1.25)	0.280	0.44 (0.25–0.75)	0.003
26–35 years	416 (80.3)	102 (19.7)	0.68 (0.48–0.96)	0.027	0.98 (0.68–1.42)	0.928
36–50 years	428 (82.1)	93 (17.9)	0.60 (0.43–0.85)	0.004	0.93 (0.63–1.36)	0.690
Over 50 years	317 (86.1)	51 (13.9)	0.45 (0.30–0.66)	< 0.001	0.58 (0.38–088)	0.012
Not stated	0	0				
Cultural background						
Anglo-celtic	1099 (81.6)	247 (18.4)	1.00			
Aboriginal or Torres Strait Islander	26 (63.4)	15 (36.6)	2.47 (1.29–4.70)	0.006		
Other	337 (79.9)	85 (20.1)	1.13 (0.86–1.48)	0.396		
Not stated	5	0				
Education						
Less than university level	544 (78.5)	149 (21.5)	1.00			
University level	920 (82.4)	197 (17.6)	0.79 (0.62–1.00)	0.052		
Not stated	3	1				
Employment status						
Full-time employed	921 (85.1)	161 (14.9)	1.00		1.00	
Part-time employed	183 (75.9)	58 (24.1)	1.91 (1.35–2.70)	< 0.001	1.66 (1.16–2.38)	0.005
Not in workforce	346 (73.6)	124 (26.4)	2.10 (1.60–2.74)	< 0.001	1.82 (1.35–2.45)	< 0.001
Not stated	17	4				
HIV testing history						
HIV-negative	1192 (81.6)	269 (18.4)	1.00			
HIV-positive	91 (82.7)	19 (17.3)	0.88 (0.52–1.51)	0.647		
Untested	184 (75.7)	59 (24.3)	1.43 (1.03–1.98)	0.031		
In relationship with regular partner						
Not in a relationship	868 (77.2)	257 (22.8)	1.00		1.00	
In a relationship	599 (86.9)	90 (13.1)	0.50 (0.38–0.65)	< 0.001	0.55 (0.41–0.73)	< 0.001
Sexual identity						
Gay	1324 (80.7)	316 (19.3)	1.00			
Bisexual	117 (83.0)	24 (17.0)	1.16 (0.74–1.84)	0.515		
Other	35 77.8)	10 (22.2)	1.39 (0.61–3.19)	0.433		
Identification as masculine/feminine						
Neither masculine or feminine	566 (77.4)	165 (22.6)	1.00		1.00	
Feminine	54 (66.7)	27 (33.3)	1.76 (1.07–2.89)	0.026	1.78 (1.05–3.03)	0.033
Masculine	777 (84.8)	139 (15.2)	0.62 (0.48–0.80)	< 0.001	0.71 (0.55–0.93)	0.012
Very masculine	68 (81.0)	16 (19.0)	0.84 (0.47–1.49)	0.544	0.96 (0.52–1.75)	0.887
Not stated	2	0				
Study enrolment years						
2014	254 (81.4)	58 (18.6)	1.00			
2015	475 (82.0)	104 (18.0)	0.96 (0.67–1.37)	0.817		
2017	747 (79.9)	188 (20.1)	1.10 (0.80–1.53)	0.560		
Sexual behavior in previous 6 months						
Number of partners						
None	101 (65.2)	54 (34.8)	1.00			
1–10	767 (81.5)	174 (18.5)	0.43 (0.30–0.62)	< 0.001		
Over 10	599 (83.4)	119 (16.6)	0.38 (0.26–0.56)	< 0.001		
Any group sex						
Did not engage in group sex	1017 (79.6)	260 (20.4)	1.00			
Did engage in group sex	450 (83.8)	87 (16.2)	0.71 (0.54–0.93)	0.013		
Sex with casual partners						
No casual partners	446 (76.6)	136 (23.4)	1.00		1.00	
No anal intercourse	113 (82.5)	24 (17.5)	0.67 (0.41–1.10)	0.112	0.85 (0.52–1.40)	0.532
Condom use only	319 (85.5)	54 (14.5)	0.53 (0.37–0.75)	< 0.001	0.55 (0.38–0.79)	0.001
Any condomless anal intercourse	589 (81.6)	133 (18.4)	0.71 (0.54–0.94)	0.015	0.71 (0.53–0.95)	0.022
Drug use						
Illicit drug use in previous six months[a]						
Amyl nitrite	576 (82.6)	121 (17.4)	0.87 (0.73–1.04)	0.126		
Cocaine	242 (86.1)	39 (13.9)	0.79 (0.62–1.01)	0.064		
Ecstasy	277 (83.7)	54 (16.3)	0.93 (0.74–1.16)	0.518		
GHB	151 (85.3)	26 (14.7)	0.82 (0.58–1.17)	0.278		
Heroin[b]	2 (100.0)	0 (0.0)				
LSD	42 (76.4)	13 (23.6)	1.36 (0.85–2.16)	0.202		
Cannabis	429 (80.5)	104 (19.5)	1.08 (0.88–1.31)	0.471		
Methamphetamine	248 (86.1)	40 (13.9)	0.63 (0.44–0.90)	0.012		
Ketamine	70 (82.4)	15 (17.6)	0.97 (0.63–1.49)	0.878		

(continued on next page)

Table 3 (*continued*)

N (%)	Normal to high self-esteem (15 +) (n = 1467)	Low self-esteem < 15) (n = 347)	Univariate analysis		Multivariate analysis	
			OR (CI 95%)	P-trend	aOR (CI 95%)	P-trend
None	646 (79.4)	168 (20.6)	0.83 (0.66–1.05)	0.126		
Erectile dysfunction medication						
Not used	1010 (78.7)	273 (21.3)	1.00			
< monthly use	221 (86.0)	36 (14.0)	0.55 (0.37–0.81)	0.003		
At least monthly use	236 (86.1)	38 (13.9)	0.56 (0.38–0.81)	0.003		
Tobacco						
Not used	997 (81.9)	220 (18.1)	1.00			
< daily use	262 (80.4)	64 (19.6)	1.09 (0.80–1.50)	0.578		
Daily use	207 (76.7)	63 (23.3)	1.36 (0.98–1.88)	0.063		
Not stated	1	0				
Mean scores (SD)						
Alcohol – AUDIT-c	2.09 (0.95)	1.99 (0.97)	0.88 (0.78–1.00)	0.056		
Mean gay social engagement (SD)	3.78 (1.63)	3.29 (1.70)	0.84 (0.78–0.90)	< 0.001		
Mean level of personal support from gay friends (SD)	3.25 (0.89)	2.88 (1.00)	0.67 (0.59–0.76)	< 0.001	0.71 (0.62–0.80)	< 0.001

[a] Items are not mutually exclusive: Could have used multiple drugs.

[b] Numbers too small to interpret.

to this. For most men participating in these subcultures, drug use is merely an enhancement to pleasure (Halkitis, Fischgrund et al., 2005; Hurley & Prestage, 2009; Prestage, Grierson et al., 2009). Given the important role of personal and social connectedness, and of experiences of stigma, social and community norms undoubtedly influence individual men's experiences, either positively or negatively.

Nonetheless, a minority of these men, whose drug use risks are considered problematic or dependent, also experience poor mental health outcomes. Whether their drug use is a causal factor in their mental health issues, or a symptom of them, is less clear. Our data suggest that harm-reduction and mental health interventions for GBM need to be carefully nuanced and targeted. They should acknowledge both the functional use of some drugs within specific gay party subcultures and the positive impact of being supported in one's sexuality on mental health, while simultaneously addressing the risk of dependent drug use, particularly in relation to poor mental health. Further research is needed regarding this relationship: to what extent does poorer mental health contribute to the likelihood of dependent or problematic drug use, or is it a symptom of such drug use? In particular, tobacco use, which was strongly associated with poorer mental health outcomes in our study, has received considerably less attention than has the use of illicit drugs among GBM.

Extrapolating these findings may be limited by differences between Australia and other locations. Although this was a large sample that was similar to other samples of Australian GBM (Lea et al., 2013), it was a volunteer convenience sample and may not be entirely representative of all homosexually active men in Australia (Hammoud et al., 2017). It is also not possible to determine any causative relationships in these cross-sectional data. Determining causality is complex and difficult, particularly in relation to stigmatized behaviors and psychopathology. In this study of prevalence and incidence of drug use among GBM, we were restricted in the range of mental health measures able to be included. The measures used in this study are limited in their capacity to identify detailed mental health states. The meaning, and interpretation, of measures of mental health, and measures of psychosocial states, need to be considered in their cultural and social context. The observed relationships in these analyses reflect relative differences within this sample, but comparisons to other populations need to considered with caution. Nonetheless, men's drug-using and sexual risk behaviors may reflect multiple factors, and for individual men, mental health issues may be a major consideration, even if this is not apparent at a population level. Longitudinal data may help to identify risk factors for changes in individuals over time.

Conclusion

The interconnections between mental health, substance use, and sexual risk behavior among GBM are complex. For the most part, GBM use drugs to enhance sexual pleasure, and neither their substance use nor their sexual behavior appears to be driven by mental health issues. Nonetheless, GBM whose substance use was considered problematic or dependent were more likely to experience both anxiety and depression.
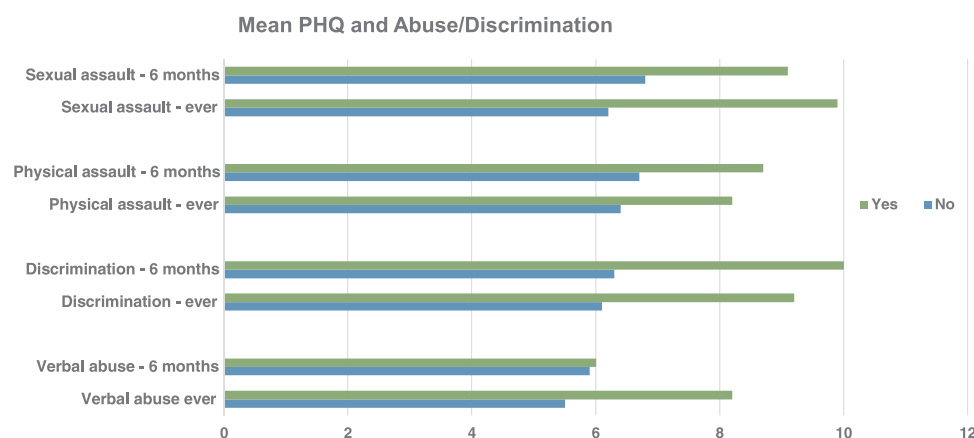
Mean PHQ and Abuse/Discrimination

Fig. 1. Depression (PHQ score) and experiences of abuse or discrimination.

Table 4
Masculinity, femininity, and sex partying N = 3013.

N (%)	Feminine (n = 187)	Neither masculine or feminine (n = 1242)	Masculine (n = 1451)	Very masculine (n = 133)	p-value
Sexual behavior in previous 6 months					
Number of partners					< 0.001
None	40 (21.4)	151 (12.2)	119 (8.2)	6 (4.5)	
1–10	113 (60.4)	688 (55.4)	756 (52.1)	60 (45.1)	
Over 10	34 (18.2)	403 (32.4)	576 (39.7)	67 (50.4)	
Any group sex					< 0.001
Did not engage in group sex	162 (86.6)	977 (78.7)	1034 (71.3)	89 (66.9)	
Did engage in group sex	25 (13.4)	265 (21.3)	417 (28.7)	44 (33.1)	
Sex with casual partners					< 0.001
No casual partners	99 (52.9)	466 (37.5)	483 (33.3)	32 (24.1)	
No anal intercourse	7 (3.7)	74 (6.0)	111 (7.6)	12 (9.0)	
Condom use only	31 (16.6)	283 (22.8)	325 (22.4)	34 (25.6)	
Any condomless anal intercourse	50 (26.7)	419 (33.7)	532 (36.7)	55 (41.4)	
Drug use					
Illicit drug use in previous six months[a]					
Amyl nitrite	44 (23.6)	410 (33.0)	538 (37.0)	53 (39.8)	0.001
Cocaine	15 (8.0)	185 (14.9)	205 (14.1)	14 (10.6)	0.040
Ecstasy	30 (16.1)	236 (19.0)	241 (16.6)	20 (15.0)	0.241
GHB	12 (6.4)	92 (7.4)	130 (9.0)	14 (10.5)	0.398
Heroin[b]	0 (0.0)	1 (0.1)	3 (0.2)	0 (0.0)	0.786
LSD	7 (3.7)	39 (3.1)	46 (3.2)	6 (4.5)	0.390
Cannabis	57 (30.5)	394 (31.7)	404 (27.8)	33 (24.8)	0.180
Methamphetamine	19 (10.2)	171 (13.8)	238 (16.4)	25 (18.8)	0.035
Ketamine	11 (5.9)	53 (4.3)	56 (3.9)	8 (6.0)	0.070
None	110 (58.8)	592 (47.7)	684 (47.1)	56 (42.1)	0.011
Erectile dysfunction medication					< 0.001
Not used	171 (92.0)	1013 (81.6)	983 (67.8)	76 (57.1)	
< monthly use	8 (4.3)	129 (10.4)	233 (16.1)	27 (30.3)	
At least monthly use	7 (3.7)	100 (8.1)	235 (16.2)	30 (22.6)	
Mean scores (SD)					
Alcohol – AUDIT-c	2.02 (0.96)	2.11 (0.98)	2.09 (0.95)	2.15 (1.15)	0.611
Mean gay social engagement (SD)	2.62 (0.98)	2.70 (1.02)	2.80 (0.96)	2.70 (1.08)	0.010

[a] Items are not mutually exclusive: Could have used multiple drugs.
[b] Numbers too small to interpret.

GBM who experience social isolation and marginalization are particularly likely to have poor mental health. Interventions addressing sexual risk behavior, substance use, and mental health among GBM need to integrate harm reduction with peer and social support that acknowledges the balance between risk and pleasure.

Author agreement/declaration

All authors certify that they have seen and approved the final version of the manuscript being submitted. All authors warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

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2.1   Trends in behaviour following PrEP initiation

2.1.1   Publication details

Prestage G, Maher L, Grulich A, Bourne A, <u>Hammoud MA</u>, Vaccher S, Bavinton B, Holt M, Jin F. Brief report: Changes in behavior after PrEP initiation among Australian gay and bisexual men. Journal of Acquired Immune Deficiency Syndromes 2019; 81(1): 52-6.

2.1.2   Items related to this thesis

Item 1: Measure ongoing PrEP use following initiation.

Item 2: Describes changes in behaviour after PrEP initiation.

2.1.3 Appendix two in context

The results presented in **chapter 5** identified that gay and bisexual men who were engaging in high-risk HIV behaviours subsequently initiated PrEP. What was not demonstrated by these results were changes in behaviours following PrEP use.

Few men who initiated PrEP subsequently stopped using it. Simultaneously, there have been increases in some behaviours that correspond to the *Australian PrEP Guidelines.* Men who initiated PrEP became more sexually active, but their drug-using behaviours have changed little. Compared to men that did not commence PrEP, those that did were more socially engaged with gay men and had higher mean scores of measures of sexual sensation seeking, regardless of when they commenced PrEP. They were also more likely to have engaged in riskier behaviours, such as receptive condomless anal intercourse with casual partners, methamphetamine use, and were more sexually active in general than were the men who never used PrEP. As these are considerations in whether one is eligible for PrEP, and presumably, in how individuals determine whether they should use PrEP themselves, this is unsurprising. It also reaffirms that PrEP tends to be being adopted by those for whom it is most suitable. Nonetheless, men who commenced using PrEP tended to become even more likely to engage in riskier sexual behaviours during the same survey period in which they commenced using PrEP, and they usually maintained these behaviours during subsequent survey rounds. Proportions of methamphetamine use before and after PrEP uptake remained stable. So, it would appear that gay and bisexual men were not using PrEP as a means to use illicit drugs.

Changes in Behavior After PrEP Initiation Among Australian Gay and Bisexual Men

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Introduction: HIV pre-exposure prophylaxis (PrEP) has been increasingly adopted by gay and bisexual men (GBM). Little is known about whether individual GBM change their sexual behavior after PrEP initiation.

Methods: Following Lives Undergoing Change (Flux) is a national, online, prospective observational study among Australian GBM. Using McNemar statistics, we compare rates of sexual behaviors before and coincident with PrEP initiation among 1518 non–HIV-positive men recruited between August 2014 and July 2017 who had not commenced PrEP at baseline and who completed at least one 6-monthly follow-up surveys by July 2018.

Results: The proportion of men using PrEP rose to 24.2% over time. In total, 348 men initiated PrEP during follow-up. PrEP initiators were more likely to report particular sexual behaviors during the follow-up period that they commenced PrEP compared with the period immediately prior: receptive condomless anal intercourse with casual partners increased from 31.0% to 48.9% (McNemar < 0.001); mean partner number increased from 21.96 partners to 34.55 partners (p-trend < 0.001). Among the 1170 men who did not initiate PrEP, prevalence of these behaviors remained lower and stable. Sexual sensation-seeking and gay social engagement were both higher among men who commenced PrEP.

Conclusions: GBM tended to increase their engagement in "adventurous" sexual behaviors after PrEP initiation. Sexual behaviors among men who did not initiate PrEP were less common and did not change over time.

Key Words: HIV, pre-exposure prophylaxis, gay men, men who have sex with men, sexual risk behavior, chemsex

INTRODUCTION

In Australia, declines in HIV infections have accompanied increases in the proportion of gay and bisexual men (GBM) using HIV pre-exposure prophylaxis (PrEP).[1] Nonetheless, rates of recent receptive condomless anal intercourse (CLAI) with casual partners (R-CLAIC) among HIV-negative men who were not using PrEP have remained stable at about 20%.[2] This could be because men who previously engaged in R-CLAIC without taking PrEP may be continuing to do so, or that men who had previously not engaged in R-CLAIC may have commenced doing so while others who had previously engaged in R-CLAIC simultaneously initiated PrEP use.

GBM represent the key population group at risk of HIV infection in Australia.[3,4] PrEP effectively reduces the risk of HIV infection among adherent GBM by as much as 99%.[5] Australia's National HIV Strategy prioritizes GBM for HIV prevention, and PrEP is now offered at minimal cost through public subsidy.[4,6,7] Eligibility criteria for access to PrEP include recent (within last 3 months) CLAI with an HIV-positive partner with detectable viral load; recent R-CLAIC; recent use of methamphetamine; or recent diagnosis with a rectal sexually transmissible infection (STI) or syphilis.[8]

More than 15,000 GBM currently use PrEP in Australia.[9] The proportion of HIV-negative GBM in Sydney and Melbourne using PrEP increased rapidly from 2% in 2013 to 24% in 2017.[2] Most men who used PrEP in these cross-sectional surveys reported behaviors consistent with PrEP prescribing guidelines, during the same period as their PrEP use.[10] Methamphetamine use remained stable with about 1 in 8 reporting use in the previous 6 months.[2] In open-label PrEP trials, men who commenced PrEP more often engaged in R-CLAIC over time.[11,12] Use of PrEP was associated with higher rates of R-CLAIC in a US cohort of young GBM and a Dutch cohort of GBM.[13,14] In a small US clinic-based sample, PrEP use was associated with increased rates of CLAI.[15] What is less clear, however, is how PrEP influences sexual behaviors and how the sexual behavior of GBM who commence PrEP compares with the behavior of those who do not use PrEP.

In this article, we use 30-month follow-up data from a cohort of Australian GBM to investigate changes in sexual behavior and drug use after initiation of PrEP compared with men who did not use PrEP.

METHODS

The methods of the Following Lives Undergoing Change (Flux) study have been described elsewhere.[16] Flux is an ongoing online prospective observational cohort study among Australian GBM. Study promotion occurred through online advertising through social media, including popular gay "dating" sites and apps, and Facebook. Once enrolled, participants completed online surveys at study virtual visits at 6-monthly intervals. Participants provided informed consent, and the study was approved by the Human Research Ethics Committee at UNSW Sydney (HC14075).

Measures

At each virtual visit, the online questionnaire included demographic items, questions on sexual identity, HIV testing history, and self-reported HIV serostatus. Men described their recent (ie, previous 6 months) methamphetamine use and their PrEP use. Sexual behavior was reported for both regular and casual partners. Data collected therefore included 3 of the 4 eligibility criteria for PrEP in Australia; STI data were not collected.

We also included a previously used measure of social engagement with gay men (gay social engagement; GSE) based on 2 items: proportion of friends who are gay and amount of free time spent with gay men.[17] Other measures included the Kalichman sexual sensation-seeking scale.[18,19]

Participants

Men who lived in Australia, aged 16 years or above, were eligible for participation if they were gay- or bisexual-identified or had any sexual contact with another man in the previous year.

Analysis

Data were analyzed with SPSS version 25 software. Descriptive statistics were used to describe demographic and other characteristics of men who used PrEP. For each virtual visit, we described use of PrEP, and changes in behaviors that met the eligibility criteria for PrEP (except STI diagnoses). Categorical variables were analyzed using Pearson's χ^2 test, and t tests were used for continuous variables. We used type I error rate of 5% for these analyses. For overall trends over time, responses at each of the 6 virtual visits were included. The McNemar method for nonparametric tests of 2 related samples was used to examine the significance of univariate relationships between the visit before commencement of PrEP and the visit concomitant with PrEP initiation. For men who never used PrEP, we compared their most recent follow-up visit with the preceding visit.

RESULTS

Overall, 1695 men were enrolled in 2014–2015 and 864 in 2017. Among these 2559 men, 151 were HIV-positive and another 393 were already using PrEP at baseline. Of the remaining 2015 men, 1518 had completed at least one follow-up virtual visit by July 2018 and were included in these analyses. Compared with the 1518 men included here, the 497 excluded men were younger (mean = 29.7 years vs mean

TABLE 1. PrEP Eligibility Behaviors and PrEP Use During Each Virtual Visit (N = 1518)

n (%)	Virtual Visit 1 (n = 1518)	Virtual Visit 2 (n = 1142)	Virtual Visit 3 (n = 1024)	Virtual Visit 4 (n = 831)	Virtual Visit 5 (n = 858)	Virtual Visit 6 (n = 871)
CLAI with HIV-positive boyfriend with detectable viral load	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)
Methamphetamine use	132 (13.0)	171 (15.2)	146 (14.3)	123 (14.8)	134 (15.6)	97 (11.1)
Use of PrEP†						
No PrEP use	1518 (100.0)	1110 (97.2)	964 (94.1)	729 (87.7)	668 (77.9)	652 (74.9)
Continued use of PrEP from previous visit	0 (0.0)	0 (0.0)	25 (2.4)	54 (6.5)	90 (10.5)	139 (16.0)
Commenced use of PrEP	0 (0.0)	32 (2.8)	31 (3.0)	47 (5.7)	88 (10.3)	71 (8.2)
Stopped use of PrEP from previous visit	0 (0.0)	0 (0.0)	4 (0.4)	1 (0.1)	4 (0.5)	9 (1.0)
Incomplete data	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (0.9)	0 (0.0)
Sex with casual partners*						
No R-CLAIC	1226 (80.8)	907 (80.5)	806 (78.7)	636 (76.5)	610 (71.1)	744 (85.4)
R-CLAIC protected by PrEP	0 (0.0)	20 (1.8)	45 (4.4)	72 (8.7)	132 (15.4)	80 (9.2)
R-CLAIC unprotected by PrEP	280 (18.4)	198 (17.6)	156 (15.2)	117 (14.1)	111 (12.9)	45 (5.2)
Incomplete data	12 (0.8)	17 (1.5)	17 (1.7)	6 (0.7)	5 (0.5)	2 (0.2)

Virtual visit 6 includes 269 men enrolled into the cohort in 2017 for whom this was their second virtual visit.
*p-trend < 0.01.
†p-trend < 0.001.

= 34.7 years; $P < 0.001$), less likely to have university-level education (40.7% vs 60.2%; $P < 0.001$), and had lower GSE scores (Mean = 2.50 vs Mean = 2.73; $P < 0.001$) but were no more or less likely to engage in R-CLAIC and had similar partner numbers and sexual sensation-seeking scores.

At baseline, the mean age was 34.7 years (SD 13.07; median = 31 years). Participants were mostly university-educated (60.2%) and in full-time employment (58.6%). Three quarters (77.0%) were of Anglo-Celtic background. Most identified as gay (90.4%) or bisexual (7.6%). Most participants (1397, 92.0%) had been tested for HIV.

Very few men reported condomless sex with an HIV-positive "boyfriend" whose viral load was detectable (Table 1). PrEP use increased over time and few of those who commenced PrEP subsequently stopped using it. The proportion of men who engaged in R-CLAIC that was protected by PrEP increased while R-CLAIC that was not protected by PrEP declined by 71.7%. Methamphetamine use remained stable at about 1 in 7.

Among the 348 men who initiated PrEP during follow-up, the proportion reporting R-CLAIC increased by 57.4% between the visit before commencing PrEP and the visit when they reported commencing PrEP (Table 2; McNemar < 0.001). Multiple instances of R-CLAIC increased by 87.3%. Group sex increased by 33.7% (McNemar < 0.001). Mean partner number increased from 21.96 in the period before commencing PrEP to 34.55 during the period when they commenced PrEP (p-trend = 0.002).

Among the 1170 men who never used PrEP, the proportion reporting R-CLAIC remained steady between visits and group sex declined (McNemar = 0.001) (Table 2). Mean partner number also remained steady at 9.31 in the previous survey period and 8.59 during the most recent follow-up (p-trend = 0.185).

Methamphetamine use increased slightly among both PrEP initiators and PrEP nonusers (Table 2).

Men who initiated PrEP were more likely to engage in R-CLAIC than were men who did not, both in the period before PrEP initiation (Table 2; $P < 0.001$) and in the period during which they commenced PrEP ($P < 0.001$). They were also more likely to have engaged in group sex and to have used methamphetamine in both survey periods. Mean partner number among men who initiated PrEP was twice that of men who never used PrEP during the period before PrEP initiation ($P < 0.001$) and almost 4 times as high during the period they commenced PrEP ($P < 0.001$). Men who initiated PrEP had higher mean scores on the measure of gay social engagement than did men who never used PrEP, both before (3.08 vs 2.66; $P < 0.001$) and after (3.16 vs 2.65; $P < 0.001$) PrEP initiation. They also had higher scores on sexual sensation-seeking both before (31.90 vs 28.32; $P < 0.001$) and after (32.84 vs 28.49; $P < 0.001$) PrEP initiation.

DISCUSSION

Uptake of PrEP in this sample of Australian GBM increased dramatically over time and few men subsequently stopped using PrEP. PrEP initiation coincided with significant increases in R-CLAIC, sexual partners, and group sex. Although prevalence of those behaviors was higher among PrEP initiators before commencing PrEP than among men who never used PrEP, their engagement in those behaviors increased substantially coincident with initiation of PrEP. PrEP users effectively became more adventurous than they already were. Men whose behaviors shifted in the direction of greater (perceived) "risk" during the follow-up period may have decided to commence PrEP to minimize the possibility of HIV infection. Alternatively, initiating PrEP may have led to some men becoming less concerned about the need to sustain other methods of risk reduction.

Although more men engaged in R-CLAIC over time, the increased uptake of PrEP means that the proportion of R-CLAIC not protected by PrEP has declined. Among men who did not initiate PrEP, the proportion who engaged in R-CLAIC remained stable over time. Although men who did not initiate PrEP were less likely to engage in "risky" behaviors than men who did, they nonetheless continued to engage in those behaviors at the same rate over time.

Men who initiated PrEP also used methamphetamine at higher rates than men who never used PrEP, but commencing PrEP was only accompanied by small increases in methamphetamine use. "Chemsex" has previously been strongly associated with "sexual risk behavior" and HIV infection among GBM.[20–22] That methamphetamine use was not substantially affected by PrEP initiation suggests that post-PrEP changes in behavior were mostly restricted to sex.

Men who initiated PrEP also scored higher on sexual sensation-seeking than men who did not, both before and after they commenced PrEP. Men who participated in intensive sex partying networks, despite being at elevated risk of HIV infection, may nonetheless have been somewhat restrained because of concerns about the risk of HIV infection. Even among high-risk GBM, most men use some forms of risk-reduction most of the time.[10,23] Men who do not access PrEP despite being eligible for it are often less consistent over time in their likelihood to engage in the behaviors that make them eligible for PrEP than are the men who initiate PrEP.[24] Among men who initiate PrEP, the desire to engage in such behaviors is often felt strongly.[25]

TABLE 2. Behavioral Changes and PrEP Initiation (N = 1518)

PrEP Users (n = 348)	Virtual Visit Before PrEP Initiation, n (%)	Virtual Visit Coinciding With PrEP Initiation, n (%)
Receptive CLAIC	108 (31.0)	170 (48.9)
Repeated R-CLAIC	74 (21.3)	139 (39.9)
Group sex	130 (37.4)	174 (50.0)
Methamphetamine use	69 (19.8)	83 (23.9)

PrEP Nonusers (n = 1170)	Penultimate Visit, n (%)	Most Recent Visit, n (%)
Receptive CLAIC	154 (13.2)	146 (12.5)
Repeated R-CLAIC	97 (8.3)	89 (7.6)
Group sex	254 (21.7)	195 (16.7)
Methamphetamine use	107 (9.1)	129 (11.0)

The initiation of PrEP by men inclined toward more "adventurous" behaviors will certainly reduce their risk of HIV infection. However, whereas, prior to their initiation of PrEP, their more constrained, though still occasionally high-risk sexual behavior may have minimized the possibility of other STIs, after they had initiated PrEP, their increased frequency of R-CLAIC, and of multiple partners may increase exposure to these other infections.[26,27] Although this is potentially mitigated by the regular sexual health screening that accompanies PrEP.[28] Nonetheless, observed changes in behavior after PrEP initiation were presumably because men felt safe from HIV infection. Distinguishing between perceptions of "safe" and "risky" sex before and after PrEP is an evolving issue.[28] Rather than being viewed as increases in risk-taking behavior, these changes need to be understood in the context of changing definitions of "safe sex" and may represent broader changes in gay community "safe sex culture."[29–31]

Although this volunteer, online convenience sample was similar in characteristics and behaviors to those of participants in other samples of Australian GBM,[4,10,32,33] it may not be representative of all homosexually active men in Australia. Questions referred to the 6-month period before each visit, so we were unable to identify the precise timing of commencement of PrEP in relation to changes in behavior.

CONCLUSIONS

PrEP offers a means for some men to engage in sexually adventurous behaviors that they may have previously desired but were cautious about practicing without the protection now offered by PrEP. It is important that all GBM have access to high-quality regular sexual health screening to offset any potential increases in non-HIV STIs that may follow these changes in behavior.

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Appendix Three

Peer reviewed publications relating to my PhD research

2019

1 Grulich AE, Guy R, Amin J, Jin F, Selvey C, Holden J, Schmidt HA, Zablotska I, Price K, Whittaker B, Chant K, Cooper C, McGill S, Telfer B, Yeung B, Levitt G, Ogilvie EE, Dharan NJ, Hammoud MA, Vaccher S, Watchirs-Smith L, McNulty A, Smith DJ, Allen DM, Baker D, Bloch M, Bopage RI, Brown K, Carr A, Carmody CJ, Collins KL, Finlayson R, Foster R, Jackson EY, Lewis DA, Lusk J, O'Connor CC, Ryder N, Vlahakis E, Read P, Cooper DA. Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. Lancet HIV 2018; 5(11): e629-e37.

2 Prestage G, Maher L, Grulich A, Bourne A, Hammoud MA, Vaccher S, Bavinton B, Holt M, Jin F. Brief Report: Changes in Behavior After PrEP Initiation Among Australian Gay and Bisexual Men. Journal of Acquired Immune Deficiency Syndromes 2019; 81(1): 52-6

3 Lea T, Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Bath N, Grierson J, Prestage G. Attitudes and perceived social norms toward drug use among gay and bisexual men in Australia. Substance use & misuse 2019; 54(6): 944-54.

4 Hammoud MA, Jin F, Maher L, Bourne A, Haire B, Saxton P, Vaccher S, Lea T, Degenhardt L, Prestage GP. Biomedical HIV protection among gay and bisexual men

who use crystal methamphetamine. Currently under review at AIDS and Behavior. Submitted July 2019.

5   Hammoud MA, Vaccher S, Jin F, Bourne A, Maher L, Holt M, Bavinton BR, Haire B, Degenhardt L, Grulich A. HIV Pre-exposure Prophylaxis (PrEP) Uptake Among Gay and Bisexual Men in Australia and Factors Associated With the Nonuse of PrEP Among Eligible Men: Results From a Prospective Cohort Study. Journal of Acquired Immune Deficiency Syndromes 2019; 81(3): e73-e84.

2018

6   Jin F, Hammoud MA, Maher L, Degenhardt L, Bourne A, Lea T, Vaccher S, Grierson J, Haire B, Prestage GP. Age-related prevalence and twelve-month incidence of illicit drug use in a cohort of Australian gay and bisexual men: Results from the Flux Study. Drug and alcohol dependence 2018; 188: 175-9.

7   Hammoud MA, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Prestage G. The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe. International Journal of Drug Policy 2018; 55: 197-204.

8   Prestage G, Hammoud MA, Jin F, Degenhardt L, Bourne A, Maher L. Mental health, drug use and sexual risk behavior among gay and bisexual men. International Journal of Drug Policy 2018; 55: 169-79.

9   Bui H, Zablotska-Manos I, Hammoud MA, Jin F, Lea T, Bourne A, Iversen J, Bath N, Grierson J, Degenhardt L. Prevalence and correlates of recent injecting drug use among gay and bisexual men in Australia: results from the FLUX study. International Journal of Drug Policy 2018; 55: 222-30.

10   Zablotska IB, Selvey C, Guy R, Price K, Holden J, Schmidt H-M, McNulty A, Smith D, Jin F, Amin J. Expanded HIV pre-exposure prophylaxis (PrEP) implementation in communities in New South Wales, Australia (EPIC-NSW): design of an open label, single arm implementation trial. BMC Public Health 2018; 18(1): 210.

2017

11   <u>Hammoud MA</u>, Bourne A, Maher L, Jin F, Haire B, Lea T, Degenhardt L, Grierson J, Prestage G. Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men–results from the Flux Study. Sexual Health 2018; 15(2): 123-34.

12   Prestage G, <u>Hammoud MA</u>, Lea T, Jin F, Maher L. Measuring drug use sensation-seeking among Australian gay and bisexual men. International Journal of Drug Policy 2017; 49: 73-9.

13   <u>Hammoud MA</u>, Jin F, Lea T, Maher L, Grierson J, Prestage G. Off-label use of phosphodiesterase type 5 inhibitor erectile dysfunction medication to enhance sex among gay and bisexual men in Australia: results from the FLUX study. The Journal of Sexual Medicine 2017; 14(6): 774-84.

14   <u>Hammoud MA</u>, Jin F, Degenhardt L, Lea T, Maher L, Grierson J, Mackie B, Pastorelli M, Batrouney C, Bath N, Bradley J, Prestage G. Following Lives Undergoing Change (Flux) study: implementation and baseline prevalence of drug use in an online cohort study of gay and bisexual men in Australia. International Journal of Drug Policy 2017; 41: 41-50.

Appendix Four

Peer reviewed conference presentations relation to my PhD research

2019

1   Use of HIV pre-exposure prophylaxis reduces HIV anxiety among high risk gay and bisexual men
Keen P, <u>Hammoud MA</u>, Bourne A, Bavinton B, Holt M, Vaccher S, Grulich A, Saxton P, Jin F, Maher L, Haire B, Prestage G
10th IAS Conference on HIV Science. Mexico City, Mexico

2   Anxiety about HIV and use of HIV pre-exposure prophylaxis among gay and bisexual men
Keen P, <u>Hammoud MA</u>, Bourne A, Bavinton B, Holt M, Vaccher S, Grulich A, Saxton P, Jin F, Maher L, Haire B, Prestage G
Joint Meeting of the 23rd ISSTDR and 20th IUSTI. Vancouver Convention Centre, Canada

3   "Flux NZ": An online national cohort investigating HIV, STI and drug-related practices among New Zealand gay and bisexual men
Saxton P, <u>Hammoud MA</u>, Andrews S, Newcombe D, Walton A, Stewart S, Te Akau R, Fisher M, Leafe K, Greenwood C, Green JA, Prestage G
Joint Meeting of the 23rd ISSTDR and 20th IUSTI. Vancouver Convention Centre, Canada

2018

4   Understanding chemsex in New Zealand: research methods and initial findings
Andrews A, Saxton P, <u>Hammoud MA</u>, Newcombe D, Walton A, Stewart S, Te Akau R, Fisher M, Leafe K, Greenwood C, Green A, Prestage G,
<u>Hammoud MA</u>, Clackett S, Prestage G, on behalf of the Flux Study Investigators
ACON NSW Community Feedback Session, Sydney, Australia

5   A longitudinal analysis of the impact of PrEP on sexual behaviour and drug use among Australian gay and bisexual men.
Prestage G, Maher L, Jin F, Degenhardt L, Vaccher S, Bourne A, <u>Hammoud MA</u>
Association for the Social Sciences and Humanities in HIV (ASSHH), Amsterdam, the Netherlands.

6   Predictors of non-use of PrEP among gay and bisexual men.
<u>Hammoud MA</u>, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Grulich A, Bavinton B, Holt M, Degenhardt L, Prestage G.
Association for the Social Sciences and Humanities in HIV (ASSHH), Amsterdam, the Netherlands

7	The new MTV generation: Using methamphetamine, Truvada and Viagra to enhance sex and stay safe. Hammoud MA, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Prestage G Association for the Social Sciences and Humanities in HIV (ASSHH), Amsterdam, the Netherlands
8	Sexualised drug use among gay, bisexual and other MSM: exploring assumptions, motivations and implications. Hammoud MA. Australasian HIV & AIDS Conference, Sydney, Australia https://ashm.eventsair.com/QuickEventWebsitePortal/2018-australasian-hivaids-conference/program/Agenda/AgendaItemDetail?id=760316af-7b19-49ec-9192-4a7cdef2ceb6
9	What drugs are Gay, Bisexual, or Men who have Sex with Men (GBMSM) using and what role do they play? Hammoud MA, Prestage G. Australasian HIV & AIDS Conference, Sydney, Australia
10	Mental health as a factor in gay men's involvement in chemsex. Prestage G, Hammoud MA Australasian HIV & AIDS Conference, Sydney, Australia conference/program/Agenda/AgendaItemDetail?id=760316af-7b19-49ec-9192-4a7cdef2ceb6
11	Initiation pf PrEP among gay and bisexual men who met the eligibility criteria for PrEP Hammoud MA, Prestage G. Australasian HIV & AIDS Conference, Sydney, Australia
12	Increase in uptake and incidence of HIV pre exposure prophylaxis (PrEP) among gay and bisexual men in Australia Hammoud MA, Prestage G. Australasian HIV & AIDS Conference, Sydney, Australia
13	Initiating sex work among Australian gay and bisexual men. Prestage G, Hammoud MA Australasian HIV & AIDS Conference, Sydney, Australia
14	The Current State of Drug Use Among Australian Gay and Bisexual Men: Factors Associated with Drug Use, Initiation, and Dependence Hammoud MA Australasian Professional Society on Alcohol and other Drugs, Auckland, New Zealand
15	The new MTV generation: Using Methamphetamine, Truvada, and Viagra to enhance sex and stay safe. Hammoud MA, Vaccher SJ, Bourne A, Haire BG, Lea T, Maher L, Prestage G. Australasian Professional Society on Alcohol and other Drugs, Auckland, New Zealand
16	Incidence and predictors of the initiation of methamphetamine use among gay and bisexual men Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, Prestage G. Australasian Professional Society on Alcohol and other Drugs, Auckland, New Zealand
17	What behaviours predict crystal methamphetamine dependence among gay and bisexual men in Australia? Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, Degenhardt L, Prestage G Australasian Professional Society on Alcohol and other Drugs, Auckland, New Zealand

18	Gamma-hydroxybutyrate (GHB) used for chemsex and its association to HIV risk behaviours and overdose Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, Degenhardt L, Grierson J, Prestage G. Australasian Professional Society on Alcohol and other Drugs, Auckland, New Zealand
19	Initiation of illicit drug use in the Flux cohort of Australian gay and bisexual men Prestage GP, Hammoud MA, Maher L, Degenhardt L, Bourne A, Lea T, Mackie B, Bath N, Haire B, Batrouney C, Jin F Australian and New Zealand Addiction Conference
20	The current state of chemsex among gay and bisexual men in Australia: Results from the Flux Study Hammoud MA, Bourne A, Mackie B, Prestage G. Health in Difference Conference, Sydney Australia
21	A Longitudinal Analysis of the Impact of PrEP on Sexual Behaviour and Drug Use among Australian Gay and Bisexual Men Prestage G, Hammoud MA. International Union against Sexually Transmitted Infections, Asia Pacific, Auckland, New Zealand
22	Increase in Uptake and Incidence of HIV Pre-Exposure Prophylaxis (PrEP) among Gay and Bisexual Men in Australia Prestage G, Hammoud MA. International Union against Sexually Transmitted Infections, Asia Pacific, Auckland, New Zealand
23	Social Media as a research tool and the insights it provides on gay, bisexual and other MSM's sexual networks and behaviours Hammoud MA International Union against Sexually Transmitted Infections, Asia Pacific, Auckland, New Zealand
24	Why are Some Australian Gay and Bisexual Men Choosing not to Initiate PrEP? Hammoud MA, Philpot S, Prestage G. International Union against Sexually Transmitted Infections, Asia Pacific, Auckland, New Zealand
25	Gay and Bisexual Men's Perceptions of PrEP in Australia: A Setting of High Accessibility. Philpot S, Hammoud MA, Prestage G. International Union against Sexually Transmitted Infections, Asia Pacific, Auckland, New Zealand
26	Methamphetamines and PrEP: Helping or Hindering Health Outcomes in Gay Men? Vaccher S, Hammoud MA, Prestage G. Methamphetamine and Health Symposium, New York, United States of America
27	PrEP in the real world Hammoud MA. 22nd International AIDS Conference, Amsterdam, the Netherlands
28	Predictors of non-use of PrEP among gay and bisexual men Hammoud MA, Vaccher S, Jin F, Bourne A, Haire B, Maher L, Lea T, Grulich A, Bavinton B, Holt M, Degenhardt L, Prestage G 22nd International AIDS Conference, Amsterdam, the Netherlands
29	A longitudinal analysis of the impact of PrEP on sexual behaviour and drug use among Australian gay and bisexual men Prestage G, Hammoud MA 22nd International AIDS Conference, Amsterdam, the Netherlands

30	The new MTV generation: Using methamphetamine, Truvada and Viagra to enhance sex and stay safe Hammoud MA. 22nd International AIDS Conference, Amsterdam, the Netherlands

2017

31	Self-Perceived Problematic Relationship with Drugs and the Use of Alcohol and Other Drug (AOD) Services among Gay and Bisexual Men. Bourne A, Hammoud MA, Bath N, Batrouney C, Prestage G. Australasian HIV & AIDS Conference, Canberra, Australia
32	PrEP and other drugs in the Flux cohort: The new MTV generation. Hammoud MA, Vaccher S, Jin F, Prestage G. Australasian HIV & AIDS Conference, Canberra, Australia
33	Why Are Some Gay and Bisexual Men Eligible for PrEP but Not Taking It? Prestage G, Maher L, Jin F, Degenhardt L, Vaccer S, Hammoud M. Australasian HIV & AIDS Conference, Canberra, Australia
34	Prevalence and initiation of illicit drug use in the Flux Study. Hammoud MA, Prestage G, on behalf of the Flux Study Investigators. Australasian HIV & AIDS Conference, Canberra, Australia
35	Does mental health drive gay men's sexual risk behaviour and drug use? Prestage G, Maher L, Jin F, Degenhardt L, Hammoud MA. Australasian HIV & AIDS Conference, Canberra, Australia. 2017
36	Changes in sexual behaviour and methamphetamine use following commencement of PrEP among Australian gay and bisexual men Prestage G, Maher L, Jin F, Degenhardt L, Vaccher S, Hammoud MA. Australasian HIV & AIDS Conference, Canberra, Australia
37	Incidence and predictors of the initiation of HIV pre-exposure prophylaxis use among gay and bisexual men. Hammoud MA, Vaccher S, Prestage G. 9th International AIDS Society (IAS) conference on HIV Science, Paris, France. 2017.
38	Incidence and predictors of the initiation of crystal methamphetamine use among gay and bisexual men. Hammoud MA, Vaccher S, Prestage G. 9th International AIDS Society (IAS) conference on HIV Science, Paris, France. 2017.

2016

39	Associations with PrEP Initiation among Gay and Bisexual Men Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
40	Use of Erectile Dysfunction Medications and Risk Behaviour Among Gay and Bisexual Men Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
41	Party Drug Use and Sexual Risk Behaviours Among Gay and Bisexual Men. Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
42	Characteristics of gay and bisexual men who use little to no HIV risk reduction Strategies during condomless anal intercourse. Hammoud MA.

43	Key predictors with the initiation of crystal methamphetamine, and HIV Pre-exposure Prophylaxis, among gay and bisexual men. Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
44	Attitudes towards illicit drug use among gay and bisexual men in Australia: Evidence for normalization. Lea T, Hammoud MA, Prestage G. Australasian Professional Society on Alcohol and other Drugs, Sydney, Australia
45	Party drug use within gay community networks in an online cohort of gay and bisexual men Hammoud MA. Australasian Professional Society on Alcohol and other Drugs, Sydney, Australia
46	Party drug use and sexual risk behaviours among gay and bisexual men. Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
47	Risk behaviours among gay and bisexual male sex workers in Australia. Hammoud MA. Australasian HIV & AIDS Conference, Adelaide, Australia
48	The Highs and Lows of Methamphetamine use among Gay and Bisexual Men. Hammoud MA. Australasian HIV & AIDS Conference, Brisbane, Australia

2015

49	Gay and Bisexual Men Alternate Ways of Obtaining Erectile Dysfunction Medication and their Reasons for Use. Hammoud MA. Australasian HIV & AIDS Conference, Brisbane, Australia
50	Gay and bisexual men's alternate ways of obtaining erectile dysfunction medication and their reason for use Hammoud MA. Australasian Professional Society on Alcohol and other Drugs, Brisbane, Australia
51	Does psychological well-being affect HIV risk behaviours among male sex workers in Australia Hammoud MA. Australasian HIV & AIDS Conference, Brisbane, Australia
52	Party drug use and sexual risk behaviours among gay and bisexual men. Hammoud MA. Australasian Professional Society on Alcohol and other Drugs, Brisbane, Australia
53	The highs and lows of methamphetamine use among gay and bisexual men. Hammoud MA Australasian HIV & AIDS Conference, Brisbane, Australia

Appendix Five

Community presentations relation to my PhD research

2019

1. Sex, drugs, and PrEP in Flux.
   <u>Hammoud MA</u>, Vaccher S, Keen P, Philpot, Prestage G, on behalf of the Flux
   Study Investigators
   Kirby Institute Seminar Series. Sydney, Australia.

2. Amyl nitrite use among gay men.
   Prestage G, <u>Hammoud MA</u>
   Australian Government. Department of Health. Therapeutic Goods
   Administration. Alkyl nitrites – public meeting. Sydney, Australia

3. Key findings from a cohort study of gay and bisexual men's health.
   Prestage G, <u>Hammoud MA</u>, on behalf of the Flux Study investigators.
   ACON NSW

2018

4. The current state of chemsex among Australian gay and bisexual men.
   Bourne A, <u>Hammoud MA</u>, Prestage G.
   Australian Federation of AIDS Organisations (AFAO) members meeting,
   Sydney, Australia.

5. Changes in drug use behaviour over time among Australian gay and bisexual
   men. Results from the Flux Study: Two years later
   <u>Hammoud MA,</u> Bourne A, Prestage G.
   Australian Research Centre in Sex, Health and Society Community Feedback,
   La Trobe University, Melbourne, Australia

6. Chemsex among gay and bisexual men in Australia: Results from the Flux
   Study
   <u>Hammoud MA</u>, Prestage G.
   HIV Epidemiology and Prevention Program Scientific Meeting, Sydney,
   Australia.

7. PrEP uptake and behavioural data among men in the Flux Study.
   Prestage G, <u>Hammoud MA.</u>
   NSW HIV Prevention Partnership Project 2018 Scientific Meeting, Sydney,
   Australia

8. Changes in drug use behaviour over time among Australian gay and bisexual
   men
   <u>Hammoud MA</u>, Prestage G.
   QuAC community feedback session, Brisbane, Australia

9. Changes in drug use behaviour over time among Australian gay and bisexual
   men
   Prestage G, <u>Hammoud MA.</u>
   SAMESH community feedback session, Adelaide, Australia

10	Using Methamphetamine, Truvada, and Viagra to enhance sex and stay safe. Hammoud MA, Vaccher S, Prestage G. UNSW Postgraduate Research Symposium, Sydney, Australia
11	Changes in drug use behaviour over time among Australian gay and bisexual men Hammoud MA, Prestage G. WAAC community feedback session, Perth, Australia
12	The Flux Study: Drug use incidence, and trends in patterns of use over two years of follow up. Hammoud MA, Prestage G, on behalf of the Flux Study Investigators Kirby Institute Seminar Series, Sydney, Australia.

2017

13	Starting and stopping drug use over time: Gay men's perceptions of their drug use in the Flux Study Hammoud MA, Prestage G, on behalf of the Flux Study Investigators ACON NSW. Sydney, Australia.
14	Starting and stopping drug use over time: Gay men's perceptions of their drug use in the Flux Study. Hammoud MA, Fengyi F, Prestage G. Centre for Social Research in Health Seminar Series. Sydney, Australia
15	The Flux Study Prestage G, Hammoud MA. Gilead Sex Conference, Sydney, Australia
16	Drug Use & Sex. Prestage G, Hammoud MA. HIV Treatment Update Seminar, Auckland, New Zealand. 2017.
17	Drug use and mental health among Australian gay and bisexual men: Results from the Flux Study. Prestage G, Hammoud MA. St Vincent's Hospital, Sydney, Australia
18	The Flux Symposium Hammoud MA, Prestage G, on behalf of the Flux Study Investigators The Kirby Institute. UNSW Sydney. Sydney, Australia.
19	Following Lives Undergoing Change: Baseline key findings from an online cohort Hammoud MA, Prestage G. Australian Federation of AIDS Organisations, Sydney, Australia
20	Why is drug research among gay and bisexual men important? Hammoud MA. HIV Epidemiology and Prevention Program Scientific Meeting, Sydney, Australia
21	Incidence and predictors of the initiation of HIV-pre-exposure prophylaxis among gay and bisexual men. Prestage G, Hammoud MA. NSW Ministry of Health, Sydney, Australia
22	Flux preliminary findings Hammoud MA, Prestage G, on behalf of the Flux Study Investigators. ACON NSW. Sydney, Australia.

23   The Flux Study: A cohort study of drug use among gay men. Preliminary data.
<u>Hammoud MA</u>.
Kirby Institute Seminar Series, Sydney, Australia

24   The Highs and Lows of methamphetamine use among Australian Gay and Bisexual men
<u>Hammoud MA.</u>
UNSW Postgrad Symposium, UNSW Sydney, Australia