EPIDEMIOLOGY, SEASONAL VARIATION AND FACTORS ASSOCIATED WITH HIV TESTING AND SEXUALLY TRANSMITTED INFECTIONS AMONG MEN WHO HAVE SEX WITH MEN AND HETEROSEXUALS IN SOUTH AUSTRALIA

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A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

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LIST OF ACRONYMS AND ABBREVIATIONS

Acronyms	Abbreviations
ABS	Australian Bureau of Statistics
ACCESS	The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood-borne Viruses
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Treatment
ASHC	Adelaide Sexual Health Centre
BBV	Blood Borne Virus
CDC	United States Centers for Disease Control and Prevention
Chemsex	Drug use for or during sex
CT	Chlamydia trachomatis
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
ESSTI	European Surveillance of Sexually Transmitted Infections
EU	European Union
EuroHIV	European Centre for the Epidemiological Monitoring of AIDS
FSWs	Female sex workers
GC	Gonococcal/Gonorrhea
GRID	Gay-related immune deficiency
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
LGV	Lymphogranuloma Venereum
MeSH	Medical Subject Headings
MG	Mycoplasma genitalium

MSCH	Melbourne Sexual Health Centre
MSM	Men who have sex with men
MSW	Men who have sex with women
NAAT	Nucleic Acid Amplification Testing
NG	Neisseria gonorrhoeae
NGOs	Non-Government Organisations
NNDSS	National Notifiable Diseases Surveillance System
PEP	Post-exposure prophylaxis
PrEP	Pre-exposure prophylaxis
RAH	Royal Adelaide Hospital
RCT	Randomised control trial
SSHC	Sydney Sexual Health Centre
SSuN	STD Surveillance Network
STI	Sexually Transmitted Infection
TasP	Treatment as prevention
UAI	Unprotected Anal Intercourse
UK	The United Kingdom
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNSW	University of New South Wales
USA	The United States of America

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DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Signed: …… …….

Bin Li (PhD Candidate)

Date: 01/09/2018

LIST OF PUBLICATIONS CONTRIBUTING TO THIS THESIS

Published

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Published

Li B, Bi P, Chow EPF, Donovan B, McNulty A, Ward A, Bell C, Fairley CK. Seasonal variation in gonorrhoea incidence among men who have sex with men. **Sexual Health**. 2016 Nov; 13(6):589-592; **doi: 10.1071/SH16122.**

Published

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Published

Li B, Hocking JS, Bi P, Bell C, Fairley CK. The efficacy of Azithromycin and Doxycycline Treatment for Rectal Chlamydial Infection: A Retrospective Cohort Study in South Australia. ***Internal Medicine Journal***. 2017 Oct 2; **doi: 10.1111/imj.13624.**

PRESENTATIONS ARISING FROM THE THESIS

Transit increase in gonorrhoea among heterosexuals attending a sexual health clinic in South Australia temporally associated with increase prostitution policing: Poster presented at the Australasian Sexual Health Conference, Sydney, Australia; October 2014.

Seasonal variation in gonorrhoea incidence among men who have sex with men: Poster presented at the Australasian Sexual Health Conference, Adelaide, Australia; November 2016.

Trends and predictors of recent HIV testing over 22 years among a clinic sample of men who have sex with men in South Australia: Poster presented at the Australasian HIV&AIDS Conference, Adelaide, Australia; November 2016.

The efficacy of Azithromycin and Doxycycline Treatment for Rectal Chlamydial Infection: A Retrospective Cohort Study in South Australia: Poster presented at the Australasian Sexual Health Conference, Canberra, Australia; November 2017.

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THESIS ABSTRACT

Background and objectives: Sexually transmitted infections (STIs) have a profound impact on sexual and reproductive health. Despite decades of control efforts, STIs are still common in Australia and remain the major public health concern. This research was conducted within the context of increased diagnoses of STIs, control of STIs and prevention of HIV transmission in South Australia. The objectives of this research project were to: (1) explore and compare the trends in gonococcal diagnoses among heterosexuals, and investigate the plausible reasons for the gonorrhoea epidemic among heterosexuals; (2) examine the trends in gonorrhoea diagnoses among MSM and to determine whether seasonal variations in gonorrhoea diagnoses were evident in MSM; (3) determine the trends in HIV testing and examine factors associated with recent HIV testing among MSM; and (4) evaluate treatment efficacy of two treatments for rectal chlamydial infection, in order that future public health policy, clinical practice and future research are informed by the best evidence.

Methods: The research project was a quantitative analysis of medical records using longitudinal clinical data. The first study was a cross-sectional and retrospective analysis to understand how the gonorrhoea trends observed in South Australia compare to those seen in other Australian state capitals, Melbourne (Victoria) and Sydney (New South Wales). Additional analyses were undertaken to investigate factors associated with the gonorrhoea epidemic among heterosexuals in Adelaide to explore whether the observations were unique or part of an Australia-wide phenomenon. In the second project, cross-sectional study was conducted to assess whether seasonal variations in urethral gonorrhoea diagnoses were evident in MSM in

three Australian states. The third study explored computerised medical records of MSM who attended the Adelaide Sexual Health Centre (ASHC) at their first visit between 1994 and 2015 to determine whether HIV testing had changed and examine factors associated with recent HIV testing among MSM. The fourth study was a retrospective analysis to evaluate treatment efficacy of two treatments for rectal chlamydial infection.

Results: In the first study, a gonorrhoea epidemic has been identified between 2006 and 2010 among heterosexual men, women and female sex workers (FSWs) compared with other years; the odds of gonorrhoea were significantly associated with FSWs in the epidemic years at ASHC. No corresponding trend in gonorrhoea diagnoses was seen at Melbourne Sexual Health Centre (MSHC) and Sydney Sexual Health Centre (SSHC). It is noted that around the same time convictions against FSWs peaked in Adelaide and newspaper reports of increased police activity against FSWs where carrying condoms had been used as evidence of sex work by police. In the second study, peaks of gonorrhoea cases were observed in the first quarter of the year in Adelaide and Sydney but in the second and fourth quarter in Melbourne. The third study showed the proportion of newly registered MSM who reported ever being tested for HIV declined; recent HIV testing did not change and current HIV testing increased between 1994 and 2015. The proportion of MSM who returned for HIV testing within 12 months did not change, with less than 40% of MSM returning for HIV testing. In the last study, rectal chlamydia prevalence was 6.7% and 8.1% respectively in men and women. Treatment with azithromycin was significantly associated with 3-fold higher risk of repeat rectal chlamydial infection. The significant association of treatment regimen with repeat rectal chlamydia remained after adjusting for other factors.

Conclusions: The first study suggests that increased policing against sex workers may reduce access to condoms, thereby increasing rates of unprotected sex. SA government should consider legislative revisions to stop using possession of condoms as evidence of sex work. The second study finds that gonorrhoea among MSM occurs in a seasonal pattern, particularly late summer into early autumn. This has implications for the provision of health services and resource allocation over the year and for the timing of health promotion activities. The third study highlights that HIV testing rate among MSM attending ASHC was suboptimal and new approaches are needed to increase the uptake and early detection of HIV infection among the high-priority MSM population. The last study identifies that azithromycin was associated with repeat rectal chlamydial infection compared to doxycycline, suggesting that doxycycline may be more effective than azithromycin in the treatment of rectal chlamydia infection in men and women. Given that STIs remain a neglected area of research and many countries observed simultaneous increases of HIV and STIs today including Australia, especially among men who have sex with men (MSM), the findings from this research project have implications for sexual health policy, clinical practice and future research in this area.

Key words: Sexually transmitted infections, epidemiology, men who have sex with men, heterosexuals, gonorrhoea, rectal chlamydia, HIV testing, azithromycin, doxycycline, treatment, risk factors, Australia

CHAPTER 1 INTRODUCTION

1.1 Background

The human immunodeficiency virus (HIV) and sexually transmitted infections (STIs) constitute the most common public health problem throughout the world and represent a huge burden in both mortality and morbidity, causing detrimental health effects [1-3]. Despite decades of global control effort has been made to reduce their high global incidence and prevalence, STIs other than HIV have been neglected as a public health priority [4,5]. Control efforts continue to fail and simultaneous increases of HIV and STIs notifications have been observed in many countries including Australia, especially among men who have sex with men (MSM) [3]. Globally, MSM are disproportionately burdened by HIV and other STIs. The reasons for the disproportionate infection burden among MSM are complex; In addition to biological and medical reasons, behavioural, social, political and economic factors also make great contributions [6,7]. Effective control of STIs include basic epidemiological and surveillance data, high quality evidence about effectiveness of individual interventions, better methods to get effective intervention onto the policy agenda, and better advocacy and more commitment to get them implemented properly [8].

The World Health Organisation (WHO) estimated 36.7 million people living with HIV/AIDS (acquired immune deficiency syndrome), 1.8 million people became newly infected with

HIV and 53% of people living with HIV were receiving antiretroviral treatment worldwide in 2016 (Figure 1.1) [9]; Globally, there were 357·4 million new cases of four common curable STIs: chlamydia (130·9 million cases), gonorrhoea (78·3 million cases), syphilis (5·6 million cases), and trichomoniasis (142·6 million cases) in 2012 (Figure 1.2) [10]. The estimated annual incidence of non-HIV STIs has increased by nearly 50% between 1995 and 2008 [11]. Additionally, HIV and STIs such as gonorrhoea, syphilis and Lymphogranuloma venereum (LGV) have re-emerged in high-income countries [12-16]; there are alarming increases in antimicrobial resistance in Neisseria gonorrhoeae (NG) and Mycoplasma genitalium (MG), particularly among MSM [4]. Meanwhile, there is growing evidence that the epidemiology of HIV and STIs is changing, control efforts may be severely challenged once again [4]. The increases in STIs and HIV have been caused by a combination of factors: lack of accurate, inexpensive diagnostic tests, particularly for chlamydia and gonorrhoea; insufficient resources to strength healthcare systems that can deliver necessary services for diagnosis and management of STIs; inefficient of surveillance and disease notification systems in many countries; political, socioeconomic and cultural barriers that limit recognition of STIs as an important public health problem; and failure to implement policies that are known to work [11].

In Australia, the notifications of sexually transmissible infections (STIs) are on the rise including gonorrhoea, chlamydia and syphilis. The recent Annual Surveillance Report from Kirby Institute, the University of New South Wales (UNSW) showed that there has been a 63 per cent increase of gonorrhoea in Australia over the last five years, with 23,000 people diagnosed in 2016 alone.

Gonorrhoea notification rates have nearly tripled from 35.6 per 100,000 in 2004 to 100.8 per 100,000 in 2016 and similar trends were observed in South Australia [17,18]. Chlamydia was still reported as the most commonly diagnosed STI in Australia, with an estimated 154,000 men and 100,000 women aged between 15 and 29 with new chlamydia infections in 2016. The notifications for infectious syphilis increased from 6.9 per 100,000 in 2012 to 14.3 per 100,000 in 2016. There were over 3000 new reports of infectious syphilis in 2016, with 87 percent of them in males. Gonorrhoea occurs predominantly among gay and bisexual identified men who reported both male and female sexual partners whereas rates in heterosexuals are low except in some minority populations [19-21].

The relationship between HIV and STIs is complex due to biological and behavioral factors [22]. Studies have shown gonorrhoea, chlamydia and syphilis can increase the risk of HIV among MSM [23,24]. HIV and STIs may interact with each other in the following ways (Figure 1.3) [25,26]:

- HIV, by causing immunosuppression, can modify the natural history (duration), clinical presentation (severity), and response to treatment of certain STIs, notably other viral infections such as genital herpes simplex virus infection or human papillomavirus.
- STIs, by causing ulceration or inflammation of the genital tract, may enhance the transmission of HIV by increasing infectiousness of HIV-positive individuals and/or the susceptibility of HIV-negative persons.

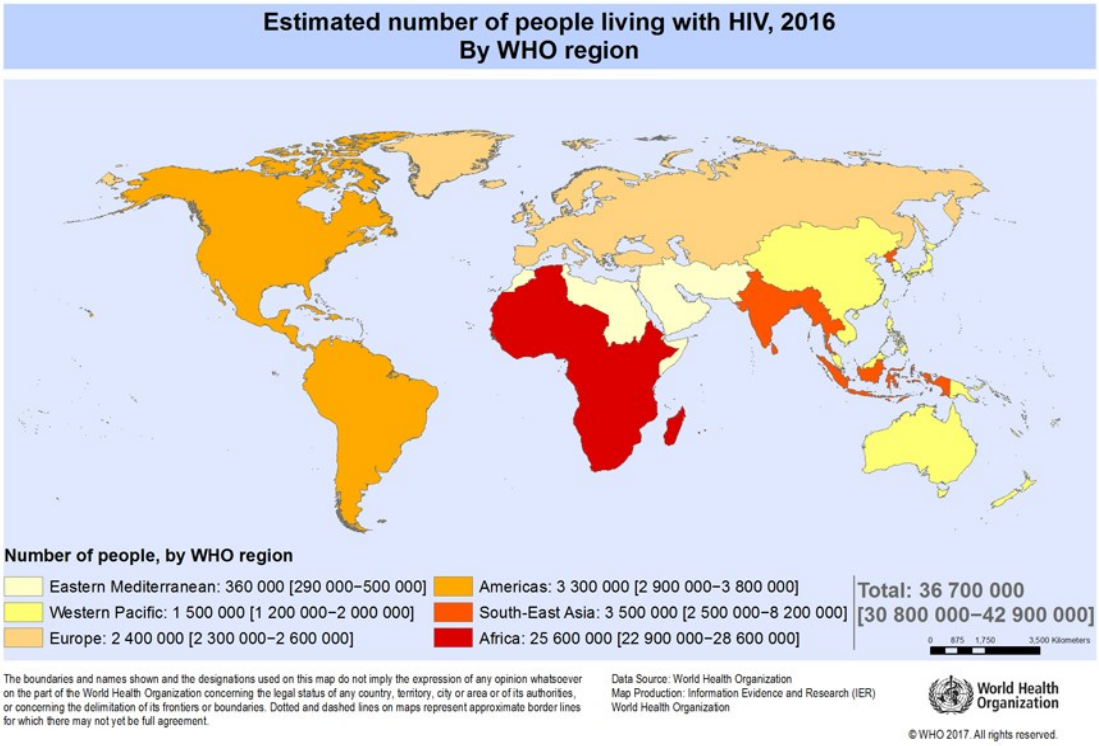

Figure 1.1 WHO estimates of number of people (all age) living with HIV, 2016 [4]

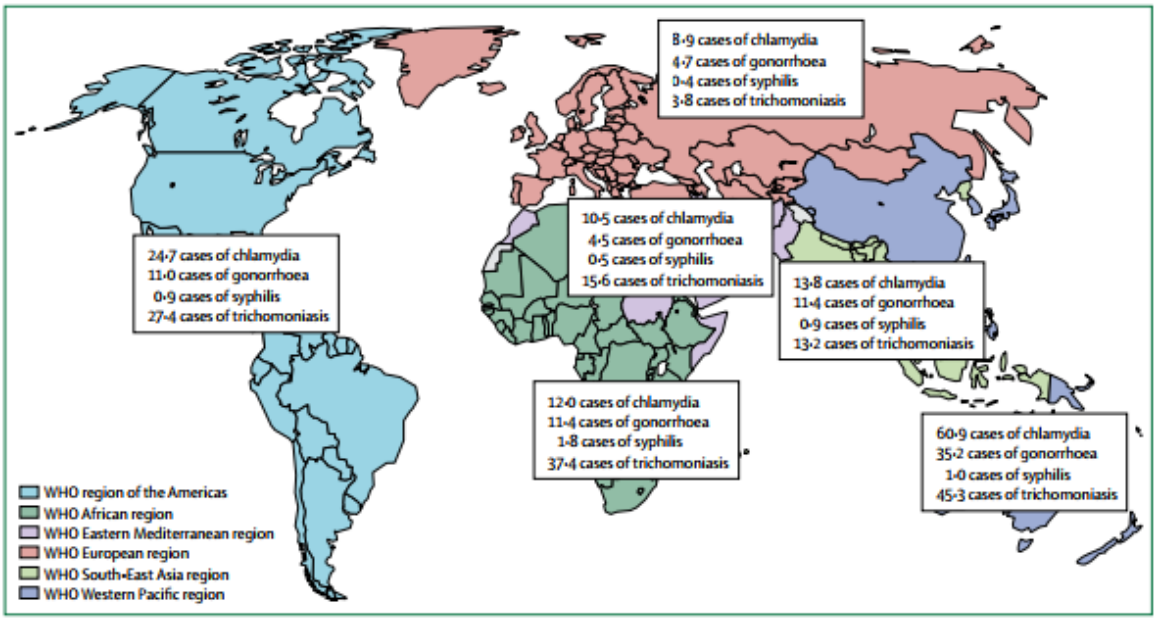

Figure 1.2 WHO regional estimates of new cases of four curable sexually transmitted infections 2012 [10]

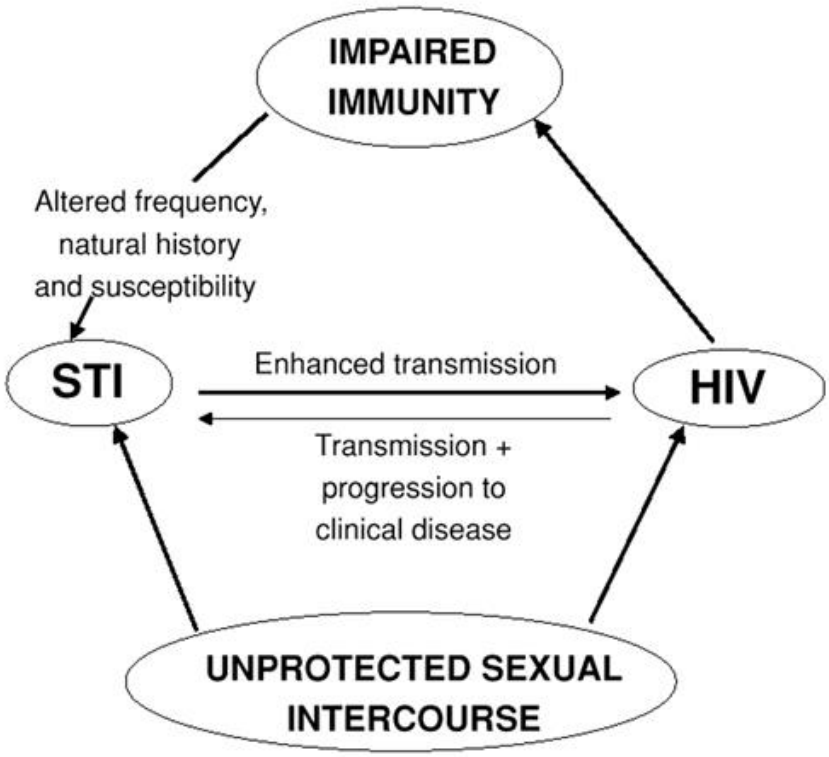

Figure 1.3 Relationships between HIV and other STIs [25]

The importance of periodic HIV testing as a preventive strategy in the programmatic response to the HIV/AIDS epidemic has been highlighted at the global level, especially in disproportionately affected MSM population. Increasing the rates of HIV testing is supported across a number of strategic documents addressing HIV [27,28]. In Australia, it is estimated that 21,391 people living with diagnosed HIV infection with 80% of them attribute their infection to male-to-male sexual contact. The prevalence of HIV among all MSM in Australia is approximately 11.2% [17]. A significant percentage of HIV infections are from people who do not know their HIV status. An estimated 31% of new HIV infections are transmitted from the approximately 9% of MSM with undiagnosed HIV. Rates of undiagnosed HIV among MSM have

been estimated between 10% and 20% in Australia [29]. The average time between a person becoming infected with HIV and being diagnosed is estimated at approximately four year [30]. Hence Monitoring trends and predictors of HIV testing among gay men and other MSM will increase the number of MSM aware of their HIV status, minimize the time between infection and diagnosis and treatment, and reduce further transmission. Meanwhile, increased testing and more people knowing their HIV status will improve health outcomes for people with HIV and reduce health impacts of late diagnosis. Recent research has shown large reductions in HIV transmission from people on effective antiretroviral treatment (ART), also known as 'Treatment as prevention' (TasP), the strategy of treating HIV-positive people with ART to prevent onward sexual transmission of HIV [31-33]. Optimising TasP is a goal of the current national HIV strategy, which aims to '. . .work towards achieving the virtual elimination of HIV transmission in Australia by 2020' and to '. . .increase the proportion of people living with HIV on treatments with an undetectable viral load' [27]. WHO has announced ambitious new HIV treatment guidelines which will see the number of people eligible for HIV treatment rising substantially. The new guidelines recommended earlier commencement of ART for people with HIV, increasing the treatment initiation threshold from a CD4 count of less than 350 to less than 500 as well as recommendations for earlier commencement of treatment for people with HIV [34].

Extragenital chlamydia and gonorrhoea are common and may be important reservoirs for ongoing STI transmission [35]. They are more likely to be asymptomatic among MSM [36]. MSM reporting unprotected receptive anal intercourse (RAI) had a high prevalence of rectal

gonorrhoea and rectal chlamydia. HIV-positive status was significantly associated with prevalent rectal chlamydia [37]. However, many MSM were not tested and most extragenital infections would not have been identified, and remained untreated, with urethral screening alone, in which patients is less likely to seek medical assistance (Figure 1.4 and Figure 1.5). There are also increasing reports of rectal chlamydia among women coinciding with studies showing that anal sex among heterosexuals is more common [38]. Prevalence of rectal chlamydia has been reported to be as high as 24.4% among MSM and 17.5% among women [39]. Studies across 11 STI clinics demonstrated that 70% – 88% of rectal chlamydia and gonorrhoea infections have no concurrent urethral infection as rectal STIs among MSM [36]. The use of nucleic acid amplification testing (NAAT) has enhanced the ability to detect frequently asymptomatic gonococcal and chlamydia infections of the rectum and other sites [40]. The rates of chlamydia among MSM are relatively low in the pre-AIDS era, but the infection rates have now been continuously increasing among MSM over the past decade [30,41]. It is possible that further increases in rectal chlamydia infection will occur due to the widespread uptake of biomedical prevention, such as pre-exposure prophylaxis (PrEP) for HIV [42]. There are ongoing concerns about treatment failure with azithromycin for the treatment of rectal chlamydia [43,44], with a systematic review and meta-analysis finding that the efficacy of single-dose azithromycin treatment may be considerably lower than 1 week of doxycycline for treating rectal chlamydial infection (82.9% vs 99.6%) [45]. As rectal chlamydial infection is associated with an increased risk of HIV seroconversion, evaluation of effective treatment for rectal chlamydial infection is critical for HIV prevention which may provide guidance for clinical medication usage.

This thesis aimed to examine the STI epidemiology at a clinic setting in Adelaide in order to further our understanding of STI distribution and HIV testing in the community, to explore the potential risk factors associated with STI epidemic by comparing the differences at three sexual health services, one each in Adelaide, Melbourne and Sydney; to evaluate the effectiveness of STI treatments in order to inform prevention efforts, to provide policy implications and suggestions for governments and non-government organisations (NGOs) for the effectiveness of prevention interventions, especially among MSM population.

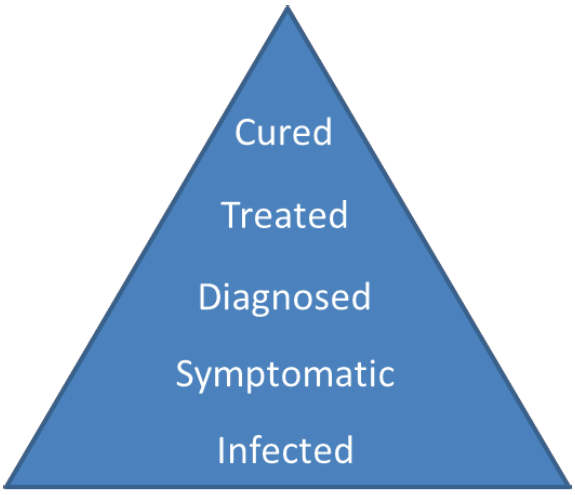

Figure 1.4 From infection to cure: system challenges to efficiently detect and treat all infected [46]

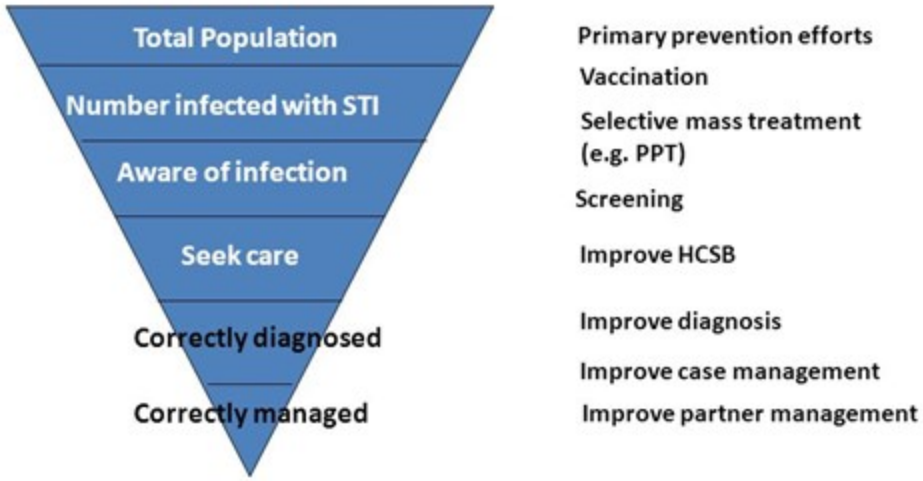

Figure 1.5 A public health perspective on STI prevention and care [47]

1.2 Aim, research questions and objectives

The increased prevalence and re-emergence of STIs over the last decade necessitate renewed interest and awareness of STIs. The mortality and morbidity of STIs and their facilitation of new HIV infections are of clinical significance, which is particularly important for clinicians providing care to higher risk populations such as MSM. Although diagnostic and treatment options are fortunately well established to offer higher sensitivity, specificity and cure and may have a clinical impact in slowing the progression of STIs, increases in STIs have been rising at an alarming rate [48].

The purpose of this research project was to understand how the STI trends, seasonal patterns and STI epidemic observed in South Australia compare to those seen in other Australian state

capitals: Melbourne (Victoria) and Sydney (New South Wales). Longitudinal data were used to determine whether there is a change in STI diagnoses, seasonal patterns, HIV testing and factors associated with them. Moreover, investigation was conducted to evaluate the efficacy of two treatments for rectal chlamydial infection at ASHC.

This thesis therefore attempts to provide new and important information in relation to STI epidemiology, seasonal variation patterns of STI, HIV testing and treatment efficacy for STI in Adelaide. The specific research questions were:

- What caused the substantial rise in diagnoses of gonorrhoea among heterosexuals between 2006 and 2010 in Adelaide? How did the epidemic of gonorrhoea and rates of diagnoses compare over time to other settings? (Chapter 3)
- Do the seasonal patterns of STI observed in South Australia in comparison to trends in other Australian state capitals reveal a seasonal variation in STI among MSM? (Chapter 4)
- What are the trends and predictors associated with HIV testing among MSM in Adelaide? (Chapter 5)
- Are the ongoing concerns about the failure of azithromycin treatment for rectal chlamydia infection applicable to Adelaide? (Chapter 6)

1.3 Thesis structure and outline

This thesis has been structured into three main parts. The first part includes the introduction and the literature review (Chapters 1 and 2). The second part consists of four chapters (Chapters 3 to 6) presented in the form of published papers from studies conducted using quantitative research methods. Each article addresses one of the four above research questions. The third part is the conclusion (Chapter 7) which highlighted the key findings, implications, recommendations and areas for future research. The schematic diagram of the thesis structure is shown in Figure 1.6.

I present this thesis for examination in the form of "**thesis by publication**". Four studies were conducted for this research project. All chapters presented in this thesis have been published in peer-reviewed journals. The first paper was published in *Sexually Transmitted Infections* (STI) Journal. The second and third papers were both published in *Sexual Health*. The fourth paper was published in *Internal Medicine Journal*.

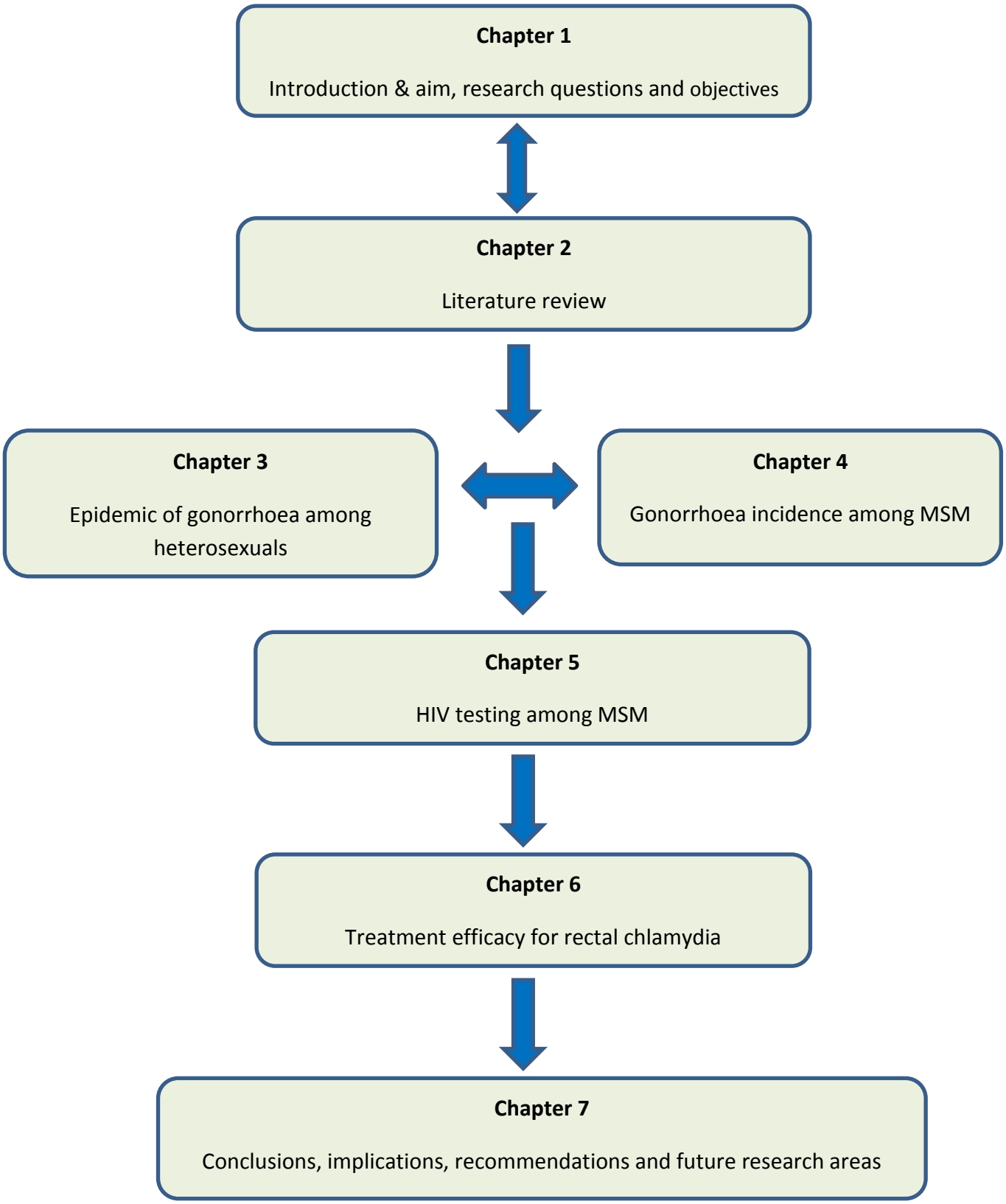

Figure 1.6 Schematic diagram of thesis structure

Below is a brief description of contents from each chapter:

Chapter 1 presents an overview of the research project by describing the research background and research questions. The aim, objectives and research questions of the research project are outlined.

Chapter 2 reviews the literature on the epidemiology of the human immunodeficiency virus (HIV) and Sexually Transmitted Infections (STIs) among men who have sex with men (MSM). The aim of this chapter is to provide a comprehensive review of the literature on major STIs and HIV infection among MSM and to identify effective prevention intervention strategies for MSM. The review examined the epidemiology of STIs and HIV infection among MSM, described the factors associated with sexual risk in this population and provided recommendations for effective prevention intervention and further research to better understand the sexual risks among MSM in Australia and other industrialised countries.

Chapter 3 investigates the substantial rise in gonorrhoea diagnoses among heterosexuals between 2006 and 2010 in Adelaide and to explore factors that could have influenced the epidemic. The Chapter addressed the research question "What caused the substantial rise in diagnoses of gonorrhoea among heterosexuals between 2006 and 2010 in Adelaide?" This study was a quantitative study with retrospective analyses of gonorrhoea diagnoses made by

sexual health services between 1990 and 2012 in Adelaide, with the comparison with that from Melbourne (Victoria) and Sydney (New South Wales).

Chapter 4 is an extension of the previous study to examine the gonorrhoea incidence among MSM. The aim of this study was to formally test the hypothesis of seasonal variations of STI against data at three sexual health services, one each in Adelaide, Melbourne and Sydney. The data suggest that gonorrhoea among MSM occurs in a seasonal pattern, particularly late summer into early autumn. This has implications for the provision of health services over the year and for the timing of health promotion activities. The chapter addressed the research question two "Is there a seasonal variation in STI among MSM?"

Chapter 5 presents the article to determine whether there has been a change in HIV testing among MSM at the Adelaide Sexual Health Centre (ASHC) over the past two decades. Computerised medical records of MSM who attended ASHC at their first visit between 1994 and 2015 were used to determine whether HIV testing had changed among MSM. First HIV tests in each calendar year and return tests within 12 months were analysed. Factors associated with recent HIV testing were also explored. The chapter addressed the research question three "What are the trends and factors associated with HIV testing among MSM in Adelaide?"

Chapter 6 compares treatment efficacy of two treatments for rectal chlamydial infection to provide evidence on ongoing concerns about treatment failure with azithromycin for the treatment of rectal chlamydia. A retrospective analysis of all patients diagnosed with rectal chlamydial infection between 2009 and 2015 in Adelaide, Australia was undertaken. The chapter addressed the research question four "Ongoing concerns about treatment failure with azithromycin for the treatment of rectal chlamydia, is this the case in Adelaide?"

Chapter 7 summarises the key finding of this thesis, presents conclusions and recommendations based on research results, and provides future directions for research to address actions for policy makers that need to be taken for HIV and STI prevention and intervention, especially among MSM in Australia.

CHAPTER 2 LITERATURE REVIEW

The human immunodeficiency virus (HIV) and Sexually Transmitted Infections (STIs) among men who have sex with men (MSM): a comprehensive epidemiologic review

2.1 Introduction

Globally, MSM are disproportionately burdened by HIV and other STIs. The reasons for the disproportionate infection burden are complex, including biological, behavioural, and sociocultural factors [49].

Surveillance data suggest that human immunodeficiency virus (HIV) and sexually transmitted infections (STIs) are increasing among domestic and international populations of MSM [50-53]. The epidemics of HIV in MSM continue to expand not only in many high income countries, including the USA, UK, France, Australia and the Netherlands where highly active antiretroviral therapy (HAART) is available, but also in low, middle income countries [51].

The rates of new infection have been consistently high among young MSM. The prevalence of HIV among MSM was reported ranging from 3% to 25%. Prevalence and incidence rates are particular higher in the countries of Sub-Sahara Africa, the Caribbean, North, Central and South America and Eastern Asia compared to those from Europe, the Middle East, North Africa, Oceania and Central Asia, where the prevalence rates have been reported to be less than 10% [54]. MSM are primarily at risk of HIV infection through unprotected anal intercourse (UAI). The estimated per-contact risk of acquiring HIV through receptive UAI with a known HIV-positive partner is 1-in-70 sexual contacts for a receptive partner (with ejaculation) and 1-in-909 for the insertive partner [55].

The acquired immune deficiency syndrome (AIDS) epidemic that started more than 30 years ago remains one of the greatest public health concerns worldwide. The re-emergence of HIV epidemic among MSM has posed a significant public health concern in different parts of the world including Western Europe, North America, Australia and China since the mid-1990s [50,56-59]. MSM have increased rates of HIV infection and STIs compared with general population [6,60]. MSM may be exposed to STIs in various ways. It is essential for clinicians to obtain a thorough sexual history in a culturally competent manner [7].

Many governments have identified MSM population as a high-risk group in their STIs and HIV strategy [3 3,61]. However, current prevention and treatment strategies are insufficient for the control of HIV epidemics [54]. In contrast to the overall slow decline in new HIV infections, the number of people living with HIV has significantly increased globally, largely due to the expansion of highly active antiretroviral therapy (HAART). There is still no efficient vaccine to protect against HIV infection despite decades of HIV research and programmes [62].

In Australia, since the beginning of national HIV surveillance, MSM have accounted for more than 70 % (19,855) of total positive HIV diagnoses over the period 1990-2016, and have been estimated to carry the greatest number of diagnosed and undiagnosed HIV infections [50]. According to the Third National Sexually Transmissible Infections Strategy 2014-2017, Department of Health and Ageing (Australia Government), MSM are also targeted as the

priority population at high risk for STIs, including gonorrhoea, chlamydia, syphilis, and the human papillomavirus (HPV) [63].

In order to better understand the epidemiology of HIV and STIs among MSM, as well as how these trends may inform public health policies, intervention programs, and community activities, this Chapter applies a comprehensive review and analyses of the scientific literature published in English on HIV and STIs (including gonorrhoea, chlamydia, infectious syphilis) in MSM based on multiple sources, including published findings, surveillance reports and prevention and interventions; to provide evidence on current epidemiologic trends relating to STIs/HIV among MSM; to explore the factors associated with the high rates of HIV and STIs among MSM; and to provide policy implications and recommendations for future endeavors targeting this high-risk group. These recommendations would impact all levels of government (nation and state wide), as well as Non-Government Organisations (NGOs). A better understanding of STIs and HIV epidemiology will allow implementation of more effective public intervention strategies to limit the transmission of STIs and HIV among MSM.

2.3 Methods

2.3.1 Data Sources

This comprehensive epidemiological review utilised a targeted literature search strategy at three levels.

First, global prevalence and incidence estimates for HIV and STI infections in 2008 and report on global sexually transmitted infection surveillance by World Health Organisation (WHO) in 2015, which could retrieved from the WHO website;

Second, incidence rate of HIV and STIs from surveillance reports in European Union (EU), the United States of America (USA) and Australia, which could be obtained from relevant government websites;

Third, a comprehensive literature search of online database PubMed (2000-2017) was conducted to identify peer-reviewed journal articles related to epidemiology and risk factors associated with HIV and STIs among MSM. We selected peer-reviewed articles directly related to HIV and/or STI among MSM. We used a combination of Medical Subject Headings (MeSH) and keywords in our search strategy including using terms such as “men who have sex with men,” ‘‘MSM,” “homosexual,” “the human immunodeficiency virus,” “HIV,” “gonorrhoea,”

“neisseria gonorrhoeae,” “gonococcal infection,” “chlamydia trachomatis,” “chlamydia,” “syphilis,” “epidemiology,” “incidence” and “prevalence” to identify the potential studies of interest in the search engine. Risk factors and preventions of HIV and STIs infections have been summarised. We also examined the reference lists of all identified studies to identify other studies. The search was limited to English language articles and published in peer-reviewed journals.

Questions raised will be covered in the thesis and addressed in the literature review including:

1) Comparison of STI rates between MSM and heterosexual men,
2) Trend and variations in STI incidence among MSM,
3) Trend and predictors of HIV testing among MSM,
4) Treatment efficacy of azithromycin and doxycycline treatment for rectal chlamydia

2.3.2 Definition of Men who have sex with men (MSM)

Over the past three decades, HIV and STIs among MSM have emerged as a research field for those with an interest in sexually transmitted infections. But what is the definition of MSM? MSM are male persons who engage in sexual activity with other males, regardless of how they personally identify themselves. The term 'MSM' is an all-encompassing term and has been used to recognise that not all homosexually active men have a gay or bisexual identity. The term excludes men who identify as gay or bisexual, but who have never had sex with another man. MSM attempts to indicate the population of men, including transgender men, engaged in same-sex sexual behaviour inclusive of sexual identity (gay, bisexual, straight, experimenting, etc.) and sexual desire (e.g. it includes men who experience no sexual desire for other men but who engage in sex with men for money or favours) [64]. The term was created in the 1990s by epidemiologists as a surveillance tool to better identify the route of HIV transmission and spread of the disease through male-male sexual activity. But, the term has been attributed to Glick *et al.*, because their usage in a 1994 study solidified the concept in medical terminology [65]. It has now become a standard term within HIV prevention work and research, encompasses both men who have sex with men only, and those who have sex with both men and women. The term represents an exposure category which refers to sexual behaviour and not a person's self-identified sexual identity". It is often used in medical literature and social research to focus on behavior rather than cultural or social self-identification thereby providing a clearer picture of HIV infection rates. That, in turns, provides us a better understanding of the implications of HIV prevention, including which prevention tools to use in which populations [66].

2.4 Epidemiology and disease burden of HIV among MSM

Since the first description of Pneumocystis pneumonia in homosexual men in Los Angeles in 1981 [67] and the discovery of the pathogen of HIV which was related to gay-related immune deficiency (GRID), currently known as AIDS identified in 1983 [68], MSM have been disproportionately affected by HIV as compared to the men from the general population [69-71]. A meta-analysis of surveillance data in low- and middle-income countries found that MSM are 19.3 times more likely to be HIV-infected than the general population [6]. Emerging and consistent data highlight that the risk for HIV infection remains high among MSM and HIV remains a critical health issue for this subpopulation although an overall decline in HIV prevalence has been noted in many geographic regions [6]. There has been a resurgence of HIV infection and increasing trend of HIV prevalence among MSM in different part of the world, particularly in industrialized countries [72]. There were approximately 36.7 million people living with HIV at the end of 2016 with 1.8 million people becoming newly infected in 2016 globally. It is estimated that MSM are 24 times more likely to become infected with HIV than the general population [28].

Reported HIV prevalence among MSM ranges from 0% to 32.9% and HIV incidence among MSM ranges from 1.2 to 14.4 per 100 person-years [71]. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that men who have sex with men (MSM) accounted for about 5–10% of the global burden of HIV, with considerable variation between countries and regions. MSM are a recognized high-risk group for HIV infection in Western Europe, North America, and

Australia, and HIV epidemics among MSM are well described in some low- and medium-income countries in Latin America and Asia [73]. Recent studies from sub-Saharan Africa reported that HIV prevalence among MSM ranges from 6% to 31%. In Asia, the odds of MSM being infected with HIV are 18.7 times higher than in the general population; and the HIV prevalence ranges from 0% to 40%. In Latin America, it is estimated that half of all HIV infections in the region have resulted from unprotected anal intercourse between men [71]. MSM account for a substantial proportion of HIV infections and compose a "bridging population" for transmission to heterosexuals due to high frequency of reported bisexuality [1].

New diagnoses among MSM are increasing in some regions, with a 17% rise in Western and Central Europe and a rise of 8% in North America between 2010 and 2014 [52]. In 2014, MSM accounted for 54% of new HIV infections in Western Europe, 68% in North America and 30% in Latin America and the Caribbean. In Jamaica, one in three men who have sex with men are living with HIV [74]. In 2016, an estimated 2.1 million people were living with HIV in Western and Central Europe and North America. In the same year, there were roughly 73,000 new HIV infections and 18,000 people died of AIDS-related illnesses [52]. According to the UNAIDS report, more than half of all new HIV infections occurred in the United States of America (USA), and more than a quarter occurred in six countries: France, Germany, Italy, Spain, Turkey and the United Kingdom [52].

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and partners launched the 90–90–90 targets; the aim was to diagnose 90% of all HIV-positive persons, provide antiretroviral therapy (ART) for 90% of those diagnosed, and achieve viral suppression for 90% of those treated by 2020 [75-77].

2.5 Epidemiology and disease burden of STIs among MSM

STIs are defined as infections that can be transmitted during unprotected sex with an infected partner, including vaginal, anal and oral sex. However, STIs can also be transmitted through skin to skin contact, blood and tissue transfer, bodily fluids, as well as mother to child contact. There are a number of bacteria, viruses, parasites, and other organisms known to cause STIs. According to WHO report, there are more than 30 different infectious pathogens known to cause STIs in humans [78].

STIs can be symptomatic or asymptomatic and may require complex clinical management. Common symptoms of STIs include discharge, dysuria, ulcers, and lumps and bumps. However, most of the STIs do not lead to symptomatic presentations, especially at extragenital sites (pharynx and rectum). Pharyngeal and rectal STIs are prone to be asymptomatic and particularly unrecognized and under detected. Without testing for the right microbes in relevant anatomical sites, infections will be missed. The seriousness and severity of STIs may vary; many cause only minor discomfort, while others can result in more complicated health

issues [79]. Most common symptoms and signs of STIs, besides genitourinary manifestations, include anorectal pain or discomfort, anal discharge, rectal bleeding and constipation. A recent study has shown that specific sexual practices of MSM result in having a high prevalence of asymptomatic infection in particular anatomic sites and that these infections are the primary drivers of transmission [80]. WHO has updated the STI syndromic management guidelines, which will include a management algorithm for anorectal infections in 2011 [71].

MSM are considered as a high-risk group for HIV infection and STIs in many countries. According to epidemiological data, MSM are more frequently diagnosed with STIs compared to general population and continue to experience disproportionately high prevalence of STIs including gonorrhoea, chlamydia, and infectious syphilis and HIV worldwide [6,81]. According to WHO report, incidence of STIs disproportionately affected racial and ethnic minority MSM, MSM of lower socioeconomic status, and young MSM. These STIs are being diagnosed in MSM with and without HIV infection in the context of changing patterns of sexual behaviour [78].

There is a high prevalence and incidence of almost all STIs in MSM, which is a significant cause of preventable morbidity worldwide and become a major public health concern among MSM. Elevated burden of STIs is of concern because it may indicate high risk for subsequent HIV infection. In Australia, more than 80% of newly acquired HIV and greater than 90% of syphilis and gonorrhoea diagnosed in major cities and regional areas are among MSM population [82]. There is a strong correlation between the spread of conventional bacterial and viral STIs and

the transmission of HIV and associated with severe disease [83]. Several studies have shown that both ulcerative and non-ulcerative STIs have been found to facilitate HIV transmission [24,84-86]. Treatment for some STIs, especially gonorrhoea, has been compromised by antimicrobial drug resistance [87-89]. Many new STIs are elevating among young MSM. However, a substantial burden of HIV and STI morbidity continued to occur among middle-aged and older men [90].

Since the publication of the WHO Guidelines for the Management of Sexually Transmitted Infections in 2004, the prevalence and incidence of STIs in MSM have continued to increase in the world. STI incidence among MSM may also be an indicator of higher risk for subsequent HIV infection [91]. Many countries have established the STI surveillance system to monitor STIs with a high burden, detect outbreaks and monitor progress towards national or international control targets. WHO/UNAIDS has published the second generation surveillance systems including HIV/STI and information on risk behaviours in order to warn of or explain changes in levels of infection in 2013 [92]. Surveillance of STIs is important to assess the disease burden in the population, to monitor and evaluate changes in trends over time.

The relatively high prevalence and incidence of STI infection among MSM may be related to multiple factors, including individual behaviours, sexual network characteristics and socioeconomic factors. Individual behaviours include number of lifetime or recent sex partners, rate of sex partner exchange, frequent penetrative and receptive sex, frequency of unprotected sex and use of disinhibiting substances, including alcohol, crystal methamphetamine, and other

recreational drugs use during sex (Chemsex), which will influence individual's probability of exposure to STIs. Sexual networks include high prevalence of STIs, interconnectedness and concurrency of sex partners and these will affect individual's risk of acquiring an STI. Socioeconomic factors include ignorance and myths exist around male-male sexual contact, loss of fear regarding HIV transmission in the era of widespread uptake of biomedical prevention, such as PrEP for HIV, the use of Internet or dating App as an efficient way to find sex partners and experiences of stigma and criminalization of homosexuality, which are associated with increased sexual risk behavior among MSM [93].

Sustained transmission of gonorrhoea and syphilis is a marker of high risk sexual activity and the relative burden of these infections is particularly high among MSM [94]. In order to reduce STIs in MSM, many countries have established STI testing guidelines [95-97]. The current Australian STI guideline recommends STI screening at least once a year, and up to 4 times a year for MSM who are at high risk for STIs. (e.g., MSM who have engaged in any unprotected anal sex, have had more than 10 sexual partners in previous six months, have participated in group sex or used recreational drugs during sex, or are HIV-positive) [95].

Increases in STIs among MSM may also be partly explained by increased detection screening policies for asymptomatic MSM at extragenital sites using highly sensitive nucleic acid amplication tests. Increasing resistance and decreased susceptibility to antimicrobials are emerging public health concerns, especially for gonorrhoea [98,99] . Most STIs are asymptomatic

and may not be diagnosed in the clinic settings. Thus, the case-based surveillance system may underestimate the prevalence of STIs in the population.

2.5.1 Neisseria gonorrhoea Infections

Gonorrhoea is a one of the very common bacterial sexually transmitted infections among MSM in Australia and other developed countries. It is caused by infection with the bacterium *Neisseria gonorrhoeae (NG).* This bacterium tends to infect warm, moist areas of the body, including urethra, throat, anus, vagina, eyes and female reproductive tract (the fallopian tubes, cervix, and uterus) [100]. Gonorrhoea passes from person to person through unprotected oral, anal, or vaginal sex. People with numerous sexual partners or those who do not use a condom are at greatest risk of infection. Risk behaviours making a person more likely to engage in unprotected sex also increase the likelihood of infection, including alcohol use, illegal drug use, particularly intravenous drug use and drug use for or during sex (Chemsex) [101,102].

Gonococcal infection can occur at genital as well as extragenital sites (Pharynx and rectum). The primary sites for gonorrhoea among MSM include the pharynx, urethra and ano-rectum [103-105]. Rectal GC is an independent risk factor for HIV acquisition among MSM after adjustment for sexual behaviors and other concurrent infections [24,91]. Gonorrhoea can occur at all three sites or at a single site, with the pharynx being the most common. The prevalence of pharyngeal gonorrhoea in MSM ranges from 3% to 15% worldwide. Symptoms of gonorrhoea usually occur within two to 14 days after exposure. However, some people may never develop any symptom.

Extragenital infections are often asymptomatic among MSM. Infections can result in dysuria, discharge, epididymitis, anal itching, soreness, bleeding and painful bower movements. Gonorrhoea is normally asymptomatic in approximately 10% of males. The rate of gonorrhoea is much higher in men who have sex with men than in heterosexuals [106]. Rises in gonorrhoea among MSM raised the concerns because rising rates will increase the probability of antimicrobial drug resistance and possible associated rises in HIV acquisition [107-110].

2.5.2 Chlamydia trachomatis

Chlamydia trachomatis (CT) is a common bacterial sexually transmitted infection for both men and women. It is one of the most common sexually transmissible infections (STIs) among MSM worldwide. It can be transmitted by vaginal, anal or oral sex. Most men and women with CT infection have no symptoms [100]. If it is untreated, serious sequelae may arise, including ectopic pregnancy and infertility in women and epididymitis and proctitis in men. High-risk groups for *Chlamydia* infection are characterized by a large number of partners and an infrequent use of preventive measures, such as condom use. Among MSM, the transmission of infection is often via anal intercourse.

GC and CT are the most commonly reported notifiable infections among MSM. The Centers for Disease Control and Prevention recommends that men who have sex with men (MSM) be screened for urogenital GC/CT, rectal GC/CT, and pharyngeal GC. GC and CT, and the behaviors

associated with acquiring them, may increase the likelihood of acquiring and transmitting human immunodeficiency virus (HIV) infection.

Notifications of Chlamydia infection in MSM have been rising in Australia and globally [10,50]. Studies conducted in the last decade have convincingly demonstrated that the usual standard testing of urogenital sites for gonorrhoea and chlamydia misses most infections in MSM, which occur at extragenital sites in the pharynx and rectum, and are mostly asymptomatic [111-113]. While pharyngeal infections are self-limiting and usually clear within two to three weeks even without treatment [114], rectal infections can persist over longer periods, often without severe symptoms [115]. The majority of pharyngeal and rectal GC and CT infections are asymptomatic [24]; these infections are unlikely to be detected without routine screening. It is estimated that chlamydia infected over 100 million people each year worldwide by sexual transmission. The majority of persons with anogenital CT infection are not aware of their infection because it is frequently asymptomatic. Urogenital chlamydial infection can lead to serious adverse outcomes in women, e.g. pelvic inflammatory disease (PID) that can result in tubal factor infertility, ectopic pregnancy and chronic pelvic pain. Urogenital chlamydial infections do not result in any sustained immunity [116].

2.5.3 Infectious Syphilis

Syphilis is a chronic bacterial infection caused by *Treponema pallidum*. Transmission of the bacterium occurs during vaginal, anal, or oral sex. There are four stages of syphilis: primary (10-90 days), secondary, latent (within or after 1 year of infection), and tertiary (3 or more years after infection). Primary and secondary syphilis are the most infectious stages [100]. Syphilis is of both individual and public health importance. In addition to its direct morbidity, increases risk of HIV infection and can cause lifelong morbidity in children born to infected mothers [117].

Incidence of many acute STIs including Syphilis infection fell substantially among MSM after the mid-1980s due to sexual behavioural modification in response to the emerging HIV epidemic. However, despite the promising decline of syphilis infections in the late 1990s in many developed countries, the Syphilis re-emerged in 2000 and continued to rise recently [118]. The reemergence in cases of infectious syphilis coincided with an increase with other STIs following the introduction of antiretroviral therapy in 1996 which has improved survival and sexual wellbeing of people with HIV [119]. From 2000 to 2013, the proportion of syphilis diagnoses reported among MSM versus non-MSM in high-income countries increased from 26.8% to 55%, with all 18 countries reporting an increase of syphilis prevalence among MSM [120]. An increase has been reported in the numbers and rates (per 100,000) of syphilis infections among MSM in the USA and Western Europe since 1998, particularly those with coexistent HIV infection [117,121] .The reemergence of syphilis occurred almost exclusively among MSM and were attributed to increases in risky sexual behaviors such as unprotected anal sex with casual partners, HIV

'serosorting' and oral sex ,exchange sex, illicit drug use before sex, multiple sexual partners, and high-risk anonymous sexual contacts [122].

MSM and men with HIV infection account for a disproportionate burden of syphilis infections [123,124]. WHO estimates 12 million new syphilis cases worldwide each year and MSM are estimated to constitute over 60% of the cases [48]. Moreover, syphilis has been reported to be strongly associated with prevalence of HIV infection among MSM thereby playing an important role in the increase of HIV infection in the MSM subpopulation. Syphilis cases are occurring in both HIV-negative and HIV-positive MSM, with repeat infections often overrepresented in the latter group. In some industrialized countries, the HIV infection increase has been coincided with the outbreak of syphilis among the MSM population. Oral sex between men seems to be important in the transmission of syphilis outbreaks as unprotected oral sex is considered a safe practice among MSM [125]. Syphilis transmission attributed to oral sex has been reported between 20% and 46% [126]. Syphilis causes inflammatory genital ulcers and lesions in the skin which raised concern that syphilis appears to promote the acquisition and transmission of HIV [127]. Syphilis also complicates the clinical course of HIV by increasing viral load [128]. It has also been associated with a higher rate of treatment failure in HIV-infected persons [129]. The interaction between HIV infection and syphilis is complex and remains the great interest of ongoing research for the epidemiological and clinical implications that apply to both heterosexuals and MSM [126].

Syphilis remains a global problem despite the existence of simple and validated screening tests because syphilis infection is frequently asymptomatic. Annual serological screening for syphilis is recommended for the MSM subpopulation and frequent syphilis screening for MSM with higher risk in many countries [130,131]. This includes serological testing for syphilis every time when HIV testing is undertaken and each time HIV viral load testing is performed in HIV-positive MSM [132,133]. Moreover, only one drug, penicillin, is recommended for syphilis treatment and response to therapy is assessed based on changes over months in serological test titres. Treatment for patients who cannot receive penicillin and management of patients who do not serologically respond to treatment are common clinical problems [117].

2.6 Epidemiology of HIV infection among MSM in Australia

The first AIDS diagnosis in Australia was in October 1982, with the first AIDS death in Melbourne on the 8th July 1983 [134]. HIV testing was introduced in Australia in 1985 and the first antiretroviral drugs for HIV infection became available in Australia in 1987, which were initially used as monotherapy and then as dual therapy from 1992 [135]. Cases of newly diagnosed HIV peaked at 2,773 in 1987 and then declined to the lowest level in 1999 [136]. The decline in HIV incidence has been largely attributed to the rapid adoption of HIV prevention practices, including safe sex education, and world leading needle and syringe programs [135,137]. AIDS cases in Australia have plummeted from its peak in the early 1990s since the advent of anti-retroviral medication in the mid-1990s, which stops HIV from progressing to AIDS. Of the 16,765 newly

diagnosed cases of HIV infection between 1984 and 1992, the majority were reported in NSW (67%). New HIV diagnoses declined rapidly from 14% in 1985-1986 to 1% in 1991-1992 [138].

Trends in HIV diagnoses differ across Australia and are primarily driven by men who have sex with men (MSM) [139]. The rate of HIV transmission through male-to-male sex reached a peak in 1983-1984 and declined rapidly in subsequent years. After the Millennium, HIV diagnoses have remained stable in Australia over the past decade, and the epidemic remains concentrated among gay and bisexual men. Male‑to‑male sex continues to be the major HIV risk exposure in Australia with low levels of heterosexual transmission and transmission among people who inject drugs. The pattern of HIV diagnoses attributed to male-to-male sex was 86% in earlier years. However, females are increasingly being affected by the HIV epidemic in recent years [135,138]. In 2016, 1,013 people were newly diagnosed with HIV [140] and male-to-male sexual contact accounted for 712 (70%) new HIV diagnoses, while (209) 21% of the cases were attributable to heterosexual sex and both male‑to‑male sex and injecting drug use for 51 (5%) diagnoses, and injecting drug use only for 14 (1%) diagnoses [50].

By the end of 2016, an estimated 26,444 people were living with HIV in Australia, with an estimated 19,855 (75%) infections were attributable to male-to-male sex exposure. The rate of HIV diagnosis is 2.2 times higher among the Aboriginal and Torres Strait Islander people than Australian born non-indigenous people (6.4 vs 2.9 per 100,000). Between 2012-2016, there has

been a 33% increase in HIV diagnosis among Aboriginal and Torres Strait Islander people compared to a 22% decline among Australian born non-Indigenous people [140].

HIV incidence over the five years 2012-2016 varied between 0.58% and 0.85 per 100 person-years (0.85 per 100 person-year in 2016) among gay and bisexual men attending sexual health clinics in the ACCESS network. The self-reported HIV prevalence among gay and bisexual men participating in the Gay Community Periodic Survey was 7.3% and 1.4% in people who inject drugs [141]. Another clinic based study showed the incidence of HIV was above 2.0% in subgroups of MSM with specific characteristics at the last HIV negative test [108]. The number and rate of notifications of HIV infection in Australia in the past 10 years has been relatively stable at about 1000 per annum and 4.2–4.9 per 100,000 population [50]. This is relatively low compared with other industrialised countries [142].

2.7 Epidemiology of STIs among MSM in Australia

2.7.1 Gonorrhoea

In Australia, gonorrhoea is predominantly diagnosed in MSM, among young heterosexual Aboriginal and Torres Strait Islander people living in remote and very remote areas and travelers returning from high prevalence areas overseas. A national epidemiological study on gonorrhoea demonstrated that a dual epidemic in Australia among Aboriginal people in remote

areas, and non-Aboriginal men in metropolitan areas contributed substantially to the overall rise in gonorrhoea notifications [18].

According to the Australian Bureau of Statistics (ABS), over half a million people or 3% of the adult population identified as gay, lesbian or 'other' in 2014 [143]. A study has shown that rates of unprotected anal intercourse with casual male partners have increased among MSM in Australia since 2004 [144]. Studies have shown that greater sexual risk and potential increase in STIs will occur due to widespread uptake of biomedical prevention, such as PrEP for HIV [145,146].

In 2016, there were 23,887 gonorrhoea notifications in Australia, an increase of 185% compared to the 8,388 notifications in 2006. Around 75% of notifications were in males (17,325 notifications). Gonorrhoea notification rates in males were higher in all age groups in 2016 than in females except in the 15-19 age group. The rate of notified gonorrhoea in males has nearly tripled over the past decades from 53.1 per 100,000 in 2005 to 145.5 per 100,000 in 2016 with the majority of cases in MSM [50]. However, the surveillance data do not provide a valid measure of either the prevalence or change in STI in the general population [21].

Incidence is the best indicator of changes in transmission in a population. Gonorrhoea incidence from The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of STIs and BBVs (ACCESS) project showed that gonorrhoea incidence was 33.7 per 100 person‑years in HIV

-positive gay and bisexual men, 46% higher than that in HIV-negative gay and bisexual men (23.1 per 100 person-years). In the past five years (2012–2016) gonorrhoea incidence has increased in both HIV-positive (29% increase) and HIV-negative (30% increase) gay and bisexual men, but remained steady between 2015 and 2016. However, these incidence estimates represent populations attending sexual health clinics and may not be generalised to the broader priority populations [50].

In MSM, gonorrhoea is commonly infected at three sites: pharynx, rectum, and urethra. MSM population-based studies have shown that gonorrhoea positivity is increasing among MSM in Australia in recent years, particularly among those MSM who had more than 10 sexual partners in the last 12 months [147,148]. A study conducted in Melbourne among a total of 12, 873 MSM reported that the proportion of pharyngeal, urethral and rectal gonorrhoea positivity was 1.7%, 2.3% and 2.9% respectively among MSM population. 0.9% of MSM were infected at multiple sites for gonorrhoea and among the positive cases, 19.1% of MSM were infected at 2 or more sites of gonorrhoea [149]. It is also noted that a decrease in consistent condom use between MSM and their casual partners and an increase in STI testing have been observed during the same time [149]. Another MSM population based analysis showed similar increase in gonorrhoea positivity has been reported in Sydney [148,150]. A recent study has reported that among MSM with urethral gonorrhoea, the proportions with concurrent pharyngeal or rectal gonorrhoea were 32% (134/210) and 64% (74/235) respectively [151].

2.7.2 Chlamydia

Chlamydia is the most frequently diagnosed and notified STI followed by gonorrhoea, HIV and syphilis in Australia. According to the national surveillance for STIs in 2017, there were 96, 721 notifications. However, the unavailable sex preference information making the estimation of chlamydia prevalence in MSM impossible because national surveillance is based on reports by clinicians or laboratories of newly diagnosed cases of STI and BBV infection to local State and Territory Health Departments [152]. The annual surveillance report form The Kirby Institute showed that the notification rate of chlamydia was increased steadily between 2007 and 2011, remained relatively stable between 2011 and 2015, and increased by 8% from 378.3 per 100 000 in 2015 to 409.0 per 100 000 in 2016 [50]. It is important to examine trends in chlamydia notifications in the context of patterns of testing, as changes in notification rates can be an indication of changes in testing, changes in disease incidence, or both [50].

In 2016, Chlamydia incidence data from The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of STIs and BBVs (ACCESS) showed that chlamydia incidence in HIV-positive gay and bisexual men was 37.9 per 100 person-years, which was 1.9 times as high as in HIV-negative gay and bisexual men (19.5 per 100 person-years) in 2016. There was a 20% increase in chlamydia incidence in HIV-positive gay and bisexual men (from 31.6 to 37.9 per 100 person-years) and 13% increase in HIV-negative gay and bisexual men (from 17.3 to 19.5 per 100 person-years) from 2012 to 2016 [50].

There are few published data on the rate of chlamydia infection in MSM in Australia. One Victorian study on 12,873 MSM showed that the proportion of MSM who were infected with anal chlamydia was 5.6%, with an average increase of 6% (95% CI, 3%–10%) each year between 2007 to 2013; however, no significant change was observed in urethral chlamydia positivity (adjusted odds ratio, 1.02; 95% CI, 0.98–1.06). Increases in chlamydia positivity were primarily restricted to MSM who reported more than 10 partners in 12 months [149]. Another study at MSHC found that 3.70% (95% CI: 3.30-4.14) were urethral chlamydia positive and 5.36% (95% CI: 4.82-5.96) were anal chlamydia positive in MSM between 2002 to 2009 [21].

2.7.3 Infectious syphilis

In Australia, there were 4,400 notifications of early syphilis cases in 2017 and majority of early syphilis cases are currently found among men (85%). The notification rate of early syphilis cases among men has increased in the past ten years, from 4.9 per 100,000 population in 2004 to 30.6 per 100,000 population in 2017 with the highest notification rates among men aged 25–29 years [152]. Over 90% of syphilis and gonorrhoea diagnosed in major cities and regional areas are diagnosed in MSM [50]. Nearly half of the cases were in HIV positive MSM, and among these MSM, a significant proportion are re-infections [153].

There are very few studies to investigate the rate of infectious syphilis in MSM in Australia. One study showed that the proportion of MSM serologically tested for syphilis annually increased in

HIV-negative (48% to 91%; P_{trend} < 0.0001) and HIV-positive MSM (42% to 77%; P_{trend} < 0.0001) among MSM attending a national sentinel network of 46 clinics in Australia between 2007 and 2014. Among HIV-negative MSM, the proportion of infections that were early latent increased from 27% to 44% (P_{trend} <0.0001), while the proportion that were secondary decreased from 24% to 19% (P_{trend} =0 .030). Among HIV-positive MSM, early latent infections increased from 23% to 45% (P_{trend} <0.0001), while secondary infections decreased from 45% to 26% (P_{trend} = 0.0003). Among HIV-positive MSM, decreasing secondary syphilis correlated with increasing testing coverage (r = −0.87; P =0.005) or frequency (r= −0.93; P = 0.001) [131].

2.8 Epidemiology of HIV infection among MSM in the United States of America (USA)

The epidemiology of HIV infection in the United States has changed significantly over the past 30 years since the first AIDS cases were reported there in June 1981. This earlier epidemic began predominantly in young, white, middle-class MSM living in the largest west and east coast cities [3,154-156]. Today, HIV/acquired immune deficiency syndrome (HIV/AIDS) has a broad geographic distribution involving multiple transmission risk behaviours in USA. It has become a disease affecting far greater demographic diversity, all ages, genders, races and economic status [154].

In 2016, the number of new HIV diagnoses in the United States was 39,782 with 32,131 diagnoses among adult and adolescent males (13 years or older), 7,529 among adult and

adolescent females, and 122 among children younger than 13 years. The estimated HIV number of new HIV infections (HIV incidence) in the United States was 37,600 in 2014 and the estimated annual HIV infections in the United States declined 10% from 2010 to 2014. There were more than 1.1 million persons aged 13 and older were living with HIV infection (HIV prevalence) at the end of 2015, including an estimated 162,500 (15%) persons whose infections had not been diagnosed [157].

HIV transmission patterns have shifted over time in the USA. In 2016, most diagnosed cases of HIV occurred through male-to-male sexual contact (67%, 26570) of all HIV diagnoses and 83% of diagnoses among males. An additional 3% of diagnoses occurred among gay and bisexual men with a history of injection drug use. Diagnoses attributable to injection drug use alone have declined significantly over time and accounted for 6% of new diagnoses in 2016. Transmission through heterosexual sex now accounts for more cases than at the beginning of the epidemic – 24% of new diagnoses in 2016 – but diagnoses attributable to heterosexual sex have declined 16% between 2011 and 2015 [157,158].

2.9 Epidemiology of STIs among MSM in the United States of America (USA)

2.9.1 Gonorrhoea

MSM comprise at least 4% of males in the USA [159]. A review of available national and sentinel surveillance data in USA suggested that MSM bear a disproportionate burden of gonorrhoea

and an increasing number of MSM have been diagnosed with gonorrhoea in recent years. National surveillance data which captures only a fraction of America's STI burden showed that 468,514 cases (18.5% increase) of gonorrhoea reported in 2016 with the prevalence rate of 146 per 100,000 people [160].

A narrative review showed that between 2009 and 2015, 16.6% of MSM tested positive for gonorrhoea at any sites; rectal gonorrhoea positivity rate was 11.7%, oropharyngeal 7.3%, and urogenital was 9.9%. Positivity increased 12.6% for oropharyngeal and 72.4% for rectal gonorrhoea [161]. In 2015, there were 26,878 MSM tested for gonorrhoea across the participating STD clinics. The median site-specific gonorrhoea prevalence among those tested was 19.0% (range by site: 10.9%–22.7%). The estimated incidence of gonorrhoea among MSM in STD Surveillance Network (SSuN) sites increased 151% from 1,368.6 cases per 100,000 MSM in 2010 to 3,434.7 cases per 100,000 MSM in 2015. The rates among women and men who have sex with women (MSW) increased a significantly smaller proportion (39.8% and 31.7%, respectively) over the same period [162]. In a Seattle clinic, the proportion of MSM with pharyngeal gonorrhoea was 6.5%, rectal gonorrhoea 9.7%, and urethral gonorrhoea 5.5% (7). Almost all urethral infections were symptomatic (96%), but most pharyngeal and rectal infections were asymptomatic. Most pharyngeal or rectal infections (58%) were not associated with urethral infection [163].

2.9.2 Chlamydia

Chlamydia is the most common STI in the USA, accounting for nearly three million new infections each year, according to the estimates from the Centers for Disease Control and Prevention (CDC) based on the National Health and Nutrition Examination Survey (NHANES) [164]. National surveillance data which captured only a fraction of America's STI burden showed that 1.59 million cases (4.7% increase) of chlamydia reported in 2016 with the prevalence rate of 497 per 100,000 people [160].

During July 2011–June 2012, there were 21,994 MSM tested for chlamydia, 81.4% for urogenital chlamydia, 31.7% were tested for pharyngeal CT, and 45.9% for rectal CT. Of these MSM tested, 8.4% for urogenital CT, 2.9% for pharyngeal CT, and 14.1% for rectal CT. More than 85% of extragenital CT infections were associated with negative urethral tests at the same visit and would not have been detected with urethral screening alone. In 2015, the STD Surveillance Network collects patient data from 42 STD clinics has showed that 26,694 MSM were tested for chlamydia. The median site-specific chlamydia prevalence among those tested was 16.0% (range by site: 11.8%–17.6%).

2.9.3 Infectious syphilis

In the USA, the prevalence rates of primary and secondary syphilis are highest among MSM, particularly among young and Black MSM [165]. Primary and secondary (P&S) syphilis among men

who have sex with men (MSM) has been increasing since at least 2000. The number of reported primary and secondary syphilis cases among MSM continued to rise in 2016 and the majority of primary and secondary syphilis cases remained among MSM. National surveillance data which captures only a fraction of America's STI burden showed that 27814 cases (17.6% increase) of primary and secondary syphilis reported in 2016 with the prevalence rate of 9 per 100,000 people [160]. Gay, bisexual and other men who have sex with men (MSM) accounted for 81 percent (16,155) of male cases where the sex of the sex partner is known in 2016 [160]. In the United States, approximately half of MSM with primary and secondary syphilis were also living with HIV. In addition, MSM who are HIV-negative and diagnosed with primary and secondary syphilis are more likely to be infected with HIV in the future.

Overall, the data from the studies conducted in the USA documented an increase in syphilis cases from their lowest prevalence in 1998. Syphilis cases among MSM were at their lowest between 1998 and 2000, and then increased from 2000 and beyond. Several studies have reported a consistent increase in the number of syphilis cases among MSM [166-171]. Syphilis case data from 27 States reported an increase among MSM from 3.4/100,000 males in 2005 to 4.0/100,000 males in 2008 [170]. Using national syphilis case data that was reported to the CDC from all States and the District of Columbia, Peterman examined syphilis trends and reported a consistent increase in syphilis cases among MSM from approximately 6,000 cases in 2006 to 14,000 cases in 2013 [171]. Studies have showed that syphilis increases among HIV-positive MSM [172,173]. Data from these studies suggested that the increases in syphilis trends may be more

pronounced among HIV-positive MSM and that increased syphilis transmission may be accompanied by increased HIV transmission among MSM and vice versa [172,173]. Meanwhile, research findings suggested evidence for widening racial and age disparities in syphilis trends among MSM in the USA with racial minority (Black, Hispanic, and API) MSM and young MSM, especially MSM between 20 and 29 years, may account for the greatest increases in syphilis trends among all MSM bearing a disproportionate burden in the USA [169,170,174,175].

2.10 Epidemiology of HIV infection among MSM in Europe

HIV infection has had a large impact in European countries over the last 35 years of the transmission among gay and bisexual men at different time periods and in different geographical regions. In Northern and Western European countries (Scandinavian countries, UK, France, the Netherlands, Belgium, Western Germany, Switzerland, Austria), HIV infection started to spread in metropolitan gay communities in the late 1970s and early 1980s, followed importations from North America [176]. Peak incidences were reached around 1985/1986, when the first diagnostic tests became widely available [177]. Spontaneous and promoted behaviour changes, such as reductions in numbers of anal intercourse partners and increasing condom use, contributed to declining incidence of new HIV and STI infections in the late 1980s and early 1990s. However, incidence increased again in the late 1990s and early 2000s.

In Southern Europe (Spain, Portugal, Italy), HIV initially spread mainly among Injection Drug Users (IDUs). However, transmission among gay and bisexual men increased gradually from the late 1990s onwards. In Eastern Europe, explosive HIV epidemics developed among IDUs in the mid-1990s, followed by increasing incidence of sexual transmission [178,179]. In Central and Eastern Europe HIV started to spread among MSM from the early 1990s, with incidence initially increasing slowly but then accelerating from the early 2000s.

HIV epidemics are attributed to two main modes of transmission: Injecting drug use and male-to-male sex in the EU/EEA (the European Economic Area). The highest proportion of HIV diagnoses (40%) was reported to be in MSM in 2016, which is lower than that in Australia and USA. In general, HIV prevalence tends to be higher in Western compared to Eastern European countries. In the western and central European countries, MSM account for about half of all HIV-infections with known transmission routes. In the eastern European countries, only 1% of all HIV infections are reported as being in MSM [53]. This may better reflect gender norms and unavailable or unreliable information on mode of transmission, due to high stigmatization of homosexual behaviour [53,180]. In most eastern European countries and some central European countries, MSM remain one of the most hidden parts of society. In Eastern Europe heterosexual contact and IDU remain the main modes of HIV transmission. MSM remain one of the most hidden parts of society and the epidemic among MSM remains hidden and often invisible in Eastern Europe. Little is known about their risk behaviour, including injecting drugs, international sex tourism and involvement in commercial sex [181].

In Europe, EuroHIV (European Centre for the Epidemiological Monitoring of AIDS) coordinated the surveillance of AIDS and later also HIV infection between 1984 and 2007. Since 2008, the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Regional Office for Europe have jointly coordinated HIV/AIDS surveillance in Europe and published an annual analysis of the data [181]. In 2016, a total of 29,444 new HIV diagnoses were reported by the 31 countries of the EU/EEA, with a rate of 5.9 per 100,000 population. The rate was higher among men than women (8.9 versus 2.6 cases per 100,000 population). Despite three decades of preventive efforts since the early years of the epidemic and decreases in the rate of the HIV infection in the last decade, MSM still remain the sub-population most affected by the HIV epidemic, with 40% of new HIV diagnoses in 2016 being among this group [53]. Studies have reported HIV prevalence estimates among MSM ranging from lows of 0% to 3% in some Eastern European countries (e.g. Bosnia & Herzegovina, Belarus) to between 10% and 20% in some Western European countries (e.g. France, Germany, the UK, Spain, the Netherlands). Data from 23 European countries showed an 86% increase in newly diagnosed case of HIV infection among MSM between 2000-2006 [182]. However, data suggest that in Western Europe, trends in new HIV diagnosis among MSM were stable between 2006 and 2016. In contrast, HIV diagnosis trends among MSM in Central and Eastern Europe increased over this period [181].

2.11 Epidemiology of STIs among MSM in Europe

2.11.1 Gonorrhoea

The European Surveillance of Sexually Transmitted Infections (ESSTI) network was first established in 2001 and is a collaboration of STI epidemiologists and microbiologists from 24 European countries. The key objective of ESSTI is to collate and analyse surveillance data on acute STI in order to inform public health policy and control of STI. Previously, surveillance data on STI had been collected at the European level for some time by both WHO and ECDC, until recently data on diagnoses in MSM had not been routinely collected.

Since 2008, the overall rate of reported gonorrhoea has been more than doubled across Europe. In 2014, 66,413 cases of gonorrhoea were reported by 27 EU/EEA member states with the overall notification rate 20 cases per 100,000 population, which was a 25% increase compared to that in 2013 and MSM accounted for over 40% of reported gonorrhoea cases. The highest rates were reported in the United Kingdom (60 per 100,000), Ireland (28 per 100,000) and Denmark (20 per 100,000). Majority of gonorrhoea cases were diagnosed among young MSM aged 15-34 years old [183]. Population based study in UK showed that 65% of all cases of gonorrhoea diagnosed in London in sexual health clinics in 2013 were MSM and these proportion have been steadily increasing [184].

2.11.2 Chlamydia

Incidence of chlamydia among MSM was in very low levels in EU in the mid-1990s. However, it has increased among MSM in Western Europe since late 1990s and early 2000 [185]. This may have been partly due to improved sensitivity of diagnostic tests and the expanded use of combination diagnostic tests, in addition to behavioural changes such as increases in partner numbers and declines in condom use [181,186].

Information on transmission risk group for chlamydia notifications in the EU/EEA is poor due to the availability of data which was just 40% of reported cases in 2014 [183]. In 2014, the majority of cases (87%) occurred in heterosexuals, with only 7% of notifications being among MSM [181]. In 2014, 83% of all chlamydia cases (all transmission risk categories) were reported in four countries (Denmark, Norway, Sweden and the UK) and the UK continues to contribute a large proportion of reported cases (60% in 2014). Notification rates among MSM were much lower than for all transmission risk groups combined. Countries with low but increasing notification rates among MSM between 2010 and 2014 included Latvia and Slovenia [116].

The UK had the highest notification rate among MSM, increasing from 14.2 per 100,000 men in 2009 to 36.2 per 100,000 men in 2014 [116]. Surveillance data from sexual health clinics in England indicated recent increases diagnoses of chlamydia among MSM increased over 6 times (from 2,183 in 2005 to 12,900 in 2016). Between 2015 and 2016, chlamydia diagnoses

remained relatively stable among MSM (1% increase from 12,828 in 2015 to 12,900 in 2016), consistent with the increasing trend since 2005 [187].

MSM population-based studies have shown similar pharyngeal prevalence of chlamydia with 1.5%, 1.5% and 1.2% in Germany, the Netherlands and the UK, respectively [188-190]. Rectal prevalence of chlamydia was higher at 8.0%, 8.2% and 6.5%, respectively. The Netherland and UK studies additionally reported urethral prevalence of chlamydia to be 4.0% and 4.3 respectively [189,190].

2.11.3 Infectious Syphilis

Similar to syphilis trends among MSM in the US, the epidemiological trend suggested an increase in syphilis prevalence over time among MSM in Europe, especially Western Europe. Data on the prevalence of syphilis in MSM were very limited in Eastern Europe. However, Syphilis incidence has been declining following the major epidemic in the 1990s in Eastern Europe. A recent Russian study showed that syphilis incidence declined nationally from 79.4 per 100,000 in 2004 to 28.9 per 100,000 in 2013, but remains high in some regions, particularly the Far Eastern, Siberian and Northwestern Federal districts [191]. The declines in Russia are occurring against a backdrop of increasing syphilis incidence in the EU/EEA, mainly driven by MSM, although even the highest incidence countries have considerably lower rates than Russia (e.g. 7.2 and 7.7 per 100,000 in the UK and Spain, respectively) [183]. In Western Europe, MSM also

account for the majority of primary and secondary syphilis cases and remain the group most at risk for contracting syphilis. In England, all cases of syphilis (84%) diagnosed in London residents in sexual health clinics in 2013 were from MSM. Studies from Western Europe showed that syphilis cases among MSM were lowest between 1998 and 2000 and have increased since then [121]. National surveillance data showed a consistent increase in syphilis cases among MSM, increasing by 14% from 4,185 in 2015 to 4,788 in 2016 in England [187], increasing from approximately 400 cases in 2001 to 1500 cases in 2007 in Germany and from 47 cases in 2008 to 114 cases in 2010 in Greece [192]. Studies in England, Wales, France, Sweden, Scotland and Netherland showed an overall increase among MSM despite intermittent periods of decline [121,193,194].

Very few studies conducted in Europe presented differences in syphilis trends by race and age. One study noted that demographic profile of the increasing trends in syphilis in England and Wales was comprised predominantly of White MSM [194]. Another national surveillance data from the Netherlands, did not demonstrate any age differences in syphilis trends among MSM, rather showing a decline in syphilis cases among both younger MSM (15–24 years) and older MSM (25 years and above) [195].

2.12 Factors associated with HIV and STIs among MSM

Causes of HIV and STIs among MSM are complex and multifactorial. Increases in incidence and prevalence of HIV and STIs reflect changes in biological, demographic, behavioral and social factors, which are important in understanding high HIV/STI transmission rates among MSM. Individual level risk factors for HIV and STIs have been well documented globally in MSM such as high numbers of sexual partners and anal intercourse, particularly unprotected anal intercourse [6,196]. HIV prevalence among MSM is so high in many countries means that members of this group have an increased chance of being exposed to the virus, due to mainly having sex within this group. In summary, factors that put men who have sex with men at heightened risk of HIV and STIs include:

1. Biological factors. High vulnerability to HIV infection among MSM is that unprotected anal sex carries a higher risk of transmission than vaginal sex because the walls of the anus are thin and more easily torn, creating an entry point for HIV into the bloodstream [197]. Having a STI may also facilitate HIV infection among MSM [83].
2. Behaviour factors. Having multiple sexual partners and unprotected anal intercourse are more common among this community, and many men who have sex with men do not use condoms consistently [198]. Access to HIV testing services is low among this group. Alcohol and drugs are a common part of socialising in some communities of MSM.
3. Substances & Chemsex. One of the major factors facilitating the increased risk-taking behavior by MSM is the use of disinhibiting substances, including alcohol, crystal methamphetamine, and other recreational drugs [7].

4. Legal factors. As of May 2016, 73 countries still criminalise same-sex conduct, affecting the rights of MSM. In 13 countries including Iran, Sudan, Saudi Arabia, Yemen and parts of Nigeria and Somalia, homosexuality is punishable by the death penalty [199]. As a result, men who have sex with men are less likely to access HIV healthcare services for fear of their sexual orientation and identity being revealed.
5. Social and Cultural factors. Many MSM have experienced homophobic stigma, discrimination and violence. This drives MSM to hide their identity and sexual orientation [200,201]. Many fear a negative reaction from healthcare workers. As a result, men who have sex with men are less likely to access HIV healthcare services [202].
6. Sexual network factors. Focusing on risk behavior alone does not explain why some persons and communities continue to be infected with HIV and other STIs more than others. Increases in HIV and STIs among MSM have been pronounced in urban areas where dense sexual networks, population churn and high prevalence of anonymous partnerships sustain ongoing transmission [203]. STIs affect individuals, who are part of partnerships and larger sexual networks, and in turn populations (Figure 2.1) [5].
7. Geosocial networking systems and online social networks. Geosocial networking and online dating are widely used by MSM worldwide to meet partners for sex and dating. Studies indicated that MSM are less likely to use condoms with partners met via "hookup apps" [204-207].

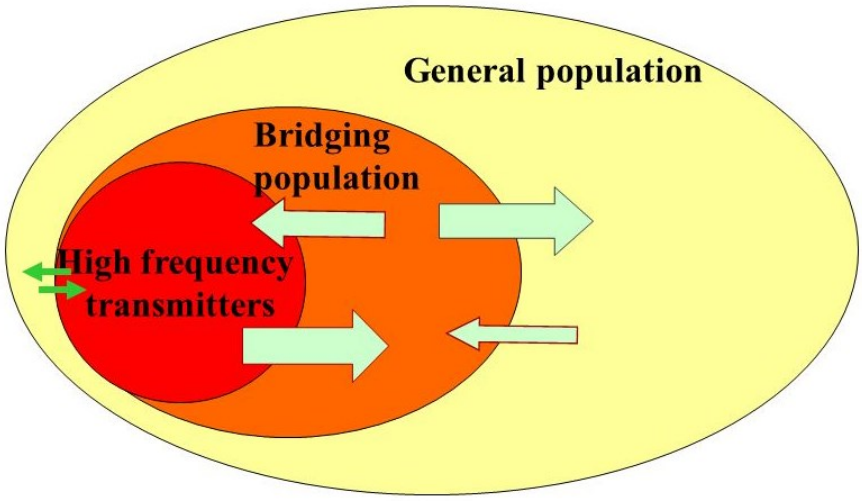

Figure 2.1 Sexually transmitted infection transmission dynamics at the population level [8]

Arrows show direction of sexual contact between core groups, bridging populations, and general population

2.13 Prevention and interventions for STI and HIV among MSM

In order to effectively prevent and reduce HIV and STI transmission among MSM and to promote sexual health among MSM, key components of public health programmes have been suggested to address HIV and STIs among MSM based on scientific evidence available by WHO Collaborating Centre for Gonorrhoea and Other Sexually Transmitted Infections and the European Centre for Disease Prevention and Control (ECDC) [4,64]. Prevention and interventions for STIs and HIV in MSM (Figure 2.1) include:

1. Vaccination: Promote and deliver vaccination to protect against Hepatitis A and B vaccination, HPV vaccination in male adolescence, vaccination for people living with HIV [208].

2. Condom: Promote condom use and provide easy access to condoms and lubricants.
3. Testing and screening for HIV and STIs: Provide voluntary and confidential HIV and STI counselling and testing, identify barriers and facilitators to testing for the target group and offer partner notification services to support the early diagnosis and treatment of contacts.
4. Treatment provision: Timely provision of treatment for HIV, viral hepatitis and STI for patients and their contacts.
5. Health promotion: Provide accurate and accessible information that enables men to understand and assess sexual health-related risks and prevention efficacy, and that promotes awareness of one's own HIV and STI status.
6. Deliver MSM competent health services: MSM-competent points of care offering a comprehensive sexual health programme including health promotion, counselling, peer support, prevention, adequate diagnostics and treatment will increase service uptake.
7. Biomedical treatment strategies that use antiretroviral therapies (ARTs) to prevent HIV infection including post-exposure prophylaxis (PEP), PrEP, and treatment as prevention (TasP) [4].
8. Targeted care for HIV-positive MSM: Provide antiretroviral treatment for HIV and vaccination; regular STI screening using adequate diagnostics; several efficacious medications exist to treat STIs [209]; individual counselling, sexual health promotion and peer-support groups for men living with HIV.

However, no single measure will effectively control all STIs at a population level. Effective STI control will require the political will to prioritise and invest in new interventions together with the optimisation of primary and secondary prevention strategies, including integrated sex education programmes in schools, strong partner notification programmes that use the latest information technology systems and legislative changes for partner delivered antibiotic treatment where appropriate, legalised frameworks for sex work, active targeted health promotion, accurate surveillance programmes, and accessible health care for all [4].

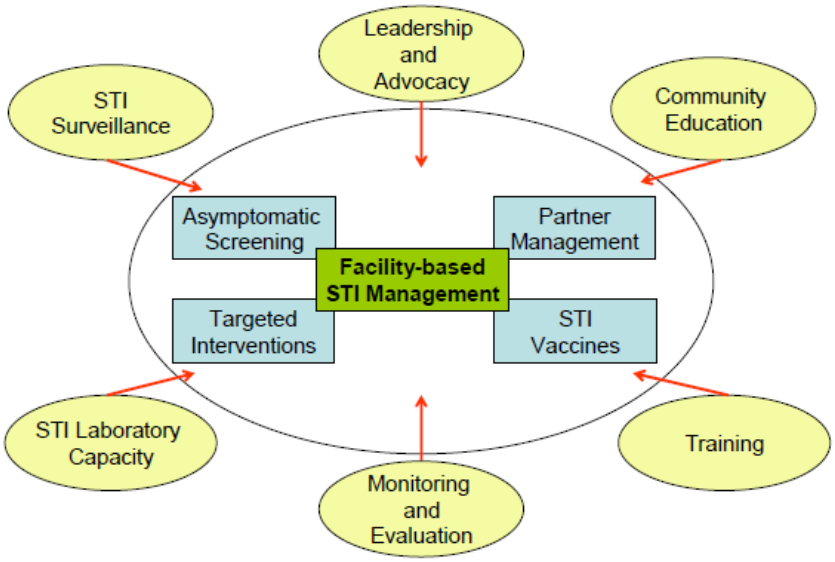

Figure 2.2 Prevention and control: Five core components and supportive elements [206]

2.14 Discussion

Despite global efforts to control HIV and STIs among MSM, new infections among MSM have been increasing since 2000, reaching or exceeding pre-HIV levels. This epidemiological review of HIV and STIs among MSM worldwide over the past decades showed a substantial change and an increasing trend in the prevalence of HIV and STIs, resurgence of some STIs and reemergence of antimicrobial resistance among MSM over the last two decades among MSM. The results showed very high prevalence rate of gonorrhoea, syphilis and HIV infection in MSM and indicated diversity and heterogeneity of STI prevalence among MSM according to geography, race and ethnicity, and HIV status. However, the rates of HIV and other STIs among MSM can vary markedly in relation to the time, setting and population whom the studies were conducted. These findings provide evidence on the epidemiology of STIs and HIV worldwide in MSM and highlight the special need for targeted prevention programmes, screening and treatment strategies in this subpopulation.

MSM have continued to be disproportionately affected by HIV and STIs. HIV and STIs diagnoses among MSM have increased since the late 1990s, reflecting social, economic and test technological changes. Gonorrhoea and syphilis have re-emerged as a major public health concerns. Additionally, the alarming increase in gonorrhoea among MSM is of particular concern given the propensity of Neisseria gonorrhoeae to develop resistance to successive antimicrobials used for treatment [19]. Although most STIs are not usually fatal, they result in a

substantial burden of disease [3]. STIs can also increase the infectiousness of and susceptibility to HIV especially among MSM [210].

Detection of gonorrhoea and chlamydia has increased in the rectum and pharynx among MSM in recent years with the widely use of nucleic acid amplification tests (NAATs) and the awareness of sexual health providers of the value of screening of non-genital sites in the absence of symptoms [103]. Extragenital screening for sexually active MSM is critical to the provision of comprehensive sexual health services for this population. However, the significance of positive NAAT at extragenital sites should be interpreted after a detailed clinical interview including presence or absence of symptoms, potential risk for reinfection, and adherence to treatment [211]. Will the increases in infections reflect true increase in incidence, or just an artifact of enhanced screening or a combination of both? More research is needed.

HIV and STIs continue to be important public health concerns among MSM and emergence of antimicrobial resistance is substantially compromising the effectiveness of treatment globally [4]. Prevention should remain a public health priority for those at greatest risk. Treatment of curable STIs has long been considered an integral component of combination HIV prevention packages [212]. Improvements in treatment with a better medication or approach, together with clinical and public health actions are needed to control STIs and HIV among MSM. STI control interventions that complement the highly effective biomedical interventions for HIV prevention are needed as part of combination prevention packages. Biomedical HIV interventions play a

positive part in STI control through frequent contacts with sexual health services that allow regular continued opportunities for primary prevention and comprehensive case management of STIs [4]. Further research is required to develop effective, evidence-based interventions among MSM. Continued research is needed to understand the effects of TasP and PrEP on sexual behaviours and networks that might increase STI transmission. Enhanced biological and behavioural surveillance activities are needed to monitor epidemiological changes in STIs in MSM who are infected or not infected with HIV, antimicrobial resistance, and the emergence or re-emergence of new sexually transmissible pathogens [4].

There are some key differences in addressing prevention strategies between HIV and STIs. Condoms have been the cornerstone of HIV and STI prevention, which can reduce the risk of other STIs, such as gonorrhea, chlamydia, herpes and syphilis [213]. Safer sex messaging and prevention counselling need to emphasize that the correct and consistent use of condoms is a very highly effective method of preventing the sexual transmission of HIV [214]. However, the simple message of "always use a condom" no longer reflects the diversity of non-condom-based HIV prevention options available to MSM in the era of non-condom HIV risk-reduction options continues to increase, such as PrEP and serosorting and strategic positioning [215,216]. Meanwhile, condoms are less effective at preventing the transmission of STIs that are spread through skin-to-skin contact, including warts, herpes and syphilis [217]. Two highly effective strategies, PrEP and use of antiretroviral treatment as prevention can reduce the risk of HIV

transmission but unfortunately cannot protect against STIs [218]. Importantly, STIs may increase the risk of HIV transmission while using some of these prevention strategies [119,219,220].

2.15 Future directions to reduce STIs and HIV among MSM

Because of the enormous burden of STIs and their wide-ranging adverse health effects, decisive action will be an essential part of efforts to meet the health component of the Sustainable Development Goals, and the targets of the global health sector strategy on sexually transmitted infections 2016–2021 [221], which were adopted by the 69th World Health Assembly in May 2016. Based on the literature review on the epidemiology of HIV and STIs in MSM, there are many implications for HIV and STIs prevention, diagnoses, treatment and care.

As the use of non-condom HIV risk reduction options continue to increase, MSM living with positive HIV need to be actively monitored in addressing the rising rates of STI among MSM population. In order to improve screening, testing and treatment for STI and HIV preventions, sexual health providers should integrate HIV and STIs preventions together with a range of preventive measures targeting MSM populations including the combinations of biomedical, behavioral, and structural interventions [222,223]. These would ideally involve an array of prevention contexts, including (1) effective health information communications and practices among sexual partners, (2) transactions between individual clients and their healthcare

providers, and (3) comprehensive population-level strategies for prioritizing prevention research, ensuring accurate outcome assessment, and formulating health policy [222].

As network factors have a significant impact on STI incidence among MSM, more interventions to reduce STIs should be focused on social and sexual networks, rather than individual factors. Prevention strategies should utilize the online or dating apps as a forum to educate MSM about HIV and STI risk behaviours and sexual health responsibilities (e.g., condom use, PrEP uptake and adherence, serostatus assumptions), and to disseminate information on how to best prevent the contraction and spread of HIV and other STIs. Future studies should focus on potential relationships between long-term or consistent use of online dating or apps and HIV and STIs incidence in MSM.

Antimicrobial resistance in Neisseria gonorrhoeae especially among MSM puts an emerging threat to effective treatment of gonococcal infections, which calls for global surveillance and international collaboration action [112,195,224,225]. Research and efforts are needed in the following areas: development of gonococcal vaccine in conjunction with early detection and screening strategies including asymptomatic infections, enhanced partner notification and treatment, develop new diagnostic and novel treatment options in order to achieve a 90% reduction of gonorrhoea incidence by 2030 [226].

Epidemiological information collected from STI surveillance system enable health authorities to conduct efficient planning, monitoring and evaluation of intervention activities for STIs and HIV. The evidence-based information on transmission patterns of HIV and STIs and potential impact on planned intervention activities are required to make appropriate political and programmatic decisions at both local and international level. Therefore, a quality HIV and STI surveillance system is an essential element of HIV/AIDS and STIs control and prevention program. STI surveillance should include (1) routine systematic recording and reporting of numbers of STI patients seen at all health care facilities or sentinel surveillance, (2) special studies to collect information on proportions of individuals infected with STIs in different population settings, (3) special studies to determine the most common microbial causes of specific STI syndromes, and (4) special studies to determine the effectiveness of selected drugs for a specific STI pathogen, or monitoring the prevalence of antimicrobial resistance among specific pathogens [51].

2.16 Gaps in the current literature and the basis for the research project

As evidence from this literature review, there is an expansive body of international literature describing the epidemiology of HIV and STIs in MSM. Studies have shown that very high prevalence rate of gonorrhoea, syphilis and HIV infection in MSM. However, there are a few gaps. These gaps suggest a need for focused epidemiologic and health services research to better characterise STI epidemiology, seasonal variation patterns of STI, HIV testing and treatment efficacy for STI. The following section highlights research gaps in this area.

The rates of sexually transmitted infections are rising rapidly in MSM. Gonorrhea is of particular concern because rising rates will increase the probability of antimicrobial drug resistance. The infection rate of gonorrhea is much higher in MSM than that in heterosexuals [80,227]. There are limited published studies that have specifically investigated the sexual orientation disparities in STIs and the relationship between sex work, policing and transient STI epidemic among heterosexuals [228]. It is therefore important for studies to be conducted to understand factors associated with the STI epidemic among heterosexuals.

Currently, the reasons for the higher rates of urethral gonorrhoea in summer remain unknown and there are limited studies that have examined seasonal variation in gonorrhoea and risk factors associated with gonorrhoea in MSM in Australia. Consequently, studies are required to assess the seasonal variations in gonorrhoea in order to allow policy makers to target demand for clinical services and health promotion activities to the periods when higher service demands are needed, to inform the design and timing of health promotion activities to reduce STI rates in Australia [229].

MSM remain the group most at risk of acquiring HIV worldwide. No single intervention measurement is likely to control HIV at a population level; however effective prevention strategies should start with HIV testing. A positive test result enables planning to effective treatment which could prevent others from becoming infected. In many countries, current HIV testing efforts are insufficient to identify new HIV infections early enough, and substantial

proportions of people with HIV are unaware of their infection [230]. HIV treatment promise to be an important public health measure for the prevention of HIV transmission [231]. A large randomised controlled trial showed early initiation of treatment reduced the risk of sexual transmission by 96% [49]. There is a gap between evidence and practice in the implementation of HIV testing programmes in populations. Studies are required to examine the current HIV testing among the MSM population in Australia in order to provide data on HIV testing rate.

As rectal chlamydial infection is associated with increased risk of HIV seroconversion, screening patients who reported receptive anal intercourse and effective treatment for rectal chlamydial infection are critical for HIV prevention [24,232]. Current STI treatment guidelines recommend rectal chlamydia to be treated with a single 1 g dose of azithromycin or 7 days (100 mg twice daily) of doxycycline [233]. Improvements to the treatment can reduce the incidence of STIs. However, there are ongoing concerns about treatment failure with rates from 13% to 21% have been reported [234,235]. The available evidence is poor and there are no pharmacokinetic data available for azithromycin in rectal mucosa. Given that HIV and STI rates continue to increase among MSM and anal sex is increasing in women, treatment for rectal chlamydia infection must be efficacious [45]. As a result, research is needed to evaluate the efficacy of single-dose azithromycin and 1 week of doxycycline for treating rectal chlamydia.

The knowledge gaps summarised above represent important areas for future research. Addressing these gaps will provide a better understanding of epidemiology of STIs among MSM

and heterosexual in South Australia. The research described in this thesis aims to address these research gaps.

CHAPTER 3

WAS AN EPIDEMIC OF GONORRHOEA AMONG HETEROSEXUALS ATTENDING AN ADELAIDE SEXUAL HEALTH SERVICES ASSOCIATED WITH VARIATIONS IN SEX WORK POLICING POLICY?

Statement of Authorship

Title of Paper	Was an epidemic of gonorrhoea among heterosexuals attending an Adelaide sexual health services associated with variations in sex work policing policy?
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
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Name of Principal Author (Candidate)	Bin Li		
Contribution to the Paper	Gained ethic approval, involved in study design, conducted data collection, performed statistical analyses, interpreted the results and wrote the manuscript. Revised the manuscript based on reviewers comments and re-submitted for publication.		
Overall percentage (%)	90%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	04/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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SHORT REPORT

Was an epidemic of gonorrhoea among heterosexuals attending an Adelaide sexual health services associated with variations in sex work policing policy?

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ABSTRACT

Background A review of historical trends in gonococcal diagnoses made at the Adelaide Sexual Health Clinic (ASHC), South Australia, identified a substantial rise in diagnoses among heterosexuals between 2006 and 2010. Sex work is illegal in South Australia, regulated in Victoria and legal in New South Wales. This and other factors that could have influenced the epidemic were explored in this analysis.

Methods Retrospective analyses of gonorrhoea diagnoses made by sexual health services between 1990 and 2012 in three Australian state capitals, Melbourne (Victoria) and Sydney (New South Wales) were undertaken.

Results At the ASHC the proportion of gonorrhoea diagnoses was higher between 2006 and 2010 among heterosexual men (5.34% vs 0.84%, p<0.001), non-sex worker women (0.64% vs 0.28%, p<0.001) and female sex workers (FSWs) (1.75% vs 0.24%, p<0.001) compared with other years. This relationship was not seen at the Melbourne Sexual Health Clinic and corresponding data from the Sydney Sexual Health Centre showed that FSWs were less likely to have gonorrhoea between 2006 and 2010 than the other groups (p=0.746, p=0.522, p=0.024, respectively). At ASHC FSWs were significantly more likely to be diagnosed between 2006 and 2010 (OR 2.8, 95% CI 1.48 to 5.27, p=0.002). Charges against sex workers peaked in 2007/2008.

Conclusions A substantial, self-limiting rise in diagnoses of heterosexual gonorrhoea was seen in Adelaide FSWs between 2006 and 2010. Removing barriers to condom use is vital to the prevention of HIV and STI transmission.

INTRODUCTION

In Australia, gonorrhoea occurs predominantly in men who have sex with men (MSM) whereas rates in heterosexuals are low except in some minority populations.[1] Nationally, gonococcal diagnoses have doubled from 35.6 per 100 000 in 2004 to 67.9 per 100 000 in 2014 and similar trends were seen in South Australia.[2] Interpreting trends in clinic level data is difficult because national surveillance does not capture contextual information on the determinant of incidence. However, the Adelaide Sexual Health Clinic (ASHC) has collected demographic, clinical and epidemiological information on every clinic attendance since 1990. A review of trends in diagnoses of gonococcal made from 1990 to 2012 suggested that there had been an epidemic among heterosexual men, women and female sex workers (FSWs) who attended the Adelaide clinic between 2006 and 2010 inclusive. Here we compared trends in diagnoses at the Adelaide clinic with those at the Sydney Sexual Health Centre (SSHC) (New South Wales) and Melbourne Sexual Health Centre (MSHC) (Victoria) and investigated factors associated with the increase in Adelaide to explore whether the observations were unique or part of an Australia-wide phenomenon.

METHODS

A retrospective analysis was undertaken using computerised sexual health service records from three Australian states. The clinics were selected because laws governing sex work vary between states. Sex work is illegal in South Australia, whereas sex work in brothels in Melbourne and Sydney is not a criminal offence.[3 4] At the ASHC, demographic, clinical and epidemiological information is collected on all clients at each clinic visit.[5] Heterosexual male sexual orientation was defined as men who reported only having sex with female sex partners in the previous 12 months. Episodes of care (all related consultations for a discrete diagnostic condition) were used at the ASHC, while individuals attending were used at MSHC and SSHC. All three clinics recorded whether a sex worker had primarily attended for testing for sex work. Prostitution offences were investigated using the data sources described in the web supplementary material (web appendices).

Diagnostic tests

The analysis was restricted to urethral infections in men and genital infections in women. Diagnostic testing strategies varied between and within centres over the 13 years studied. At ASHC culture was used until 2010 when nucleic acid amplification test (NAAT) (APTIMA COMBO 2 assay) was introduced. At MSHC gonorrhoea culture was used over the entire period. At SSHC culture was used for men and women until 1999 when it was replaced by the Roche AmplicorPCR.

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Statistical analysis

The epidemic curve of diagnoses of gonorrhoea made in heterosexual men, non-sex worker women and FSW at the Adelaide clinic was visually inspected and classified into epidemic (2006–2010) and non-epidemic years (1990–2005 and 2011–2012)[6] (figure 1). A χ^2 test was used to explore variations in the proportion of diagnoses seen at the three clinics within these time periods.

For analysis of the ASHC data set, single variable logistic regression was undertaken (outcome: diagnoses of gonorrhoea) (see web tables 1 and 2). Variables with a p value <0.05 were included in the subsequent multivariable logistic regression. Statistical analysis was undertaken using STATA V.13.

RESULTS

Diagnoses of gonorrhoea made at the three sexual health services among heterosexual men, women and FSWs varied over time (figure 1). At the ASHC diagnoses were higher between 2006 and 2010 among heterosexual men (5.34% vs 0.84%), non-sex worker women (0.64% vs 0.28%) and FSWs (1.75% vs 0.24%) compared with other years (see web tables 1 and 2). At MSHC there were similar or significantly lower proportions of all three groups with gonorrhoea between 2006 and 2010 (0.60% vs 0.75%, p=0.043), (0.27% vs 0.18%, p=0.051), (0.63% vs 0.96%, p=0.036), respectively. At SSHC the proportion with gonorrhoea was not higher for heterosexual men (1.80% vs 1.85%, p=0.746) and non-sex worker women

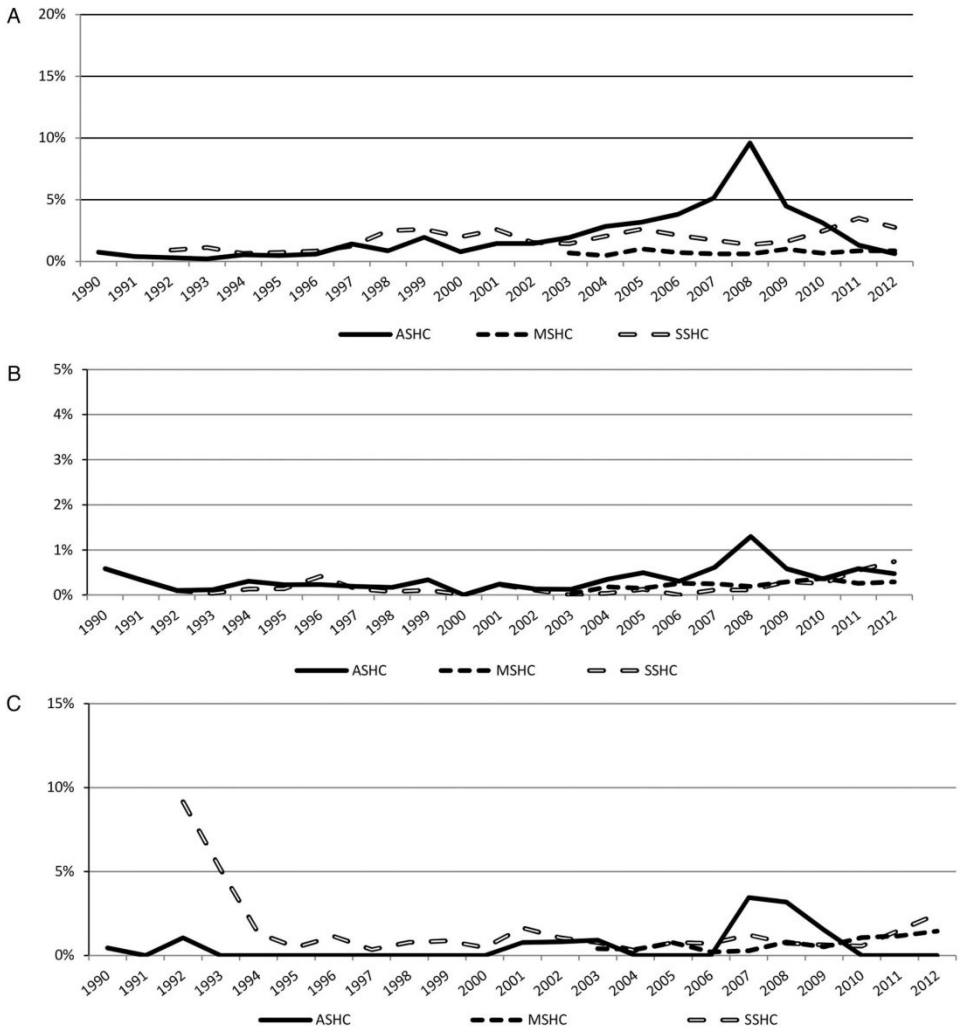

Figure 1 (A) Proportion of episodes of care or individuals seen in a year with urethral gonorrhoea in heterosexual men at ASHC (1990–2012), MSHC (2003–2012) and SSHC (1992–2012). (B) Proportion of episodes of care or individuals seen in a year with cervical or vaginal gonorrhoea in non-sex worker women at ASHC (1990–2012), MSHC (2003–2012) and SSHC (1992–2012). (C) Proportion of episodes of care or individuals seen in a year with cervical or vaginal gonorrhoea in female sex workers at ASHC (1990–2012), MSHC (2003–2012) and SSHC (1992–2012). ASHC, Adelaide Sexual Health Clinic; MSHC, Melbourne Sexual Health Centre; SSHC, Sydney Sexual Health Centre.

(0.17% vs 0.21%, p=0522); the proportion of FSW with gonorrhoea was significantly lower (0.75% vs 1.06%, p=0.024) during the epidemic years of 2006–2010.

Between 2000/2001 and 2011/2012 more than 450 charges relating to prostitution were brought against FSWs by police in South Australia which peaked at 78 in 2007/2008 although there was considerable variation over time, an initial peak being seen in 2001 (see web figure 1). In contrast, from 2000 onwards, charges fell progressively in Victoria and New South Wales, substantially lower rates were seen from 2005 onwards (data not shown) (see web reference w1–w3). For men at ASHC, having sex in another state or abroad was not significant during the epidemic years (see web table 1). For women at ASHC, the odds of gonorrhoea was significantly associated with sex worker in epidemic years (OR: 2.79, 95% CI 1.48 to 5.27, p=0.002) but not in non-epidemic years (OR: 0.85; 95% CI 0.37 to 1.94, p=0.705) (see web table 2).

DISCUSSION

The Adelaide gonorrhoea epidemic identified between 2006 and 2010 occurred in heterosexual men, women and FSWs but no corresponding trend in diagnoses seen in the Melbourne or Sydney clinics. An exploration of factors associated for gonorrhoea in Adelaide showed that there had been increased local transmission during the epidemic years which could reflect restricted access to clinical services, reduced condom use, or a transient increase in bisexual men, although these were not monitored during the period. Around the same time convictions against FSWs peaked in Adelaide with 78 prostitution offences in the 2007/2008 financial year compared with 450 over the last 12 years.

The study has a number of limitations. In Adelaide, episodes of care were used in the analysis whereas in Melbourne and Sydney individuals were used, differences that do not prevent the interpretation of a long term within centres. All centres represent only a sample of the population of each state and consequently may not necessarily reflect state-wide trends accurately. Data on the number of men who had a history of sexual contact with FSWs was not available and the accuracy of FSWs' occupation was not validated. Contextual information around sex work in South Australia was taken from a number of sources: newspaper reports of increased police activity against FSW where carrying condoms had been used by police as evidence of sex work; and reports from the Office of Crime Statistics and Research, and South Australia Police which described increased police activity against FSW during the epidemic period.[7 8] Such information could only provide circumstantial evidence of a temporal relationship between increased policing and rise in heterosexually acquired gonorrhoea which is not sufficiently robust to explore a causal relationship.

We were unable to find any other published articles which explore the relationship between sex work, policing and transient sexually transmitted infection epidemics. However, authors have suggested that increased policing can reduce access to condoms, thereby increasing rates of unprotected sex.[9] New York City stopped using possession of condoms as evidence of sex work in 2013 and, in the interests of public health interventions aimed at the prevention of HIV and STI transmission, it would appear that other governments should consider similar legislative revisions.[10]

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Contributors CKF conceived the study; BL undertook the analysis, interpreted the results and drafted the manuscript; CKF and PB supervised the data analysis. All authors contributed to the draft, and reviewed and approved the final manuscript.

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Competing interests None declared.

Ethic approval South Australia Department of Health Human Research Ethics Committee; Royal Adelaide Hospital Research Ethic Committee and Aboriginal Health Research Committee of South Australia, in addition to the human research ethics committee at the University of Adelaide. Approval number HREC/12/SAH/87.

Provenance and peer review Not commissioned; externally peer reviewed.

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Web supplement

Additional methods

To determine potential reasons for the increase in gonorrhoea, we undertook a search of the internet site for the highest circulation newspaper in South Australia (The Advertiser) to determine whether there were any reports of police using the carriage of condoms as evidence of prostitution. We also obtained Crime Statistics on the prostitution offences reported or becoming known to Police from the three States between 2000 and 2012 (w1-w3).

Additional results

We identified 119 and 32 results using the search terms ‘prostitution’ or ‘sex worker’ respectively on a search carried out on the 12th May 2014 between 2000 and 2012. After reviewing all the articles for terms ‘condom’ or ‘safe sex’, we identified one article titled ‘Police 'deter' safe sex practice’ published on June 6th 2009, which says the Adelaide's sex workers say they are facing criminal charges because they carry condoms, making it more difficult for them to carry safe sex gear (Web reference w4).

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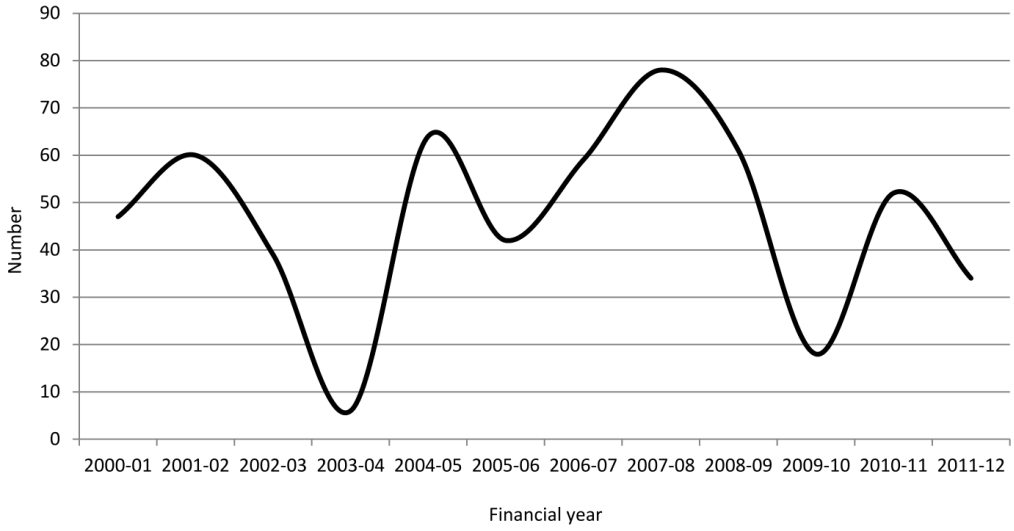
Table 1: Crude and adjusted odds ratios for with Urethral gonorrhoea among heterosexual men attending Clinic 275 during epidemic and non-epidemic years

	Epidemic years (2006-10)								Non-epidemic years (years other than 2006-10)							
	Heterosexual Men diagnosed with Urethral GC		Heterosexual Men not diagnosed with Urethral GC		Unadjusted		Adjusted		Heterosexual Men diagnosed with Urethral GC		Heterosexual Men not diagnosed with Urethral GC		Unadjusted		Adjusted	
	n	Proportion (%)	n	Proportion (%)	OR	(95% CI)	OR	(95% CI)	n	Proportion (%)	n	Proportion (%)	OR	(95% CI)	OR	(95% CI)
N	223		3955						268		31514					
Age group																
<20	15	6.7	230	5.8	1.00				18	6.7	2291	7.3	1.00			
20-24	36	16.1	1069	27.0	0.52	0.28-0.96	0.52	0.28-0.97	58	21.6	8829	28.0	0.84	0.49-1.42		
25-29	29	13.0	877	22.2	0.51	0.27-0.96	0.54	0.28-1.02	58	21.6	7168	22.8	1.03	0.61-1.75		
30-49	111	49.8	1439	36.4	1.18	0.68-2.06	1.26	0.72-2.22	116	43.3	11585	36.8	1.27	0.77-2.10		
≥50	32	14.4	340	8.6	1.44	0.76-2.73	1.69	0.89-3.23	18	6.7	1641	5.2	1.40	0.72-2.69		
Marital status																
Never married	146	65.5	2811	71.1	1.00				198	73.9	22293	70.8	1.00			
Married/de facto	35	15.7	731	18.5	0.75	0.53-1.07			37	13.8	5518	17.5	0.92	0.63-1.34	0.75	0.52-1.08
Divorced, separated or widowed	42	18.8	412	10.4	1.01	0.70-1.46			33	12.3	3674	11.7	1.96	1.37-2.81	1.06	0.73-1.55
Race																
Indigenous Australian	14	6.3	47	1.2	5.62	3.04-10.39	5.60	2.97-10.56	45	16.8	430	1.4	16.00	11.41-22.44	18.95	13.26-27.09
Asian	10	4.5	123	3.1	1.53	0.79-2.97	1.81	0.93-3.55	12	4.5	695	2.2	2.64	1.47-4.75	2.39	1.31-4.34
Caucasian	188	84.3	3546	89.7	1.00				193	72.0	29514	93.7	1.00			
other	11	6.3	238	6.0	0.87	0.47-1.62	1.05	0.56-1.97	18	6.7	862	2.7	3.19	1.96-5.20	3.09	1.89-5.07
No. partners in past 3 mths																
1	84	38.0	1607	42.3	1.00				72	27.3	15433	53.1	1.00			
2	60	27.2	1191	31.3	0.96	0.69-1.35	0.97	0.69-1.37	85	32.2	7849	27.0	2.32	1.69-3.18	2.11	1.53-2.90
3	30	13.6	464	12.2	1.24	0.81-1.90	1.32	0.85-2.04	46	17.4	2780	9.6	3.55	2.44-5.15	2.73	1.86-4.01
4	20	9.1	208	5.5	1.84	1.11-3.06	2.13	1.27-3.58	12	4.6	1255	4.3	2.05	1.11-3.79	1.62	0.87-3.04
≥5	27	12.2	330	8.7	1.57	1.00-2.45	1.62	1.02-2.56	49	18.6	1743	6.0	6.03	4.18-8.69	4.39	2.97-6.48
Sex contact in past 12mths																
SA only	152	68.2	2708	68.8	1.00				138	52.1	22935	77.0	1.00			
Interstate	17	7.6	469	11.9	0.65	0.39-1.08			37	14.0	2830	9.5	2.17	1.51-3.13	1.64	1.13-2.39
overseas	50	22.4	680	17.3	1.31	0.94-1.82			85	32.1	3737	12.6	3.78	2.88-4.96	3.39	2.53-4.53
Interstate & overseas	4	1.8	78	2.0	0.91	0.33-2.53			5	1.9	284	1.0	2.93	1.19-7.20	1.87	0.74-4.74

Table 2: Crude and adjusted odds ratios for vaginal/cervical gonorrhoea among women attending Clinic 275 during epidemic and non-epidemic years

	Epidemic years (2006-10)								Non-epidemic years (years other than 2006-10)							
	Women diagnosed with GC		Women not diagnosed with GC		Unadjusted		Adjusted		Women diagnosed with GC		Women not diagnosed with GC		Unadjusted		Adjusted	
	n	Proportion (%)	n	Proportion (%)	OR	(95% CI)	OR	(95% CI)	n	Proportion (%)	n	Proportion (%)	OR	(95% CI)	OR	(95% CI)
N	90		12970						118		41796					
Age group																
<20	20	22.2	2234	17.2	1.00				35	29.7	8816	21.1	1.00			
20-24	19	21.1	4312	33.3	0.49	0.26-0.92	0.52	0.27-0.98	39	33.1	14355	34.4	0.68	0.43-1.08	0.69	0.43-1.09
25-29	16	17.8	2691	20.8	0.66	0.34-1.28	0.71	0.36-1.38	13	11.0	7612	18.2	0.43	0.23-0.81	0.38	0.20-0.73
30-49	32	35.6	3262	25.2	1.10	0.63-1.92	1.07	0.60-1.91	29	24.6	9900	23.7	0.74	0.45-1.21	0.68	0.38-1.20
≥50	3	3.3	471	3.6	0.71	0.21-2.40	0.85	0.25-2.91	2	1.7	1113	2.7	0.45	0.11-1.88	0.45	0.10-2.03
Marital status																
Never married	54	60.0	9690	74.8	1.00				84	71.2	32020	76.7	1.00			
Married/de facto	25	27.8	1986	15.3	2.26	1.40-3.63			22	18.6	4865	11.7	1.72	1.08-2.76	1.88	1.14-3.13
Divorced, separated or widowed	11	12.2	1287	9.9	1.53	0.80-2.94			12	10.2	4890	11.4	0.94	0.51-1.71	1.13	0.56-2.29
Race																
Indigenous Australian	8	8.9	242	1.9	5.07	2.41-10.63	4.82	2.28-10.21	26	22.0	625	1.5	21.89	13.89-34.48	22.26	14.02-35.33
Asian	6	6.7	1019	7.9	0.90	0.39-2.08	0.90	0.39-2.09	15	12.7	1728	4.1	4.57	2.61-7.98	4.10	2.33-7.22
Caucasian	3	81.1	11188	86.3	1.00				73	61.9	38407	91.9	1.00			
other	73	3.3	516	4.0	0.89	0.28-2.84	0.94	0.29-3.01	3	2.5	1018	2.4	1.55	0.49-4.93	1.40	0.44-4.48
African									1	0.9	9	0.02	58.46	7.31-467.32	51.60	6.16-432.38
No. partners in past 3 mths																
1	42	46.7	7141	55.1	1.00				64	54.2	24003	57.4	1.00			
2	23	25.6	2712	20.9	1.44	0.87-2.40	1.45	0.87-2.43	32	27.1	8321	19.9	1.44	0.94-2.21		
3	9	10.0	982	7.6	1.56	0.76-3.21	1.51	0.73-3.13	8	6.8	2423	5.8	1.24	0.59-2.59		
4	2	2.2	378	2.9	0.90	0.22-3.73	0.84	0.20-3.48	0	0.0	907	2.2				
≥5	13	14.4	968	7.5	2.28	1.22-4.27	1.16	0.42-3.19	13	11.0	3155	7.6	1.55	0.85-2.81		
Sex contact in past 12mths																
SA only	75	83.3	9663	74.5	1.00				87	73.7	32655	78.1	1.00			
Interstate	10	11.1	1612	12.4	0.80	0.41-1.55			11	9.3	4196	10.0	0.98	0.53-1.84	0.98	0.52-1.85
overseas	5	5.6	1271	9.8	0.51	0.20-1.26			15	12.7	2631	6.3	2.14	1.23-3.71	2.56	1.44-4.57
Interstate & overseas	0	0.0	179	1.4					0	0.0	261	0.6				
Sex worker																
Yes	11	12.2	617	4.8	2.79	1.48-5.27	2.37	0.81-6.94	6	5.1	2470	5.9	0.85	0.37-1.94		
No	79	87.8	12353	95.2	1.00				112	94.9	39326	94.1	1.00			

Web Figure 1: Prostitution offences recorded by South Australia Police each financial year



CHAPTER 4

SEASONAL VARIATION IN GONORRHOEA INCIDENCE AMONG MEN WHO HAVE SEX WITH MEN

Statement of Authorship

Title of Paper	Seasonal variation in gonorrhoea incidence among men who have sex with men
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
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Principal Author

Name of Principal Author (Candidate)	Bin Li		
Contribution to the Paper	Involved in study design, gained ethics approval, conducted data collection, performed the analysis, interpreted the results and wrote the manuscript. Revised the manuscript based on reviewers comments and re-submitted for publication.		
Overall percentage (%)	90%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	04/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Contribution to the Paper	Supervised the development of the work, assisted data interpretation and manuscript evaluation, reviewed and revised the final manuscript.		
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	Conceived the study and acted as corresponding author. Reviewed and revised the final manuscript.		
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Short Report

Seasonal variation in gonorrhoea incidence among men who have sex with men

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Abstract. ***Background*:** After reviewing urethral gonorrhoea cases among men who have sex with men (MSM) at the South Australia Specialist Sexual Health (SASSH) in Adelaide, Australia, we noticed peaks of gonorrhoea among MSM occurred predominantly in the first quarter of the year (January–March). The aim of this study was to formally test this hypothesis against data from a similar period at three sexual health services, one each in Adelaide, Melbourne and Sydney. ***Methods*:** This study was a retrospective analysis of computerised records at the three Australian sexual health services. Potential risk factors for urethral gonorrhoea among MSM were also reviewed at the SASSH. ***Results*:** More peaks of gonorrhoea cases were observed in the first quarter of the year in Adelaide and Sydney and in the second and fourth quarter in Melbourne. Factors independently associated with urethral gonorrhoea at the SASSH were being a young MSM, especially those aged 25–29 (odds ratio (OR) 2.66, 95% confidence interval (CI): 2.00–3.54), having more than one sexual partner (OR 1.71, 95% CI: 1.43–2.04), having had sex interstate and overseas (OR 1.52, 95% CI: 1.06–2.17), and presenting in the first quarter (OR 1.30, 95% CI: 1.10–1.55). ***Conclusion*:** Our data suggest that gonorrhoea among MSM occurs in a seasonal pattern, particularly late summer into early autumn. This has implications for the provision of health services over the year and for the timing of health promotion activities.

Additional keywords: epidemiology, homosexual, sexually transmissible infections.

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Introduction

Gonorrhoea is a common sexually transmissible infection (STI) producing considerable morbidity, and the rates are higher among men who have sex with men (MSM).[1,2] In Australia, rates of gonorrhoea are increasing, with a substantial increase in rates among males from 51 per 100 000 in 2009 to 91 per 100 000 in 2013.[3,4] It is likely that rates of gonorrhoea will continue to rise with greater widespread use of biomedical HIV preventions such as pre-exposure prophylaxis for HIV which has been associated with reduced condom use and a greater number of partners.[5]

Identifying factors that are associated with sexual risk may assist in developing interventions and ensuring there are adequate health services to manage fluctuations in the rates of infection. Seasonal variation in human behaviour has a major effect on some communicable diseases, such as measles, diphtheria and chickenpox.[6] There have been several studies exploring the seasonal patterns of STI,[7–9] and some studies reported higher levels of sexual activity in young adult males during summer and autumn.[10] The warmer months are associated higher testosterone levels and with vacations, festivals and travel.[11] The majority of studies to date have only examined heterosexuals, and only one study has assessed changes in seasonal sexual activity in MSM. In that study urethral gonorrhoea diagnoses among MSM were more frequent in summer compared with winter (odds ratio (OR) 1.23, 95% confidence interval (CI): 1.04–1.46).[10]

The aim of the present study was to assess whether seasonal variations in urethral gonorrhoea diagnoses were evident in MSM in three Australian states. If there was significant variation in rates, it might allow policy makers to target demand for clinical

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services and health promotion activities to periods where demand on services was greater and risks higher.

Methods

Study population and data collection

We conducted a retrospective cross-sectional study using computerised records from three Australian sexual health services looking at the number of urethral gonorrhoea cases. We then undertook a more detailed analysis of data for all MSM attending South Australia Specialist Sexual Health (SASSH) in Adelaide, South Australia (SA) from 1 January 1990 to 31 December 2013. SASSH provides ~18 000 sexual health consultations, and ~20% of these are for MSM. It is the only public sexual health clinic in Adelaide, the capital city of SA with a population of ~1.6 million (2011 census).[12] SASSH provides a walk-in service, with free and confidential testing, diagnosis and treatment of HIV and other STI.[13] We also reviewed the available data from Melbourne Sexual Health Centre (MSHC) for 2002–2013 and Sydney Sexual Health Centre (SSHC) for 1995–2013).

For the purpose of this study, MSM were defined as men who reported having sex with male sex partners in the past12 months. The analysis was restricted to urethral infections in men because these are generally symptomatic and therefore their diagnosis is likely to be representative of recent acquisition of infection. At the SASSH, episodes of care were used and referred to clinically related consultations for one patient for a discrete diagnostic condition from the onset of symptoms until treatment was complete. At MSHC and SSHC number of individuals seen in a year who tested positive for gonorrhoea as a proportion of all MSM tested in that year is presented.

Statistical analysis

The monthly means of urethral gonorrhoea in MSM were first plotted to visualise time pattern and trends. Significant 3-month cycles were documented for all the STIs,[14] hence quarterly figures were used in the subsequent analyses. Most plots revealed obvious peaks in the first quarter in Adelaide. The proportion of MSM who tested positive for urethral gonorrhoea was calculated for the three clinics.

For the analysis of the SASSH, univariate logistic regression was undertaken to examine the association between urethral gonorrhoea and a range of risk factors. Risk factors with a P-value <0.05 in the univariate analyses were included in the subsequent multivariable logistic regression to identify risk factors associated with urethral gonorrhoea.

All statistical analyses were performed using STATA ver. 14 (StataCorp).

Ethics

The study was approved by South Australia Department of Health Human Research Ethics Committee (approval number HREC/12/SAH/87).

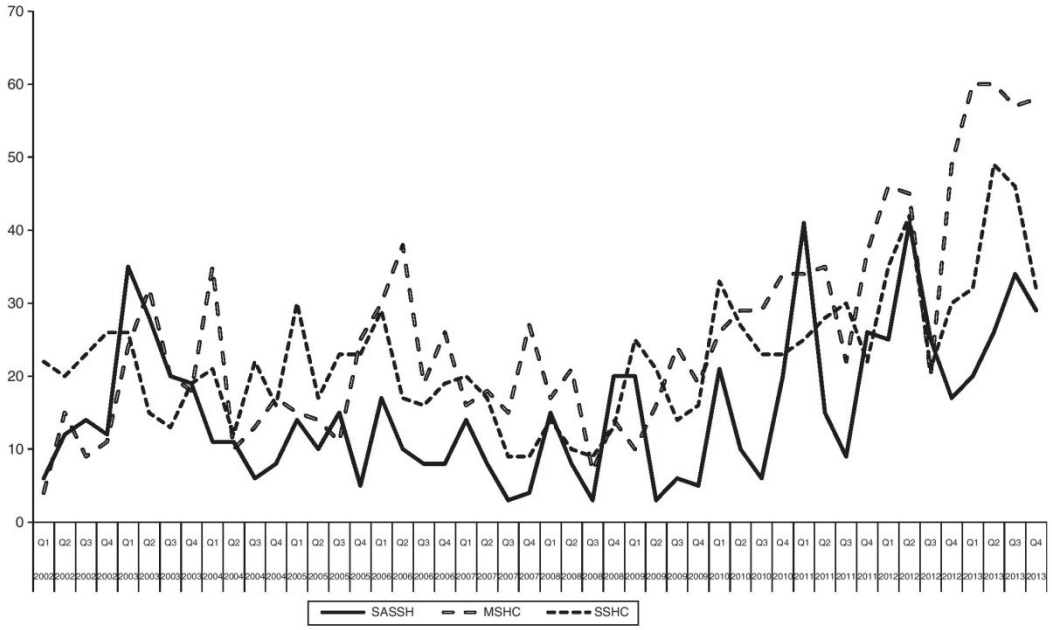

Fig. 1. Number of urethral gonorrhoea cases in men who have sex with men each quarter at South Australia Specialist Sexual Health (SASSH), Melbourne Sexual Health Centre (MSHC) and Sydney Sexual Health Centre (SSHC), 2002–2013.

Table 1. Factors associated with urethral gonorrhoea among men who have sex with men (MSM) attending South Australia Sexual Health (SASSH), 1990–2013

OR, odds ratio; CI, confidence interval

	MSM diagnosed with urethral gonorrhoea		MSM not diagnosed with urethral gonorrhoea		Unadjusted		Adjusted	
	n	Proportion (%)	*n*	Proportion (%)	OR	(95% CI)	OR	(95% CI)
	n = 1038		*n* = 20817					
Age group in years								
<20	61	5.9	1188	5.7	2.22	1.55–3.19	2.27	1.56–3.30
20–24	241	23.2	4236	20.4	2.46	1.86–3.27	2.45	1.81–3.31
25–29	238	22.9	3872	18.6	2.66	2.00–3.54	2.55	1.89–3.44
30–49	436	42.0	8839	42.5	2.14	1.63–2.80	2.03	1.53–2.67
≥50	62	6.0	2685	12.9	1.00		1.00	
Marital status								
Never married	874	84.3	16 247	78.1	1.00		1.00	
Married or de facto	106	10.2	2832	13.6	0.70	0.57–0.85	0.80	0.64–0.98
Divorced, separated or widowed	57	5.5	1724	8.3	0.61	0.47–0.81	0.78	0.59–1.05
Race								
Indigenous Australian	15	1.5	230	1.1	1.29	0.76–2.18	1.07	0.61–1.88
Asian	48	4.6	1329	6.4	0.71	0.53–0.96	0.65	0.48–0.87
African or other	21	2.0	443	2.1	0.93	0.60–1.45	0.87	0.56–1.36
Caucasian	954	91.9	18 810	90.4	1.00		1.00	
No. partners in past 3 months								
1	206	19.9	5677	27.3	1.00		1.00	
2	218	21.0	4131	19.8	1.45	1.20–1.77	1.45	1.19–1.77
3	144	13.9	2827	13.6	1.40	1.13–1.75	1.39	1.11–1.73
4	107	10.3	1638	7.9	1.80	1.42–2.29	1.78	1.40–2.27
≥5	352	33.9	5677	27.3	1.71	1.43–2.04	1.71	1.43–2.06
Sex contact in past 12 months								
South Australia only	630	60.7	13 912	66.8	1.00		1.00	
Interstate	277	27.0	4228	20.3	1.45	1.25–1.67	1.28	1.10–1.49
Overseas	87	8.4	1732	8.3	1.11	0.88–1.40	1.08	0.85–1.36
Interstate and overseas	34	3.3	495	2.4	1.52	1.06–2.17	1.35	0.94–1.94
Quarter								
Q1	317	30.5	5346	25.7	1.30	1.10–1.55	1.27	1.07–1.51
Q2	249	24.0	5012	24.1	1.09	0.91–1.31	1.09	0.90–1.31
Q3	232	22.4	5185	24.9	0.98	0.82–1.18	0.97	0.81–1.17
Q4	240	23.1	5274	25.3	1.00		1.00	

Results

At SASSH there were 1038 cases of urethral gonorrhoea in MSM between 1990 and 2013; 1244 cases of urethral gonorrhoea were reported in MSM at the MSHC between 2002 and 2013; and 1466 at the SSHC for the period of 1995–2013.

More peaks of urethral gonorrhoea cases were observed in the first quarter at SASSH and SSHC (43% and 38% respectively), but in the second and fourth quarter at MSHC (38%). There were 12 peaks in the first quarter over the 24-year study period at SASSH and nine peaks over the 19-year study period at SSHC, but at MSHC only two peaks occurred in the first quarter during the 13-year study period (Fig. 1, Supplementary Material, Table 1). The median number of urethral gonorrhoea cases peaked in the first quarter at SASSH and SSHC, with 12 and 22 cases respectively. However, the median number peaked in the fourth quarter at MSHC, with 26 cases (Supplementary Material, Table 2).

Univariate analysis showed urethral gonorrhoea was more common among young MSM at the SASSH, especially those aged 25–29 years (OR 2.66, 95% CI: 2.00–3.54), those who had more than one sexual partner (OR 1.71, 95% CI 1.43–2.04), those who had sex interstate and overseas (OR 1.52, 95% CI: 1.06–2.17) and those who presented in the first quarter (OR 1.30, 95% CI: 1.10–1.55). The first quarter remained significantly associated with urethral gonorrhoea in the adjusted analysis (adjusted OR 1.27, 95% CI: 1.07–1.51; Table 1).

Discussion

We observed 27% higher odds of urethral gonorrhoea in the first quarter when adjusted for other variables. Of the three sexual health services, two (SASSH and SSHC) saw nearly half of their peaks in the first quarter. A more detailed analysis of line data from the MSHC showed a similar pattern to Adelaide, with 23% higher odds of urethral gonorrhoea during summer.[10] The reasons for the higher rates of urethral gonorrhoea in summer are unknown but may related to biological variations in hormone levels, differences in sexual activity possibly related to social events or perhaps a greater use of antibiotics in winter. The results from the present study, together with other studies, suggest clinical services may need to increase services during the first quarter of the year.[10] This may also have policy

implications to the health authority in terms of resource allocation and timing for health promotion intervention.

The reasons for the peaks of gonorrhoea cases in the first quarter are not known. Interestingly our data also showed an increase in the total clinic attendances in the first quarter (data not shown). These findings may relate to hormonal changes causing more sexual activity during summer months, less use of antibiotics for respiratory infections in summer, or more social events during the summer months.[8,11] Several other studies support our findings, with increased sexual activity reported during summer time.[9,14]

The study has several limitations. First it was a retrospective observational study and is therefore subject to the biases associated with this type of study. Second all three centres represented only clinic patients and the trends within each clinic may not be generalisable to the entire state. Third, we had no data on seasonal changes in health-seeking behaviours, which could also influence reported gonorrhoea cases. Our hypotheses to explain the association between increased urethral gonorrhoea incidence in MSM and the warmer months are plausible but require careful scrutiny and testing in future investigations.

Despite these limitations, this study is one of few longitudinal study of seasonal variation in gonorrhoea and risk factors associated with gonorrhoea in MSM in Australia. The present findings and those from Melbourne suggest that seasonal variation in gonorrhoea occurs among MSM.[10] Gonorrhoea is rare in non-Indigenous heterosexuals in large cities in Australia so it is not possible to compare changes in incidence between heterosexuals and MSM. The observed seasonal variation in gonorrhoea among MSM has several important public health implications and has the potential to improve gonorrhoea responses in Australia and internationally. A predictable increase in gonorrhoea cases in the first quarter highlights the need for more services during this time.[14] Finally, more research is needed to understand the behavioural and biological changes underpinning seasonal fluctuations in gonorrhoea among MSM, which will be important in the development and sustainability of control strategies and policies to improve the sexual health of MSM.

Conflicts of interest

None declared.

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CHAPTER 5

TRENDS AND PREDICTORS OF RECENT HIV TESTING OVER 22 YEARS AMONG A CLINIC SAMPLE OF MEN WHO HAVE SEX WITH MEN IN SOUTH AUSTRALIA

Statement of Authorship

Title of Paper	Trends and predictors of recent HIV testing over 22 years among a clinic sample of men who have sex with men in South Australia
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Principal Author

Name of Principal Author (Candidate)	Bin Li		
Contribution to the Paper	Gained ethic approval, involved in study design, performed all the analysis, interpreted the results, wrote the manuscript and acted as the corresponding author. Revised the manuscript based on reviewers comments and re-submitted for publication.		
Overall percentage (%)	90%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	04/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Peng Bi		
Contribution to the Paper	Supervised the development of the work, helped in data interpretation and manuscript evaluation, reviewed and revised the final manuscript.		
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Contribution to the Paper	Assisted data interpretation, read the manuscript and provided feedback.		
Signature		Date	05/09/2018

Name of Co-Author	Christopher K Fairley		
	Conceived and provided oversight in the study design, reviewed and revised the final manuscript.		
Signature		Date	05/09/2018

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Trends and predictors of recent HIV testing over 22 years among a clinic sample of men who have sex with men in South Australia

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Abstract. ***Background*:** Increasing the frequency of HIV testing is crucial for effective HIV prevention and care. The aim of the present study was to determine whether there has been a change in HIV testing among men who have sex with men (MSM) at the South Australia Specialist Sexual Health (SASSH) clinic over the past two decades. ***Methods*:** Computerised medical records of MSM who attended the SASSH at their first visit between 1994 and 2015 were used to determine whether HIV testing had changed among MSM. First HIV tests in each calendar year and return tests within 12 months were analysed. Factors associated with recent HIV testing were also examined. ***Results*:** There were 24 036 HIV tests conducted among 8163 individual MSM over the study period. The proportion of newly registered MSM who reported ever being tested for HIV declined ($P_{trend} = 0.030$), the proportion who reported recent HIV testing did not change ($P_{trend} = 0.955$) and the proportion who have had current HIV testing increased ($P_{trend} = 0.008$). The proportion of MSM who returned to the clinic for HIV testing within 12 months did not change ($P_{trend} > 0.05$), with less than 40% of MSM returning for HIV testing. Factors independently associated with recent HIV testing included MSM aged ≥20 years, (odds ratio (OR) 1.79; 95% confidence interval (CI) 1.53–2.10), higher education (OR 1.28; 95% CI 1.12–1.45), non-Caucasian (African OR 1.68; 95% CI 1.30–2.17), having multiple sex partners (OR 1.47; 95% CI 1.29–1.69), having had sex interstate (OR 1.61; 95% CI 1.42–1.82) or overseas (OR 1.53; 95% CI 1.33–1.76) and injecting drug use (OR 1.56; 95% CI 1.29–1.88). ***Conclusions*:** HIV testing rate among MSM attending SASSH was suboptimal. New approaches are needed to increase the uptake and early detection of HIV infection among the high-priority MSM population.

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Introduction

HIV infections are increasing among men who have sex with men (MSM).[1–5] Increasing HIV testing is recommended among people who are at higher risk by the US Centres for Disease Control and Prevention (CDC) and the Australian Government Department of Health and Ageing.[6,7] The Sexually Transmitted Infections in Gay Men Action group (STIGMA) recommended testing for HIV at least once a year for all MSM and up to four times a year for MSM at highest risk, including any unprotected anal sex and more than 10 sexual partners in the previous 6 months.[8]

In Australia, sexual health centres have increased HIV testing substantially in MSM, and this has been analysed centrally by the Kirby Institute. The Kirby Institute obtains data from 46 sexual health services across Australia participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmitted Infections (STIs) and Blood Borne Viruses (BBVs) (ACCESS) project. Between 2011 and 2014, the proportion of MSM who attended and had an HIV test in 1 year increased from 80% to 91%.[9] Recent Australian studies show that the proportion of MSM who are unaware of their infection is approximately 9–31%,[10–12] and in 2014 there were approximately 3350 (12%) people undiagnosed and living with HIV in Australia.[9] Point-of-care HIV testing (POCT) may increase the uptake and frequency of HIV testing in individuals at high risk, but it needs to be used frequently to overcome their lower sensitivity.[13] A recent meta-analysis also suggested that within a clinic setting, POCT was

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less sensitive and should generally be restricted to situations without access to fourth-generation serological testing.[14] The aim of the present study was to report data from South Australia, to complement data from other centres in Australia on HIV testing in MSM. This will then provide national data to assess treatment as prevention (TasP) as a goal of the current national HIV strategy, which aims to '. . .work towards achieving the virtual elimination of HIV transmission in Australia by 2020' and to '. . .increase the proportion of people living with HIV on treatments with an undetectable viral load'.[6]

Methods

Study population and data collection

A retrospective analysis was conducted using computerised medical records of MSM who attended the South Australia Specialist Sexual Health (SASSH) clinic between 1 January 1994 and 31 December 2015. SASSH is the only public sexual health clinic in Adelaide, the capital city of South Australia. SASSH currently conducts over 18 000 consultations annually and provides walk-in, free and confidential testing, diagnosis and treatment of sexually transmissible infections, including HIV/AIDS.[15]

SASSH uses standardised case notes to routinely collect demographic, clinical and epidemiological information on all clients at each clinic visit. This information is then coded into an electronic clinic database.[15]

The first presentation of all MSM presenting to SASSH over the study period (1994–2015) was included to measure HIV testing rates that are unaffected by the effect of attending the clinic. For the purpose of the present study, MSM were defined as men who only reported having sex with men or who self-reported as gay or homosexual or bisexual in the previous 12 months. Transgender individuals were excluded from the analysis.

Three measures for HIV testing were analysed: ever being tested for HIV, recent HIV testing (HIV testing within the past 12 months of the most recent test) and current HIV testing (HIV testing on the day of attendance). This was done for newly registered MSM attending the clinic for that first visit. In addition, we evaluated the proportion of newly registered MSM and all MSM returning for HIV testing within 12 months of their last test at SASSH.

Statistical analysis

There are four outcomes in the present study in relation to HIV testing among the newly registered MSM on that first visit: (1) the proportion of MSM who reported ever being tested for HIV; (2) the proportion of MSM who reported recent HIV testing; (3) the proportion of MSM who have had current HIV testing; and (4) the proportion of MSM who returned for HIV testing within 12 months of their last test at SASSH. To determine whether there was a change in HIV testing over time, a Chi-squared test for trend was used. Crude and adjusted odds ratios (OR and aOR respectively) and 95% confidence intervals (CI) for HIV testing and associations with the year of test were calculated.

Univariate and multivariate logistic regression analyses were performed to assess the factors associated with the recent HIV testing. The main research question of interest was: who is recently getting tested for HIV as recommended? The analyses focused on a range of sociodemographic predictors, including age, education, ethnic background and, marital status, as well as behavioural data, such as the number of sex partners in the past 3 months, sex contacts in the past 12 months and injecting drug use. All independent categorical variables with $P \leq 0.05$ in the bivariate logistic regression analyses were selected for multivariate logistic regression analysis using the forced entry method. Variables were considered significant if $P < 0.05$. OR and aOR, as well as 95% CIs, were also included.

Trends in testing and returning for HIV testing within 12 months were examined using a non-parametric test for trend to examine trends by calendar year.

All statistical analysed were conducted using Stata 14 (StataCorp).[16]

Ethics approval

Ethics approval for this study was obtained from the South Australia Department of Health Human Research Ethics Committee, Royal Adelaide Hospital Research Ethics Committee and Aboriginal Health Research Committee of South Australia, in addition to the human research ethics committee at the University of Adelaide (Approval no. HREC/12/SAH/87).

Results

HIV testing among MSM at SASSH, 1994–2015

There were 24 036 HIV tests performed among 8163 individual MSM who attended SASSH between 1994 and 2015. Of these 8163 individual MSM, 7214 attended for the first time in the study period. The proportion of these 7214 MSM who reported ever being tested for HIV declined ($P_{trend} = 0.030$), the proportion of MSM who reported recent HIV testing did not change ($P_{trend} = 0.955$) and the proportion of MSM who have had current HIV testing increased on that first visit ($P_{trend} = 0.008$; Table 1; Fig. 1). Current HIV testing among newly registered MSM increased each year (OR 1.024; 95% CI 1.013–1.034; Table 2).

Returning for repeat HIV testing among MSM at SASSH, 1994–2015

Overall, less than 40% of all MSM (range 20–38%) or less than 22% of newly registered MSM (range 11–22%) returned for a second HIV test within 12 months at SSASH between 1994 and 2014 (Table 3). The number of return HIV tests performed within 12 months of the first HIV test increased annually ($P < 0.001$), but there was no change in the proportion of MSM who returned for HIV testing ($P > 0.05$) between 1994 and 2014 (Table 3).

Predictors of recent HIV testing among newly registered MSM at first presentation

Of all newly registered MSM at their first presentation, 2815 (39.1%) reported recent HIV testing. Univariate analysis showed that MSM older than 20 years (aOR 1.79; 95% CI 1.53–2.10), those with a higher education (aOR 1.28; 95% CI 1.12–1.45), non-Caucasian (aOR 1.67 (95% CI 1.11–2.53) for

Table 1. Description of HIV tests among newly registered men who have sex with men (MSM) at their first visit to the South Australia Specialist Sexual Health (SASSH) clinic, January 1994 to December 2015

$^{\dagger}P_{trend} = 0.000$; $^{*}P_{trend} = 0.030$; $^{**}P_{trend} = 0.955$; $^{***}P_{trend} = 0.008$. 'Recent HIV testing' refers to being tested less than 12 months before attendance at SASSH

Year	No. MSM[†]	MSM who reported ever being tested for HIV			MSM who reported recent HIV testing			MSM who have had current HIV testing		
		$n^{\dagger}$	%*	Median age (years)	$n^{\dagger}$	%**	Median age (years)	$n^{\dagger}$	%***	Median age (years)
1994	232	117	50.4	29.6	80	34.5	26.0	202	87.1	28.1
1995	245	134	54.7	28.2	98	40.0	27.5	217	88.6	27.5
1996	240	154	64.2	28.1	96	40.0	25.6	211	87.9	25.9
1997	264	159	60.2	30.0	108	40.9	28.9	225	85.2	28.5
1998	231	139	60.2	29.7	92	39.8	29.1	192	83.1	28.0
1999	197	120	60.9	34.0	82	41.6	30.5	156	79.2	29.0
2000	237	130	54.9	31.7	87	36.7	29.0	203	85.7	28.5
2001	219	135	61.6	31.6	85	38.8	30.2	179	81.7	30.1
2002	241	142	58.9	32.1	85	35.3	27.5	203	84.2	29.3
2003	280	165	58.9	31.0	122	43.6	27.9	226	80.7	30.0
2004	274	158	57.7	32.0	109	39.8	28.0	235	85.8	29.1
2005	275	167	60.7	32.0	112	40.7	28.5	235	85.5	26.7
2006	356	203	57.0	29.4	141	39.6	28.0	314	88.2	26.2
2007	321	180	56.1	31.3	120	37.4	29.3	272	84.7	27.7
2008	300	173	57.7	31.3	124	41.3	29.5	268	89.3	27.4
2009	322	181	56.2	30.5	113	35.1	30.6	289	89.8	27.0
2010	401	208	51.9	30.2	148	36.9	29.4	360	89.8	27.1
2011	510	283	55.5	29.4	193	37.8	28.0	459	90.0	26.4
2012	435	244	56.1	29.5	159	36.6	27.7	385	88.5	26.4
2013	473	244	51.6	29.0	184	38.9	27.2	435	92.0	26.5
2014	580	293	50.5	27.9	233	40.2	26.5	511	88.1	25.1
2015	581	285	49.1	29.2	244	42.0	26.6	515	88.6	25.9

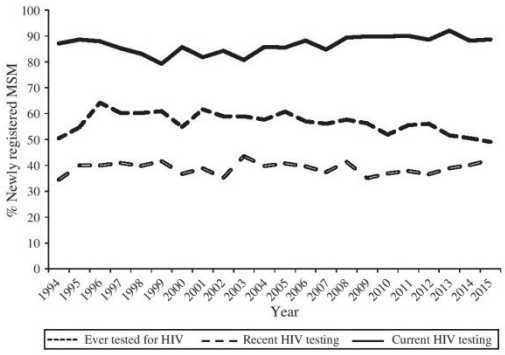

Fig. 1. Proportion of newly registered men who have sex with men (MSM) who reported ever being tested for HIV, recent HIV testing and current HIV testing at their first visit to the South Australia Specialist Sexual Health clinic between January 1994 and December 2015.

Indigenous Australians; aOR 1.68 (95% CI 1.30–2.17) for Africans; aOR 1.31 (95% CI 1.12–1.54) for Asians), those who had five or more male partners in the previous 3 months (aOR 1.47; 95% CI 1.29–1.69), those who had reported having had sex interstate (aOR 1.61; 95% CI 1.42–1.826) or overseas (aOR 1.53; 95% CI 1.335–1.76) in the previous 12 months and injecting drug users (aOR 1.56; 95% CI 1.29–1.88) were more likely to have had recent HIV testing (Table 4). Except for higher education, all factors remained statistically significant predictors of having recent HIV testing in the multivariate analysis (Table 4).

Table 2. HIV tests and associations with the year of test among newly registered men who have sex with men at their first visit to the South Australia Specialist Sexual Health clinic, January 1994 to December 2015

OR, odds ratio; CI, confidence interval

HIV tests	1994–2015		2000–2015	
	OR	95% CI	OR	95% CI
Ever tested for HIV	0.998	0.991–1.005	0.997	0.986–1.009
Recent HIV testing	1.001	0.994–1.009	1.004	0.992–1.015
Current HIV testing	1.024	1.013–1.034	1.042	1.024–1.060

Discussion

The present study used clinic data over more than two decades to describe HIV testing patterns among MSM attending the only sexual health clinic in Adelaide. Over the period 1994–2015, there has been a decline in those who have ever been tested for HIV among newly registered MSM, whereas the proportion of MSM who reported recent HIV testing did not change and the proportion of MSM who have had current HIV testing increased. Of particular concern, less frequent returning for HIV testing was seen among newly registered MSM. These results are not

Table 3. Summary of return tests within 12 months and average tests among men who have sex with men (MSM) who had their first HIV testing at the South Australia Specialist Sexual Health clinic, January 1994 to December 2015

*P_{trend} <0.001; **P_{trend} = 0.115; ***P_{trend} = 0.119; †P_{trend} = 0.252; ‡P_{trend} = 0.065

Year	Newly registered MSM				All MSM			
	No. MSM who had HIV testing*	No. MSM who had a return test within 12 months*	% MSM who had a return test within 12 months**	Mean no. tests per individual***	No. MSM who had HIV testing*	No. MSM who had a return test within 12 months*	% MSM who had a return test within 12 months†	Mean no. tests per individual‡
1994	220	37	16.8	1.24	467	93	19.9	1.20
1995	225	34	15.1	1.16	359	97	27.0	1.19
1996	221	39	17.6	1.21	313	98	31.3	1.21
1997	247	47	19.0	1.25	310	117	37.7	1.26
1998	200	41	20.5	1.25	254	87	34.3	1.27
1999	175	20	11.4	1.11	237	52	21.9	1.13
2000	210	31	14.8	1.20	255	69	27.1	1.20
2001	195	22	11.3	1.15	241	70	29.0	1.13
2002	214	38	17.8	1.21	268	71	26.5	1.23
2003	245	36	14.7	1.18	288	83	28.8	1.18
2004	250	40	16.0	1.17	298	101	33.9	1.17
2005	245	38	15.5	1.19	288	86	29.9	1.18
2006	333	60	18.0	1.20	383	117	30.5	1.22
2007	281	49	17.4	1.22	325	115	35.4	1.22
2008	276	52	18.8	1.23	317	110	34.7	1.23
2009	295	55	18.6	1.19	334	108	32.3	1.20
2010	373	54	14.5	1.16	434	107	24.7	1.17
2011	472	100	21.2	1.26	530	173	32.6	1.26
2012	398	75	18.8	1.22	474	150	31.6	1.24
2013	450	79	17.6	1.24	543	153	28.2	1.24
2014	522	117	22.4	1.27	616	198	32.1	1.29
2015	528	111		1.30	629	206		1.30

consistent with improvements reported in the Gay Community Periodic Survey (GCPS) carried out in Adelaide between 2012 and 2014; that survey reported a significant increase in those with recent HIV testing from 59.4% in 2003 to 67% in 2014.[17] The results of the present study suggest that MSM who live in Adelaide and attend SASSH are not having adequate HIV testing according to the guidelines. If interventions such as TasP are to be effective in reducing the incidence of HIV, then testing rates in Adelaide need to increase substantially.

Compared with the findings of the present study, the GCPS reported a higher proportion of ever being tested for HIV (85% between 2012 and 2014).[17] In addition the proportion of recent HIV testing in the GCPS[17] was consistently higher than that observed in the present study and a recent study from the Melbourne Sexual Health Centre (MSHC).[18] Despite guidelines recommending at least 12-monthly HIV testing for all MSM, approximately only half the newly registered MSM reported ever being tested for HIV in the present study and less than 50% of MSM reported recent HIV testing. The proportion of MSM who reported recent HIV testing at SASSH is lower than that reported in both the MSHC study[18] (56.9% in 2013) and the GCPS (67% in 2014).[17]

The present study confirmed a fall in the proportion of MSM who reported ever being tested for HIV at SASSH. Reasons for the decline among MSM who reported ever being tested for HIV are unknown. It may be related to selection bias over time, with a greater proportion of MSM with low background testing rates being attracted to SASSH in recent years. Of note, the number of newly registered MSM seen at SASSH has more than doubled, and so this could have affected the results of the present study. Despite this, possibly only 50% of MSM attending in 2015 reported ever being tested for HIV, with a median age of 29 years. The rate of returning for HIV testing in the past 12 months among MSM between 1994 and 2014 has increased marginally from 19.9% in 1994 to 32.1% in 2014. The discrepancy in the proportion of HIV testing between studies may also be due to sampling differences, whereby the GCPS participants were recruited primarily from gay community events, which would represent gay community-attached men with better HIV knowledge via their community engagement and peer education campaigns.[18,19]

Encouragingly, we did see an increase in the proportion of newly registered MSM who have had current HIV testing, with the proportion reasonably high by 2015 at approximately 90% in the present study. Importantly, recent HIV testing was more common in MSM who had higher HIV risk, including multiple sexual partners in the past 3 months and injecting drug users. In addition, demographic factors such as age and higher numbers of partners in the past 12 months were associated with a higher likelihood of being tested, which is similar to other studies among the MSM in Australia.[18,20]

Recent reviews of HIV testing in Australia suggest that HIV testing could be increased by removing barriers to HIV testing, improving health education, especially for young MSM, making HIV testing more convenient with high-quality rapid HIV tests, which allow for HIV testing without seeing a doctor,

Table 4. Factors associated with recent HIV testing among newly registered men who have sex with men at their first visit to the South Australia Specialist Sexual Health clinic, January 1994 to December 2015
OR, odds ratio; aOR, adjusted OR; CI, confidence interval

Factors	No. with HIV test in past 12 months (%)	No. without HIV test in the past 12 months (%)	OR (95% CI)	aOR (95% CI)
Year of testing	2815	4389	1.00 (0.99–1.01)	
Age (years)				
<20	243 (8.6)	602 (13.7)	1.00	1.00
20–40	2047 (72.7)	2828 (64.4)	1.79 (1.53–2.10)	1.55 (1.26–1.91)
≥40	525 (18.7)	959 (21.9)	1.36 (1.13–1.63)	1.48 (1.14–1.91)
Education				
Tertiary (university) or higher	996 (61.9)	1381 (56.1)	1.28 (1.12–1.45)	1.11 (0.97–1.28)
High school or less	612 (38.1)	1082 (43.9)	1.00	1.00
Race				
Indigenous Australian	47 (1.67)	46 (1.1)	1.67 (1.11–2.53)	2.40 (1.36–4.23)
Asian	305 (10.9)	381 (8.7)	1.31 (1.12–1.54)	1.40 (1.14–1.71)
African	124 (4.4)	121 (2.8)	1.68 (1.30–2.17)	1.75 (1.29–2.37)
Caucasian	2336 (83.1)	3837 (87.5)	1.00	1.00
Marital status				
Married or de facto	191 (6.8)	324 (7.4)	0.75 (0.65–0.87)	0.88 (0.73–1.07)
Divorced, separated or widowed	343 (12.2)	676 (15.5)	0.88 (0.73–1.05)	0.94 (0.71–1.24)
Never married	2268 (80.9)	3368 (77.1)	1.00	1.00
No. partners in the past 3 months				
2–4	1092 (41.5)	1864 (45.4)	0.98 (0.88–1.10)	1.09 (0.94–1.27)
≥5	612 (23.3)	695 (16.9)	1.47 (1.29–1.69)	1.37 (1.13–1.65)
1	925 (35.2)	1549 (37.7)	1.00	1.00
Sex contacts in the past 12 months				
Interstate	644 (23.5)	723 (17.1)	1.61 (1.42–1.82)	1.49 (1.25–1.76)
Overseas	435 (15.9)	514 (12.1)	1.53 (1.33–1.76)	1.50 (1.25–1.79)
South Australia only	1661 (60.6)	3001 (70.8)	1.00	1.00
Injecting drug use				
Yes	234 (8.3)	241 (5.5)	1.56 (1.29–1.88)	1.71 (1.25–2.35)
No	2581 (91.7)	4148 (94.5)	1.00	1.00

and involving general practitioners more in sexual health screening.[21,22] There was a suggestion that this could be achieved by POCT, but its lower sensitivity argued against it replacing standard serological testing in clinical services.[14]

The present study has several limitations. First, interpreting temporal trends with cross-sectional samples may be difficult because of variations in samples over time. Importantly, however, the clinic has operated in the same manner over the 22-year period and has not changed its clinical practices with regard to HIV testing. Second, the results from the present study may not be representative of the entire MSM population in Adelaide because the findings are based on data from a single sexual health clinic and only MSM attending the clinic. SASSH is located in the metropolitan area and close to several large tertiary institutions and therefore may represent a skewed sample of men, including highest levels of education and socioeconomic status, and ethnic backgrounds.[23] SASSH is also likely to have seen a considerable proportion of MSM living in the metropolitan area given that over 8000 individual MSM attended the centre over the time, out of an estimated 12 000 homosexual and bisexual men living in South Australia based on the Australian Study of Health and Relationships and Australian Census data in 2008.[24] Third, we may have underestimated the re-testing rate for HIV because MSM may test at general practice or at other clinics. There has been no clinic-based testing initiative during the study period and the clinic has never used text-based recall to encourage HIV testing at any point. It is unknown what number of tests may have been missed or what proportion of MSM changed clinics. Notwithstanding these weaknesses, the data are likely to provide indications of HIV testing trends. Fourth, in the calculation of returning for HIV testing within 12 months, we did not exclude MSM if they had tested before and so counted the same person if they returned in subsequent years.

The data suggest that despite an increase in current HIV testing, there is still opportunity for improved HIV testing. To improve the HIV testing rate, current services will need to reach those who have never been tested or are not tested as guidelines recommend, to engage with young gay men and to introduce faster and more convenient testing options for MSM.

Conflicts of interest

None declared.

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CHAPTER 6

THE EFFICACY OF AZITHROMYCIN AND DOXYCYCLINE TREATMENT FOR RECTAL CHLAMYDIA INFECTION: A RETROSPECTIVE COHORT STUDY IN SOUTH AUSTRALIA

Statement of Authorship

Title of Paper	The efficacy of Azithromycin and Doxycycline Treatment for Rectal Chlamydial Infection: A Retrospective Cohort Study in South Australia
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Principal Author

Name of Principal Author (Candidate)	Bin Li		
Contribution to the Paper	Gained ethic approval, conceived the study, performed all the analysis, interpreted the results, wrote the manuscript and acted as corresponding author. Revised the manuscript based on reviewers comments and re-submitted for publication.		
Overall percentage (%)	95%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	04/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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ORIGINAL ARTICLES

The efficacy of azithromycin and doxycycline treatment for rectal chlamydial infection: a retrospective cohort study in South Australia

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Key words
Chlamydia trachomatis, rectal, azithromycin, doxycycline, treatment.

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Abstract

Background: There are ongoing concerns about treatment failure with azithromycin for the treatment of rectal chlamydia.

Aim: To investigate treatment efficacy of two treatments for rectal chlamydial infection.

Methods: We performed a retrospective analysis of all patients diagnosed with rectal chlamydial infection between 2009 and 2015 in Adelaide, Australia. Patients were treated with either azithromycin (1 g single dose) or doxycycline (100 mg twice a day for 10 days) and returned for repeat testing 14–180 days after treatment commenced. Log-binomial models were used to estimate the relative risk (RR) of recurrent rectal chlamydia associated with the treatment with azithromycin versus doxycycline.

Results: In men, rectal chlamydia prevalence was 6.7%, and in women, it was 8.1%. Of the 526 patients diagnosed with rectal chlamydial infections, 419 (79.7%), 93 (17.7%) and 14 (2.6%) patients were treated with doxycycline, azithromycin or other medication respectively. Of these patients, 173 (41.3%) of 419 doxycycline-treated patients and 31 (33.3%) of 93 azithromycin-treated patients were retested between 14 and 180 days after treatment commenced ($P = 0.16$). Among these patients, the repeat rectal chlamydia test was less commonly positive in those treated with doxycycline (5.8%; 95% confidence interval (CI) 0.03–0.10) compared with those treated with azithromycin (19.4%; 95% CI 0.09–0.36) and ($P = 0.01$). In the multivariate analysis, azithromycin-treated patients had a significantly higher risk of a positive test in the 14 and 180 days after treatment commenced (adjusted relative risk (aRR) 2.96, 95% CI 1.16–7.57).

Conclusion: The findings suggest that doxycycline may be more effective than azithromycin in treating rectal chlamydial infections.

Introduction

Rectal chlamydia diagnoses have increased considerably among men who have sex with men (MSM) in recent years, and it is now more common than urethral infection.[1,2] There are also increasing reports of rectal chlamydia among women coinciding with studies showing that anal sex among heterosexuals is more common.[3] Prevalence of rectal chlamydia has been reported to be as high as 24.4% among MSM and 17.5% among women.[4] It is possible that further increases in rectal chlamydial infection will occur due to the widespread uptake of biomedical prevention, such as pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV).[5] There are ongoing concerns about rectal chlamydia treatment failure, with a systematic review and meta-analysis finding that the efficacy of single-dose azithromycin treatment may be considerably lower than 1 week of doxycycline for treating rectal chlamydial infection (82.9% vs 99.6%).[6–8]

As rectal chlamydial infection is associated with an increased risk of HIV seroconversion,[9–11] screening patients who reported receptive anal intercourse and

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effective treatment for rectal chlamydial infection are critical for HIV prevention. Current sexually transmitted infections (STI) treatment guidelines recommend azithromycin (1 g single dose) or doxycycline (100 mg twice a day for 7 days) for the treatment of rectal chlamydial infection.[12–15] To date, there is only one double-blinded randomised controlled trial planned comparing antibiotic therapy for rectal chlamydial infection.[16]

In this study, we aim to review the efficacy of 1 g of azithromycin as a single dose compared with 100 mg of doxycycline twice daily for 10 days following our clinic guidelines in the treatment of rectal chlamydial infection in men and women attending the sexual health clinic in Adelaide, Australia.

Methods

Study design and population

Using the data extracted from the Adelaide STI Clinic, a retrospective cohort of all men and women who were positive for rectal chlamydial infection diagnosed by the nuclear acid amplification test (NAAT) at the STI Clinic in Adelaide, Australia, between 2009 and 2015 was defined for analysis. Rectal specimens from women who reported receptive anal intercourse have been routinely collected since September 2012.

Data collection

All data were collected as part of routine sexual health services at the Adelaide STI Clinic. Demographic, clinical and epidemiological data were entered into a computerised database and retrieved for the purpose of this study. Since September 2012, the recommended treatment for rectal chlamydial infection at the Adelaide STI Clinic has been changed from azithromycin to doxycycline, which allowed us to assess the efficacy of azithromycin and doxycycline treatment for rectal chlamydial infection.

Throughout the study period, the clinic protocol was to obtain rectal specimens from all male patients who reported receptive anal intercourse. Prior to September 2012, we did not ask women other than sex workers about anal sex, and therefore, we did not offer rectal sampling; however, rectal specimens from all women who reported receptive anal intercourse have been collected since then. At the Adelaide STI Clinic, all rectal specimens were tested using the NAAT (APTIMA combo 2, GenProbe Diagnostics, San Diego, CA, USA) by SA Pathology.

We defined repeat testing of rectal chlamydial infection as having a positive result on the first repeat test for rectal chlamydial infection obtained in the 14 and 180 days after the date of treatment commencement. We excluded tests occurring less than 14 days after treatment to decrease the risk of false positive results from NAAT testing. We limited the analysis to all patients who were re-tested within 180 days of diagnosis to minimise the effect of spontaneous resolution of infection. We have excluded those patients if they were treated with medication other than doxycycline or azithromycin.

Statistical analysis

We used two sample *t*-tests to compare the mean time between treatment and repeat test and Fisher exact test to analyse statistically significant differences in the proportion for categorical variables. Log-binomial models were used to estimate the unadjusted and adjusted relative risk (RR) and 95% confidence interval (CI) of recurrent infection associated with treatment with azithromycin versus doxycycline. The multivariate model included demographic information (e.g. age, race and gender), clinical indicators (e.g. HIV status, previous STI, anorectal symptoms) and behavioural (e.g. number of sex partners and IDU) factors. Log-binomial models were undertaken to estimate the association between each characteristic and recurrent infection, and a backward, stepwise elimination ($P < 0.10$) to identify factors associated with recurrent infection was implemented.

All analyses were performed using Stata statistical software, version 14.1 (StataCorp, College Station, TX, USA).

Ethics

The study was approved by South Australia Department of Health Human Research Ethics Committee (approval number HREC/12/SAH/87).

Results

Rectal chlamydia prevalence was 6.7 and 8.1%, respectively, in men and women who presented to the clinic with a rectal swab over the study period. In total, 526 patients were diagnosed with rectal chlamydial infection between 2009 and 2015; 73 % ($n = 384$) were men, 379 (99%) were MSM and 27% ($n = 142$) were women. The patient age range was 16–79 years old (median age 28 years), and 4% (22/526) of patients had HIV infection. The majority of the rectal chlamydial infection was asymptomatic (330/526, 63%). Of these 526 patients, 419 (79.7%), 93 (17.7%) and 14 (2.6%) patients were treated with doxycycline, azithromycin or other medication respectively.

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Except for year of diagnosis, there were no statistically significant differences in demographic or behavioural characteristics between patients who returned for a repeat test and patients who did not return for a repeat test, and there were no statistically significant differences in demographic or behavioural characteristics for those patients who were treated with azithromycin and doxycycline (Table 1).

Of the 204 patients who returned for a repeat test within 180 days after treatment commenced, the majority of them (173, 84.8%) were treated with doxycycline, and only 31 (15.2%) were treated with azithromycin. There was no significant difference in the interval between treatment and repeat test between the azithromycin (mean = 97 days) and doxycycline (mean = 84 days) groups ($P = 0.07$) (Table 2).

Repeat rectal chlamydial infection was more commonly positive in females (12.8%) compared to males (6.4%), but this was not statistically significant ($P = 0.155$). Treatment with azithromycin was significantly associated with threefold higher risk (RR 3.35; 95% CI 1.31–8.55) of repeat rectal chlamydial infection 14–180 days after treatment commenced. The significant association of treatment regimen with repeat rectal chlamydial infection remained after adjusting for other factors (Table 2).

Discussion

In this clinical sample of patients diagnosed with rectal chlamydial infections between 2009 and 2015, we found that patients treated with azithromycin had a significantly higher risk of repeat NAAT positivity in the rectal

Table 1 Characteristics of patients diagnosed with rectal chlamydia by completion of repeat test and treatment received ($n = 438$)

Characteristics‡	Patients without a repeat test ($n = 234$)		Patients with a repeat test 14–180 days after treatment					
			Total ($n = 204$)		Azithromycin ($n = 31$)		Doxycycline ($n = 173$)	
	n	%	*n*	%	*n*	%	*n*	%
Age								
Mean	31.5		31.5		32.2		31.4	
Interquartile range	23.0–37.6		22.6–37.9		21.5–43.0		22.9–36.2	
Race								
Indigenous	2	0.9	2	1.0	1	3.3	1	0.6
Asian	19	8.2	30	14.7	3	9.7	27	15.6
Caucasian	203	87.1	163	79.9	26	83.9	137	79.2
African/other	9	3.9	9	4.4	1	3.2	8	4.6
HIV status								
Negative	220	94.0	196	96.1	29	93.6	167	96.5
Positive	14	6.0	8	3.9	2	6.5	6	3.5
No. sex partners in past 3 months								
0–1	58	24.8	45	22.1	6	19.4	39	22.5
2–4	116	49.6	85	41.7	12	38.7	73	42.2
≥5	60	25.6	74	36.3	13	41.9	61	35.3
Previous STI	53	22.7	46	22.6	7	22.6	39	22.5
Year of diagnosis†								
2009	0	0	1	0.5	1	3.2	0	0
2010	0	0	0	0	0	0	0	0
2011	1	0.4	2	1.0	1	3.2	1	0.6
2012	24	10.3	38	18.6	22	71.0	16	9.3
2013	41	17.5	56	27.5	2	6.5	54	31.2
2014	68	29.1	63	30.9	4	12.9	59	34.1
2015	100	42.7	44	21.6	1	3.2	43	24.9
Concurrent urethral/cervical chlamydia	85	38.0	57	29.5	7	24.1	50	30.5
Concurrent gonorrhoea	41	17.5	25	12.3	5	16.1	20	11.6
Any symptom	97	41.5	64	31.4	11	33.5	53	30.6
Interval between treatment and repeat test, day								
14–30			4	2.0	1	3.2	3	1.7
31–60			63	30.9	5	16.1	58	33.5
61–90			54	26.5	8	25.8	46	26.6
91–180			83	40.7	17	54.8	66	38.2

†$P < 0.05$, statistically significant difference in characteristic between patients who returned for a repeat test and who did not return for a repeat test.
‡Due to missing values, not all variables sum to column total. HIV, human immunodeficiency virus; STI, sexually transmitted infection.

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Table 2 Demographic, clinical and behavioural factors at the time of initial diagnosis associated with repeat positivity in rectal chlamydial infection among patients re-tested 14–180 days after treatment commenced (n = 204)

Factors	Repeat positive rectal chlamydia (n†)	Total number (N‡)	Repeat positive rectal chlamydia (%)	Unadjusted		Adjusted	
				RR	95% CI	RR	95% CI
Treatment							
Azithromycin	6	31	19.4	3.35	1.31–8.55	2.96	1.16–7.57
Doxycycline	10	173	5.8	Reference		Reference	
Gender							
Male	10	157	6.4	Reference			
Female	6	47	12.8	2.00	0.77–5.23		
Age							
<20	2	20	10.0	Reference			
20–24	6	55	10.9	1.09	0.24–4.97		
25–29	4	40	10.0	1.0	0.20–5.00		
30–49	2	71	2.8	0.28	0.42–1.88		
≥50	2	18	11.1	1.11	0.17–7.09		
Race							
Others	2	41	4.9	Reference			
Caucasian	14	163	8.6	1.76	0.42–7.44		
HIV status							
Negative	16	199	8.0	–			
Positive	0	5	0.0	–			
No. partners in past 3 months							
0–1	6	78	7.7	Reference			
2–4	6	76	7.9	1.03	0.35–3.04		
≥5	4	50	8.0	1.04	0.31–3.50		
IDU§							
Yes	1	14	7.1	0.93	0.13–6.56		
No	14	182	7.7	Reference			
Previous STI¶							
Yes	4	46	8.7	1.13	0.38–3.34		
No	12	156	7.7	Reference			
Symptoms††							
Yes	8	58	13.8	2.52	0.99–6.39	2.20	0.87–5.58
No	8	146	5.5	Reference		Reference	

†n = number of positive tests. ‡N = Total number of repeat test. §IDU = injecting drug use (ever). ¶Previous STI (GC, syphilis, chlamydia, herpes, warts and HBV). ††Symptoms refer to any symptom for clinic visit. CI, confidence interval; HBV, hepatitis B virus; RR, relative risk; STI, sexually transmitted infection.

specimens compared with patients treated with doxycycline. The data suggest that a 10-day course of doxycycline may be more effective than a single dose of 1 g of azithromycin in the treatment of rectal chlamydial infection. However, the proportion of repeat positivity in rectal chlamydial infection treated with doxycycline was much higher (5.8%) than that in the meta-analysis (0.4%),[6] which is possibly due to the nature of our study, where we were generally unable to exclude repeat infections.

There are several limitations that must be considered when interpreting our data. First, our data are from a retrospective observational study and, as such, are dependent on the quality of recorded data. Also, because the study was observational and not randomised, there could be confounding factors that may have influenced the results. We did adjust for potential confounding factors in the multivariate analysis, and this adjustment for confounders did not change the significant association of azithromycin with repeat positivity in rectal chlamydial infection. However, there may be unmeasured confounding factors operating (e.g. number of receptive anal sex partners, sex with anonymous partners). Second, only female sex workers were tested at the rectal site before 2012, but as there was only one female sex worker among the 204 participants, this could not have materially influenced the results. Third, because there were relatively few cases treated with azithromycin in our study, this limited the statistical power to look at subgroups in the study. Fourth, we had re-testing data on only a third of participants. Although we have shown that there was no difference in variables between patients who returned for a repeat test and patients who did not return for a repeat test, there may have been a

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difference in failure rates between those who did and did not return. If there was a systematic bias between treatment arms in those who returned for testing compared to those who did not, then this could have influenced our results. Fifth, for some patients, there was a considerable duration of follow-up time of up to 180 days. Longer follow up means that repeat infection becomes more likely, although we did have equal follow up in both treatment groups. Sixth, we did not have sexual behaviour data on the individuals between their initial and follow-up test, and so, we cannot determine whether there was a systematic bias between the two groups. Last, we cannot differentiate between persistent infection and reinfection in the absence of genotyping; thus, it is possible that at least some of the infections are the result of reinfection. We also could not assess if any patients had lymphogranuloma venereum (LGV) as our clinic does not routinely test for LGV. Undiagnosed cases of LGV may have been included, which may contribute to a lower azithromycin efficacy.

Regardless of these limitations, our findings are consistent with published observational data which suggest that doxycycline may be up to 20% more effective than azithromycin for rectal chlamydia.[17] It is also biologically plausible that azithromycin may not be as effective for rectal chlamydia as urogenital infections for several reasons, including the possibility that the immune response to infection is different in the rectal mucosa, which may impact azithromycin being delivered to the site of infection; this does not apply to doxycycline.[18] However, doxycycline has its own disadvantage as adherence to a 7-day or 10-day course of doxycycline may lead to an increased risk of treatment failure. [19]

Conclusion

Our article suggests that azithromycin was associated with repeat rectal chlamydial infection, compared to doxycycline. These findings add to the growing body of evidence suggesting that doxycycline may be more effective than azithromycin for the treatment of rectal chlamydia in men and women. A randomised control trial is needed to evaluate the treatment regimens for rectal chlamydial infection.

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CHAPTER 7

MAIN FINDINGS, CONCLUSIONS, RECOMMENDATIONS AND FURTHER STUDIES

7.1 Introduction

STIs constitute a huge health and economic burden worldwide including Australia [27,236-238]. Despite decades of global control efforts have been made to reduce their high global incidence and prevalence, HIV and STIs still remain a significant public health challenge and many countries still observed simultaneous increases of HIV and STIs including Australia, especially among MSM. STI control is a public health outcome measured by reduced incidence and prevalence [239] and STI epidemiology research provides the scientific rationale for public health decisions. One of the public health approaches to the control of STIs is to identify population-based strategies that can be targeted to these risk groups [240].

In Australia, there were a staggering 23,887 new diagnoses of gonorrhoea in 2016, with about three quarters of all diagnoses in males (17,325, 73%), up from 8,388 cases in 2006. The number of new diagnoses of gonorrhoea has nearly tripled within a decade. Similar trends were observed in syphilis and chlamydia. For instance, Syphilis cases have been more than tripled, while cases of chlamydia have increased by 43 percent in the past decade [17]. Similar increase in STIs has also been observed in Adelaide, South Australia [241].

This research was conducted within the context of increased diagnoses of STIs, control of STIs and prevention of HIV transmission in a sexual health clinic setting at the Adelaide Sexual Health Centre (ASHC). ASHC is a sentinel surveillance site for STIs in South Australia. Sentinel surveillance is an active surveillance system that can provide early indication of an outbreak and provide accurate detailed data. This thesis examined the trends in rates of diagnoses of STI, HIV testing, investigated factors associated with STI epidemic, seasonal patterns of STI and HIV testing and evaluated treatment efficacy for STI among MSM and heterosexuals. Longitudinal data were used to determine whether there has been a change in STI diagnoses, seasonal patterns, HIV testing and factors associated with them at the Adelaide Sexual Health Centre (ASHC) in South Australia and compared with those at Sydney Sexual Health Centre (SSHC) (New South Wales) and Melbourne Sexual Health Centre (MSHC) (Victoria). Findings from this study not only provide an overview of past and current STI epidemic, HIV testing and STI treatment efficacy among MSM and heterosexuals in South Australia, but also offer insights for future HIV and STI intervention programs planning and implementation, with important health policy implications for HIV and STI control and prevention.

7.2 Key findings of the study

In light of the increase in STIs and challenges and difficulties in STI control, the combined papers in this thesis contribute new and important knowledge regarding STI epidemiology, HIV testing and STI treatment efficacy among MSM and heterosexuals in Adelaide from both a clinical and a public health perspective.

Chapter 2 reviewed the local and international epidemiology of HIV and STIs among MSM to identify effective prevention intervention strategies for MSM; described the factors associated with sexual risk in this population and provide recommendations for effective prevention intervention; highlighted the knowledge gaps, and therefore the rationale for conducting this research.

Chapter 3 studied the gonorrhea notifications at ASHC over the last decades and the results showed the proportion of gonorrhoea diagnoses was higher between 2006 and 2010 among heterosexual men (5.34% vs 0.84%, $p<0.001$), non-sex worker women (0.64% vs 0.28%, $p<0.001$) and female sex workers (FSWs) (1.75% vs 0.24%, $p<0.001$) compared with other years at ASHC. Such phenomena were not found at the Melbourne Sexual Health Clinic and the Sydney Sexual Health Centre, with the data showing that FSWs were less likely to have gonorrhoea between 2006 and 2010 than the other groups ($p=0.746$, $p=0.522$, $p=0.024$,

respectively). For women at ASHC, the odds of gonorrhoea was significantly associated with sex worker in epidemic years between 2006 and 2010 (OR 2.8, 95% CI 1.48 to 5.27, p=0.002). It is also noted that charges against sex workers peaked in 2007/2008 coincided with the gonorrhoea epidemic in Adelaide. Meanwhile around the same time convictions against FSWs peaked in Adelaide with 78 prostitution offences in the 2007/2008 financial year compared with 450 over the last 12 years; newspaper reports of increased police actions against FSW where carrying condoms had been used by police as evidence of sex work. The findings suggested increased policing can reduce access to condoms for FSWs, thereby increasing rates of unprotected sex [228]. It would appear that governments should consider legislative revisions to stop using possession of condoms as evidence of sex work.

Chapter 4 analysed the trends in gonorrhoea diagnoses among MSM at ASHC. We formally tested this hypothesis of seasonal patterns in STI against data from a similar period at three sexual health services in Australia (Adelaide, Melbourne and Sydney). The results showed more peaks of gonorrhoea cases were observed in the first quarter of the year in Adelaide and Sydney and in the second and fourth quarter in Melbourne. Factors independently associated with urethral gonorrhoea at ASHC were being a young MSM, especially those aged 25–29 (OR: 2.66, 95% CI: 2.00–3.54), having more than one sexual partner (OR 1.71, 95% CI: 1.43–2.04), having had sex interstate and overseas (OR 1.52, 95% CI: 1.06–2.17), and presenting in the first quarter (OR 1.30, 95% CI: 1.10–1.55). The findings suggest that gonorrhoea among MSM occurs in a seasonal pattern, particularly late summer into early autumn. This has implications for the

provision of health services over the year and for the timing of health promotion activities and resource allocation.

Chapter 5 examined the trends in HIV testing among MSM at ASHC over the past two decades in response to effective HIV prevention and care. The findings showed the proportion of newly registered MSM who reported ever being tested for HIV declined (Ptrend = 0.030), the proportion who reported recent HIV testing did not change (Ptrend = 0.955) and the proportion who have had current HIV testing increased (Ptrend = 0.008). The proportion of MSM who returned to the clinic for HIV testing within 12 months did not change (Ptrend >0.05), with less than 40% of MSM returning for HIV testing. Factors independently associated with recent HIV testing included MSM aged 20 years, (OR 1.79; 95% CI 1.53–2.10), higher education (OR 1.28; 95% CI 1.12–1.45), non-Caucasian (African OR 1.68; 95% CI 1.30–2.17), having multiple sex partners (OR 1.47; 95% CI 1.29–1.69), having had sex interstate (OR 1.61; 95% CI 1.42–1.82) or overseas (OR 1.53; 95% CI 1.33–1.76) and injecting drug use (OR 1.56; 95% CI 1.29–1.88). The study suggests that HIV testing rate among MSM attending ASHC was suboptimal. New approaches are needed to increase the uptake and early detection of HIV infection among the high-priority MSM population.

Finally, Chapter 6 evaluated the treatment efficacy of two treatments for rectal chlamydial infection. The results showed that rectal chlamydia prevalence was 6.7% and 8.1% respectively in men and women who presented to the clinic with a rectal swab over the study period.

Treatment with azithromycin was significantly associated with 3-fold higher risk (RR 3.35; 95% CI 1.31-8.55) of repeat rectal chlamydial infection 14-180 days after treatment commenced. The significant association of treatment regimen with repeat rectal chlamydial infection remained after adjusting for other factors. Our findingssuggested that azithromycin was associated with repeat rectal chlamydial infection, comparing to doxycycline. These findings add to the growing body of evidence suggesting that doxycycline may be more effective than azithromycin for the treatment of rectal chlamydia in men and women. A randomised control trial is needed to evaluate the treatment regimens for rectal chlamydial infection.

7.3 Strengths, limitations and challenges

This research project has addressed knowledge gaps in relation to STI epidemiology, seasonal variation patterns of STI, HIV testing and treatment efficacy for STI in Adelaide. These findings make an important contribution to the knowledge of STI epidemiology and HIV testing in the South Australia and provide evidence for the SA government to stop using possession of condoms as evidence of sex work and to consider legislative revisions. The studies have also examined the potential risk factors associated with STI epidemic by comparing the differences at three sexual health services, one each in Adelaide, Melbourne and Sydney; Effectiveness of STI treatments was also evaluated in order to inform prevention efforts, to provide policy implications and suggestions for governments and NGOs for the effectiveness of prevention interventions of STIs, especially among MSM population. Interpreting STI trends in clinic level

data is difficult because national surveillance does not capture contextual information on the determinant of incidence. However, the ASHC has collected demographic, clinical and epidemiological information on every clinic attendance since 1990. A particular strength of the research project is that quantitative research design was conducted from South Australia, to complement data from other states in Australia on STI epidemiology, seasonal variation patterns of STI, HIV testing and treatment efficacy for STI.

The main limitations of this research project have generally addressed in each of the chapters, thus only a few will be mentioned in this section. All the studies used a retrospective and observational study design. Data were taken from the computerised database of the records of all the clinical visits to the ASHC since 1990. Retrospective study is subject to the selection and recall biases and therefore dependent on the quality of recorded data. Only association and not causation can be inferred from the results because the observed association is not randomised there could be confounding factors which may have influenced the results. In particular, it was not possible to measure and then control for all factors that may have affected the outcome through statistical analysis.

7.4 Policy implications and recommendations

Evidence from the data of epidemiological trends from 'Australian National Notifiable Diseases Surveillance System (NNDSS)' by the Department of Health and Ageing and 'Annual Surveillance

Report on HIV, viral hepatitis and STIs in Australia' by The Kirby Institute suggest that HIV and STIs are still major public health concerns in Australia [17,242]; STIs other than HIV have been neglected as a public health priority and control efforts continue to [3,5]. Multiple studies supported STIs can facilitate HIV transmission by increasing both HIV infectiousness and HIV susceptibility [210,243]. With the introduction of PrEP for HIV prevention in recent years, a rapid and re-emergence of reported STI cases and a high prevalence of STIs at populations with high risk will further increase the sexual transmission of HIV in Australia [146,244-247]. 'Know your epidemic, know your response' is of paramount importance in developing timely and appropriate policies, programs and strategies for HIV and STI prevention [248]. It is important to understand the epidemiological characteristics of an epidemic which is a main principle for STI control and prevention. It will not only to generate knowledge, but also to make subsequent steps to control and ultimately eradicate the infections. Based on the research findings from this thesis, the following implications are made:

7.4.1 Implications and recommendations for policy

- Legislative revisions

Prostitution in Australia is governed by state and territory laws, which vary considerably among different jurisdictions. Prostitution is illegal in South Australia, under the Criminal Law Consolidation Act 1935 [249] and the Summary Offences Act 1953 [250]. However, prostitution is regulated in Victoria [251] and legal in New South Wales [252]. Lessons learned from other countries where sex work is legal suggest that sex workers who engaged in commercial sex but do not

participate in the licensing regime are usually less healthy than licensed sex workers [253]. The legal context appeared to affect the conduct of health promotion programs targeting the sex industry. The decriminalization of prostitution is associated with better coverage of health promotion programs for sex workers [254]. New York City has stopped using possession of condoms as evidence of sex work since 2013. The research findings from Chapter 3 suggested that there had been increased local gonorrhoea transmission during the epidemic years which could reflect restricted access to clinical services, reduced condom use, or a transient increase in heterosexuals. In the interests of public health interventions aimed at the prevention of HIV and STI transmission, South Australia parliament and government should consider similar legislative revisions, after extensive consultations with different stakeholders including police and health authorities [255].

- Sexual health education and resource allocation for clinical services

A better understanding of seasonal patterns in STIs is likely to result in better implementation of the optimal control strategies [256]. A seasonal pattern may appear as a tight cluster of isolated epidemics that occurred during a relatively short time period, then spreading over a wide geographic area [257]. Possible explanations for the seasonal difference in STI diagnoses may include: (1) changes in biological rhythms in reproductive hormone concentrations and sexual activity; and (2) changes in social opportunity for sex, such as holidays and social events. Our study has demonstrated a seasonal pattern in STI diagnoses, with the peak number of gonorrhoea cases in summer. The peak of STI diagnoses is representative of corresponding variation during the year in the availability of diagnostic/clinical services [258].

The results from Chapter 4, together with other studies, have policy implications to the health authority in terms of sexual health education and promotion programs prior to the epidemic season and resource allocation including staffing, service access, service provision and quality of care. A study by Wellings found the prevalent seasonal variation in risky sexual behaviours, suggested the need to schedule pre-emptive school sexual health promotion programs prior to the times of high risk, in the spring, summer, and fall [259]. Clinical interventions should broadly incorporate STI management approaches for symptomatic patients, screening for asymptomatic infections and management of STIs in sex partner strategies [239]. Public health education and promotion should focus on promoting sexual safety and for the timing of health promotion activities, especially in warm seasons rather than in winter; perhaps health promotion campaigns should intensify during these times of year [229]. Delays in seeking preventive services may reflect the influence of seasonal barriers. Sexual health clinics may consider additional resource and staffs for increasing the availability and access to health care and counselling services in the summer and during holidays at Christmas and the New Year and social events such as Sydney's Mardi Gras [229,259,260].

- Ongoing promotion of comprehensive testing

There has been great effort made to increase the uptake of testing for HIV and other STIs, especially among MSM population at sexual health clinics over the last decade in Australia. MSM are one of the populations particularly at increased risk of STIs such as gonorrhoea, chlamydia, syphilis and HIV [237]. However, HIV and STI among the MSM are still under testing,

increasing the likelihood of undiagnosed infections and onward transmission and disease sequelae [261,262]. Apart from Australian HIV and STI testing guidelines, a variety of other approaches has been used to promote comprehensive STI testing in Australia [263]. Current Australian guidelines recommend that MSM should be tested at least once a year for a range of STIs and up to 4 times a year for HIV positive men, men who had more than 10 sexual partners in the previous 6 months, participate in group sex or use recreational drugs during sex [264]. The Chapter 5 in this thesis showed that HIV testing rate among MSM attending ASHC was suboptimal. Another Australian study showed that there was poor adherence to national guidelines that recommend regular re-testing of MSM for STIs, particularly among those at higher risk who require more frequent testing. Clinical strategies and practices are urgently needed to encourage more frequent HIV/STI testing among MSM, especially in the higher risk subgroup [261]. In addition, there is a need for the government to invest and to strengthen health systems that can deliver necessary health services for diagnosis and management of STIs, enhance the surveillance and reporting systems and encourage the development and implementation of effective strategies to increase the uptake and comprehensiveness of testing in future, particularly the promotion of regular comprehensive testing for all sexually active MSM, regardless of sexual practice.

- Clinical practice, service delivery and treatment recommendations

Management of STIs requires a multidisciplinary approach. WHO's Department of Child and Adolescent Health has expressed that research, policy, and service delivery options for STI prevention and treatment is a healthcare priority [265]. The Chapter 6 found that that patients

treated with azithromycin had a significantly higher risk of repeat NAAT positivity in the rectal specimens compared with patients treated with doxycycline, yet testing for reinfection was not routine clinical practice and we cannot differentiate between persistent infection and reinfection in the absence of genotyping. The results from Chapter 6 have policy implication for retesting guidelines relating to 'test of reinfection' for clinical practice.

Meanwhile, the research findings from Chapter 6 and other emerging data suggest increased failure rates with oral azithromycin compared to doxycycline when used for the treatment of rectal CT infections [43,44,235]. Suboptimal treatment efficacy for rectal chlamydia with azithromycin could have important implications for women who may be infected with CT at both urogenital and recital sites. Knowing whether rectal CT infection is present or absent could help guide clinicians in formulating their treatment recommendations in favour doxycycline over azithromycin [266].

7.4.2 Implications and recommendations for research

- Epidemiological studies

Epidemiological data on STI epidemic, HIV and STI testing activity and trends, health services accessibility (including resource allocation) and timing for health promotion intervention, especially for high risk populations are lacking in South Australia. There is a need for the health authorities, hospitals, and public health organisations to regularly evaluate STI trends and

prevalence; to establish behavioural surveillance among the risk populations; to assess behaviour and risks related to STI transmission among different populations; to develop guidelines to promote HIV and STI testing in South Australia. The findings from this thesis highlighted important features of STI epidemiology, trends in STI diagnoses, seasonal patterns in STI, HIV testing and factors associated with testing and treatment efficacy for STI among MSM and heterosexuals at ASHC in South Australia, using existing clinical records for analyses. This methodology can be used where routine STI surveillance is limited and offers a new approach to obtaining critical information on STI prevalence.

- Behaviour studies

Sexual behaviour remains the key determinant for STI transmission. Behavioural surveillance programmes have enabled the description of population patterns of risk behaviours for STI and HIV transmission, which are helpful in the understanding of how epidemics of STI are generated [267]. Behavioural surveillance paired with monitoring of comprehensive of STI trends yielded good results and provided information for recommendations [268].

Despite decades of global control effort to reduce their high global incidence and prevalence, many countries still observed simultaneous increases of HIV and STIs. In Australia, between 2012 and 2016, gonorrhoea notification rates have increased by 63% (62 to 101 per 100,000) [17]. These increase have been attributed to increasing high risk sexual behaviour, including unprotected sex and high rates of partner change particularly in young heterosexuals and MSM [17].

Since the late 1990s, combined analysis of both behavioural surveillance data and STI biological surveillance data forms a "second generation surveillance", and has been recommended by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organisation (WHO) working group of Global HIV/AIDS and sexually transmitted infection (STI) Surveillance [269]. Although Australia has established the behavioural surveillance and has been a joint project of the National Centre in HIV Epidemiology and Clinical Research and the National Centre in HIV Social Research since 1996, the sample sizes and source population are very limited in the scope of analyses in South Australia [270,271]. The lack of behavioural data limits the understanding of the changes in the HIV and STI epidemic among populations including MSM [271]. In order to assess the risks related to STI epidemic and provide information for planning and public health interventions, current STI surveillance should be supported by regular behavioural studies using set of indicators, targeted particularly at MSM, where most STI infection occur. There is a need for consistent and dedicated data collection on systematic HIV/STI behavioural surveillance among high-risk populations for better understanding of the HIV/STI epidemic and better targeted prevention strategies.

7.5 Future research directions

This research project has answered defined research questions related to trends and factors associated with STI diagnoses, seasonal patterns and HIV testing, as well as treatment efficacy for STI among MSM and heterosexuals. However, there is a need for regular evaluation of

sexual behaviours and trends, HIV/STI testing, HIV treatment as prevention, substance use, etc. Future studies should be focused in the following areas:

7.5.1 Further investigation of relationship between sexual behaviors and HIV/STIs

Monitoring trends in sexual behaviours plays an important role in HIV/STI control and prevention. Available study has highlight the improvements that need to be made to ensure that MSM achieve the best prevention outcomes such as willingness to participate in annual HIV and STI testing, and consistent condom use for sexually active MSM [272]. There is currently limited research on changes in sexual behaviour, especially HIV-seroadaptive behaviours; changing patterns of drug use and associated behaviours and evaluation of STI testing and treatment as prevention as an effective prevention strategy, specifically with respect to prevention outcomes among MSM. More research is therefore needed to evaluate whether changes in sexual behaviour, especially HIV-seroadaptive behaviours have probably led to the increased incidence and prevalence of STIs in this population [187,272-275].

7.5.2 Enhancing and promoting the update of regular HIV/STI testing among MSM

Barriers to HIV/STI testing may include fear of positive results, difficulties accessing sexual health services, provider perceptions of low risk, lack of provider knowledge, and limited clinic capacity to meet STI testing needs [276]. Study has shown that testing behaviour was associated

with sexual risk behaviour, but motives to test consistently remain unclear [277]. Evidence-based testing guidelines are needed to achieve optimal reductions in STI transmission in the future.

7.5.3 Evaluation of HIV treatment as prevention (TasP) and pre-exposure prophylaxis (PrEP) strategy

TasP and PrEP are important strategies to reduce HIV transmission, which may be particular relevance of for MSM, who accounts for more than half of the HIV infections [17,278]. Current data are limited regarding treatment as prevention as an isolated prevention strategy, specifically with respect to prevention outcomes among MSM. According to the available literature, treatment as prevention appears to significantly reduce HIV transmission. In randomized control trials, treatment as prevention has significantly prevented onward HIV transmission [49,279], but several observational studies have not consistently replicated the findings [55,280]. In the era of biomedical HIV prevention, STIs are increasing in many populations, bringing new challenges and opportunities. PrEP has created a tension between HIV and STI prevention that needs to be confronted: condomless sex is becoming more frequent [281]. Additional research is needed to evaluate the effectiveness of antiretroviral therapy in the real world sexual practices and clinical practice to further inform clinical guidelines and recommendations [282-285]. Studies primarily aimed at biomedical HIV prevention are needed to incorporate designs to include STI as well as HIV [281].

7.5.4 Demand for more knowledge of increasing resistance and decrease susceptibility to antimicrobials

Antimicrobial resistance in Neisseria gonorrhoeae is increasing relentlessly and adverse consequences of chlamydia infection remain prevalent [61,286]. Neisseria gonorrhoea has developed resistance to all classes of antibiotics of used for empirical treatment, and clinical treatment failure caused by extensively resistant strains [286]. Limited studies that investigated factors contributing to antimicrobial-resistant Neisseria gonorrhoeae, especially from low- and middle-income countries where both gonorrhoea and antimicrobial resistance are most common [286]. Future research studies should focus on associations with increased risk of antimicrobial-resistant neisseria gonorrhoeae in older age groups and amongst travelers, as well as those with decreased risk of Antimicrobial-resistant Neisseria gonorrhoeae in black and Aboriginal groups living in high-income countries. Establishment of surveillance systems for antimicrobial resistance, improved currant surveillance system that collects key information such as age, same sex partnerships, travel-associated sexual partnerships, and sentinel surveillance in specific groups, might allow earlier identification of emerging resistance and of risk factors that could alert more intensive follow-up and prevention interventions in groups at high risk of Antimicrobial-resistant Neisseria gonorrhoeae [286].

7.5.5 Exploring substance use during sex ('chemsex'), alcohol and illicit drug use among MSM population

Intensive recreational drug use may be facilitating increase STI transmission [274,287,288]. Interest in substance use among MSM has emerged from a concern about how 'chemsex' might increase the likelihood of acquiring or transmitting of HIV/STIs. Despite being the focus of widespread research, health provider and media attention, data relating to the prevalence and profile of substance use among MSM are incompleted and the role of substances in sexual risk-taking behaviours is still poorly understood [289]. Changing patterns of drug use and associated behaviours should be monitored to enable sexual health services to plan for the increasingly complex needs. MSM attending sexual health services should be assessed for recreational drug use and disclosure should prompt health promotion, harm minimization and wellbeing interventions.

Many challenges still remain to be addressed, including identifying political, socioeconomic and cultural factors that limit recognition of HIV/STIs as an important public health problem; and finding effective ways to target priority populations with HIV/STI prevention measures. More research is needed to develop and implement effective and long-lasting policies and prevention measures, which should focus on behavioural risks, enhance HIV/STI testing and treatment guidelines in order to control HIV/STI prevalence and transmission among priority populations in Australia.

7.6 Closing remarks

Sexually transmitted infections (STIs) are a growing and major public health concern, which can facilitate the transmission of HIV and are associated with severe disease. In recent years, some STIs have begun to (re)emerge at high rates, particularly among MSM in high-income countries. Moreover, treatment for some STIs, especially gonorrhoea, has been compromised by antimicrobial drug resistance. Much progress has been made in the detection, treatment, and prevention of HIV and other STIs in Australia. However, notifications of HIV and other STIs have been on the rise for the past decade in Australia. The studies described in this thesis have increased our knowledge and understanding of STI epidemiology, seasonal variation patterns of STI, HIV testing among MSM and heterosexuals. Furthermore, the study sheds light on the treatment efficacy of antibiotics for STI in South Australia.

The research described in this thesis was an exploratory look at STI epidemiology, seasonal variation patterns of STI, HIV testing and treatment efficacy for STI in South Australia. Based on quantitative analyses, a number of important findings emerged regarding STI epidemiology among MSM and heterosexuals. The results of this study will be helpful to increase the awareness of the scope of the STI problem and to demonstrate the application of biology, epidemiology, and behavioral aspects of STIs to the development of public health policy and programmes. Public health policy development and practice for STI control and prevention should include behavioral interventions and medical screening/treatment intervention of sexually transmitted infections. Epidemiological studies are needed to monitor changing

epidemics and trends of HII/STIs over time, evaluate interventions and clinical outcomes, and to guide public health policies and strategies to minimise further burden of STIs. To enrich the STI control and prevention strategies, a multidisciplinary collaborative approach is required. Moreover, consolidate and consistent surveillance is warranted to identify new and re-emerging infections[90,290].

To continue the battle against HIV/STIs epidemic, resources, regular HIV/STI testing, effective and availability of therapy, appropriate (biomedical) interventions, and the infrastructure and resources to provide implementation are needed for success. Clinicians, scientists, public health practitioners and social workers should work together to better understand the epidemiology of HIV/STIs and the priority populations, the performance and characteristics of diagnostic tests, the effective treatment for the infection, and promote and enhance high coverage of testing and treatment in populations at highest risk of infection.

7.7 References

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APPENDICES

Appendix A: Ethical Approval Letter (SA Health)

Government of South Australia
SA Health

SA Health Human Research Ethics Committee
Level 10, Citi-Centre Building
11 Hindmarsh Square
ADELAIDE SA 5000
Telephone: (08) 8226 6367
Facsimile: (08) 8226 7088

Mr Bin Li
STD Services
Department of Internal Medicine Services
Royal Adelaide Hospital
Level 1, 275 North Terrace
ADELAIDE SA 5000

Dear Mr Li,

HREC reference number: HREC/12/SAH/87

Project title: Epidemiology of Gonorrhoea and its interaction with other major STDs in South Australia.

RE: HREC Application – Approval

Thank you for submitting the above project, which was considered by the SA Health HREC at its meeting held on 5th December 2012.

I am pleased to advise that your application has been granted full ethics approval and appears to meet the requirements of the *National Statement on Ethical Conduct in Human Research*.

Please note the following conditions of approval:

- Approval must be sought from the Aboriginal Health Research Ethics Committee.
- The research must be conducted in accordance with the 'National Statement on Ethical Conduct in Human Research.'
- A progress report, at least annually, must be provided to the HREC.
- When the project is completed, a final report must be provided to the HREC.
- The HREC must be notified of any complaints by participants or of adverse events involving participants.
- The HREC must be notified immediately of any unforeseen events that might affect ethical acceptability of the project.
- Any proposed changes to the original proposal must be submitted to and approved by the HREC before they are implemented.
- If the project is discontinued before its completion, the HREC must be advised immediately and provided with reasons for discontinuing the project.

HREC approval is valid for 3 years from the date of this letter.

Should you have any queries about the HREC's consideration of your project please contact Sarah Lawson, Executive Officer of the HREC, on (08) 8226 6367 or hrec@health.sa.gov.au

You are reminded that this letter constitutes ethical approval only. You must not commence this research project at a SA Health site until separate authorisation from the Chief Executive or delegate of that site has been obtained via the completion of a Site Specific Assessment form. Please contact David van der Hoek via email at ResearchGovernance@health.sa.gov.au to discuss this process further.

The HREC wishes you every success in your research.

Yours sincerely

Rebecca Horgan
CHAIRPERSON
HUMAN RESEARCH ETHICS COMMITTEE

6/12/12

Appendix B: Ethical Approval Letter (Royal Adelaide Hospital)

Government of South Australia
SA Health

Central Adelaide Local Health Network
Research Governance Office
Level 3, IMVS South Building
Frome Road, Adelaide SA
Australia 5000
T : 08 8222 3839
F : 08 8222 3414

22 January 2012

Mr Bin Li
Data Management – STD Services
Department of Internal Medicine Services
Royal Adelaide Hospital
Level 1, 275 North Terrace
Adelaide SA 5000

Dear Mr Li

HREC reference number: HREC/12/SAH/87
SSA reference number: NA
Project title: Epidemiology of Gonorrhoea and its interaction with other major STDs in South Australia

RE: Site Specific Assessment Review

Thank you for submitting an application for authorisation of this project. I am pleased to inform you that authorisation has been granted for this study to commence at the following site: **Royal Adelaide Hospital**

The following conditions apply to the authorisation of this research project. These are additional to those conditions imposed by the Human Research Ethics Committee that granted ethical approval to this project.

Please note the following conditions of authorisation:

1. Authorisation is limited to the site/s identified in this letter only.

2. Project authorisation is granted for the term of your project outlined in Section 9 of the SSA, or until the project is complete (whichever date is earlier).

3. The study must be conducted in accordance with the conditions of ethical approval provided by the lead HREC, and in conjunction with the standards outlined in the *National Statement on Ethical Conduct in Human Research* (2007) and the *Australian Code for the Responsible Conduct of Research (2007).*

4. The Coordinating Principal Investigator is responsible for notifying the institution via the Research Governance Officer of any changes to the status of the project within a timely manner:

   a. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project, and which are submitted to the HREC for review, are copied to the research governance officer;
   b. Proposed amendments to the research protocol or conduct of the research which only affects the ongoing site acceptability of the project, are to be submitted to the research governance officer;
   c. Proposed amendments to the research protocol or conduct of the research which may affect both the ongoing ethical acceptability of the project and the site acceptability of the project are to be submitted to the research governance offer after a HREC decision is made.

5. A copy of this letter should be maintained on file by the Coordinating Principal Investigator as evidence of project authorisation.

6. Notification of completion of the study at this site is to be provided to the Research Governance Officer.

Should you have any queries about the consideration of your Site Specific Assessment form, please contact the Research Governance Office. The SSA reference number should be quoted in any correspondence about this matter.

Yours sincerely

Bernadette Swart

Manager Research Governance, IP and Contracts
Royal Adelaide Hospital and SA Pathology
Ph: 8222 3890
Email: bernadette.swart@health.sa.gov.au

Appendix C: Ethical Approval Letter (Aboriginal Health Research Ethics Committee)

AHREC

ABORIGINAL HEALTH
RESEARCH ETHICS COMMITTEE

14 February 2013
Mr Bin Li
Department of Internal Medicine Services
Royal Adelaide Hospital/The Discipline of Public Health
University of Adelaide
Level 1, 275 North Terrace
Adelaide SA 5000

RE: Epidemiology of Gonorrhoea and its interaction with other major STDs in South Australia
REFERENCE NO: 04-13-492

Dear Bin

Thank you for submitting your research project *Epidemiology of Gonorrhoea and its interaction with other major STDs in South Australia* on the 7 February 2013 for ethical consideration.

At our last meeting your application was assessed and I am pleased to inform you that this proposal has met with support and that the committee has decided that your application be recommended. The duration of approval is from 7 February 2013 until the expected completion date of your project indicated as 31 December 2015.

While you study is granted approval the committee has asked if you could provide some additional information. First, members wanted to know how this study will inform policy. Second, they noted that as these data sets are already available and reported on publicly, what new knowledge is this study intending to create that is not already available? Third, they questioned whether or not there are methodological issues of bias in the additional information from Clinic 275. Finally, they requested your assurance as to sensitive and understanding reporting of gonorrhoea in the APY Lands in relation to this study.

In accordance with the NHMRC guidelines, *National Statement on Ethical Conduct in Human Research* (2007), we require at regular periods, at least annually, reports from principal researcher(s). An 'Annual Progress or Final Report' template is available at: http://www.ahcsa.org.au/research-ethics/

If you require any further information please do not hesitate to contact the Executive Officer or myself. We wish you well with the project and look forward to receiving a copy of your report.

Sincerely yours

MS LUCY EVANS
CHAIRPERSON
Ref: Proposal/Approval/14February2013

Aboriginal Health Council of South Australia Inc.

AHREC is a sub-committee of AHCSA

9 King William Road Unley SA 5061 PO Box 981 Unley SA 5061
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Appendix D: Clinical Case Notes for Female at ASHC

Sexually Transmitted Disease Services **Female** **Clinic 275**

Record Number ☐☐☐☐☐☐ Clinic Number

Drug sensitivity	Hepatitis B status	Hepatitis C status

Family Name..... Given Names.....

Residential Address.....

Residential Address.....

Residential Address.....

Residential Address.....

Residential Address.....

Contact Address.....

Phone.....

Mobile.....

Email.....

1. Residential Post Code	
2. Date of Birth	
3. Martial Status 1. Never Married 2. Married/Defacto 3.W/S/D	
4. Sex 2. Female	2
5. Race 1. Aboriginal 2. Asian 3. Caucasian 4. Other 5. African	
6. Country of Birth	
7. Level of Education 1. yr 7 2. yr 8 3. yr 9 4. yr 10 5. yr 11 6. yr 12 7. TAFE Cert/App. 8. TAFE Dip. 9. Uni Deg/High Deg	

8. Drug Allergy	1. None 2. Penicillin 3. Other 4. Multiple	
10. Previous STD	1. None 2. GC 3. Syphilis 4. Chlamydia/NGU 5. Herpes 6. Warts 7. HBV 9. Other	
11. Ever had a HIV test	1. No test 2. Negative 3. Positive 4. Indeterminate Date of test:-___/___/_____	
12. Ever any Blood risk	1. Nil 2. Tattoos 3. IDU 4. Blood Trans 5. (2&3) 6. (2&4) 7. (3&4) 8. (2,3,4)	
13. HBV Vaccination	1. No 2. Yes	

DATE	COMMENT

Record Number | | | | | | |

Female STD Episode

Referral By:

Postcode | | | | |

FAMILY NAME.....

SEEN BY

DAY

GIVEN NAME.....

TIME IN

DAY

TIME OR

HOUR

WAT

1. Date of visit — 2 0

Occupation

History

2. Employment: 1. U/E 2. Student 3. CSW 4. Home duties 5. Employed 9. Other

3. Occupation: 1. Manager 2. Professional 3. Tech 4. Commun 5. Clerical 6. Sales 7. Machin 8. Labourer 9. N.A.

4. Reason for visit: 1. Asym vol 2. Sym vol 3. Contact 4. Doctor ref 5. Other ref 6. Clinic

5. Symptoms & signs: 1. None 2. Discharge 3. Dysuria 4. Genital lump 5. Genital ulcer 6. Itch 7. Rash 8. Pelvic pain/mass 9. Other

6. Duration of main symptom (days): 1. Asym 2. 0 – 3 3. 4 – 7 4. 8 – 14 5. Over 14 6. Ausc

7. Current Medication (14 days): 1. None 2. Antibiotic 3. Other 4. Antibiotic & other

8. Blood risk (12 months): 1. Nil 2. Tattoos 3. IDU 4. Bld transf 5. (2&3) 6. (2&4) 7. (3&4) 8. (2,3,4) 9. Other

9. HIV test (12 mths): 1. No 2. Yes 9. Unknown

11. Pregnant: 1. No 2. Yes 3. Uncertain — LMP: K: G: P:

12. Contraception: 1. None 2. Pill 3. IUCD 4. Other

13. No. Partners/3mth LSI: 1. One 2. Two 3. Three 4. Four 5. Five or more 6. None

14. Sex partner (12 months): 1. Solely male 2. Male & female 3. Solely female 4. Nil

15. Sex contacts (12 months): 1. Nil 2. S.A. only 3. Interstate 4. Overseas 5. (3&4)

16. Steady partner: 1. No 2. Yes — Duration

Genital Examination

Examination

1. Yes 2. No — LPU:

20. Vaginal smear: 1. Not done 2. Negative 3. GC 4. Candida 5. Trich 6. G Vag 7. Candida & Trich 8. Other — pH=

21. Vaginal culture: as for smear

22. Cervical smear: 1. Not done 2. Vag contam 3. GC 4. +poly 6. ++poly 5. +++poly

23. Cervical culture: 1. Not done 2. Negative 3. Positive 4. Other

24. Cervical chlamydia: 1. Not done 2. Negative 3. Positive

M. Genitalium: 1. Not done 2. Negative 3. Positive

25. Throat culture: 1. Not done 2. Negative 3. GC 4. Other 5. Chlamydia 6. GC & Chlamydia

26. Rectal culture: 1. Not done 2. Negative 3. GC 4. Other 5. Chlamydia 6. GC & Chlamydia

Rectal Chlamydia: 1. Not done 2. Negative 3. Positive

27. Herpes culture: 1. Not done 2. Negative 3. Type 1 4. Type 2 5. Detected

28. Syphilis EIA: 1. Not done 2. Non reactive 3. Prev reactive 4. Equivocal 5. Reactive

29. Syphilis MPH: 1. Not done 2. Non reactive 3. Weak reactive 4. 1:1 or more — Titre=

30. Syphilis TPPA: 1. Not done 2. Non reactive 3. Prev reactive 4. Reactive minimal 5. Positive Igm 6. Positive IgG

31. Hepatitis B: 1. Not done 2. Negative 3. sAb+ 4. sAg+ eAg+ 5. sAg+ eAg- 6. Other

Assessment

32. Hepatitis C: 1. Not done 2. Negative 3. Prev reactive 4. Reactive 5. Indeterminate

33. HIV serology: 1. Not done 2. Negative 3. Prev reactive 4. Reactive 5. Indeterminate

34. Diagnosis: 1. No illness 2. HIV positive 3. GC 4. Syphilis 5. Herpes 6. Chlamydia 7. Warts 8. Trich 10. Candida 11. Crabs 12. Scabies 13. Molluscum 14. B vag 15. Hep B 16. Ur. Irritation 17. Balanitis 19. Non STD Illness 20. Uncertain 21. Other STD 22. PCC 23. Hep C 24. nPEP 25. M Gen

Treatment

35. Treatment: 1. None 2. Penicillin 3. Tetracycline 4. Cryotherapy 5. Nitroimidazoles 6. Antifungals 7. Podophyllin 8. Miticides 9. Macrolides 10. Cephalosporins 11. Other 12. Quinolones 13. Hep B Vaccine 14. Antivirals

Follow up: 1. None 2. M.O. 3. Results 4. Referral 5. Recall

Time out

FIRST FOLLOW-UP VISIT Seen By 1. Doctor 2. Nurse

Time In Day Time Dr

36. Date 20

37. Main symptom 1. Worse 2. Unchanged 3. Improved 4. Resolved 5. Other

38. CC Test of Cure 1. Not done 2. Indicates cure 3. Indicates no cure 4. Other

Date of Test: 20

39. Further follow-up 1. None 2. M.O. 3. Results 4. Referral

HIV result given: ___/___/ 20___ Signature

SECOND FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

THIRD FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

FOURTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. referral

FIFTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

SIXTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

COMPLETION OF EPISODE DATE COMPLETED 20

No. visits 1. One 2. Two 3. Three 4. Four 5. Five 6. Six 7. Seven

Status 1. Completed Survey 2. Did not attend (neg) 3. Absconded 4. Referred 5. Recall

Doctor 1. RMO 2. Reg/RMP 3. MP 4. SMP 5. Consultant 6. Clinical Nurse 8. Med Student 9. Other

FINAL CHECK

Episode No

Referred To: .....

Letter Sent: .....

Revised 2011

Appendix E: Clinical Case Notes for Male at ASHC

Sexually Transmitted Disease Services **Male** **Clinic 275**

Record Number | | | | | | | Clinic Number

Drug sensitivity	Hepatitis B status	Hepatitis C status

Family Name..... Given Names .....

Residential Address .....

Residential Address .....

Residential Address .....

Residential Address .....

Residential Address .....

Contact Address .....

Phone .....

Mobile .....

Email.....

1.	Residential Post Code	
2.	Date of Birth	
3.	Marital Status 1. Never Married 2. Married/Defacto 3. W/S/D	
4.	Sex 1. Male	1
5.	Race 1. Aboriginal 2. Asian 3. Caucasian 4. Other 5. African	
6.	Country of Birth	
7.	Level of Education 1. yr 7 2. yr 8, 3 yr 9, 4. yr 10, 5. yr 11, 6. yr 12 7. TAFE Cert/App, 8. TAFE Dip, 9. Uni Deg/High Deg	

8.	Drug Allergy 1. None 2. Penicillin 3. Other 4. Multiple	
9.	Circumcision 1. Yes 2. No	
10.	Previous STD 1. None 2. GC 3. Syphilis 4. Chlamydia/NGU 5. Herpes 6. Warts 7. HBV 9. Other	
11.	Ever had a HIV test 1. No test 2. Negative 3. Positive 4. Indeterminate Date of test:-___/___/_____	
12.	Ever any Blood risk 1. Nil 2. Tattoos 3. IDU 4. Blood Trans 5. (2&3) 6. (2&4) 7. (3&4) 8. (2,3,4) 9. Other	
13.	HBV Vaccination 1. No 2. Yes	

DATE	COMMENT

Record Number | | | | | | |

Male STD Episode

Postcode | | | | |

Referral By:

SEEN BY

DAY

HOUR

FAMILY NAME

GIVEN NAME

TIME IN	DAY		TIME OR	WAIT	
1. Date of visit			1	2 0	Occupation
2. Employment	1. U/E	2. Student	3. CSW		History
	4. Home duties	5. Employed	9. Other		
3. Occupation	1. Manager	2. Professional	3. Tech		
	4. Commun	5. Clerical	6. Sales		
	7. Machin	8. Labourer	9. N/A		
4. Reason for visit	1. Asym vol	2. Sym vol	3. Contact		
	4. Doctor ref	5. Other ref	6. Clinic		
5. Symptoms & signs	1. None	2. Discharge	3. Dysuria		
	4. Genital lump	5. Genital ulcer	6. Itch		
	7. Rash	8. Pelvic pain/mass	9. Other		
6. Duration of main symptoms (days)	1. Asym	2. 0 – 3	3. 4 – 7		
	4. 8 – 14	5. Over 14	6. Audit		
7. Current Medication (14 days)	1. None	2. Antibiotic	3. Other		
	4. Antibiotic & other				
8. Blood risk (12 months)	1. Nil	2. Tattoos	3. IDU		
	4. Bld transf	5. (2&3)	6. (2&4)		
	7. (3&4)	8. (2,3,4)	9. Other		
9. HIV test (12 mths)	1. No	2. Yes	9. Unknown		
11. No. Partners/3 mth LSI:	1. One	2. Two	3. Three		
	4. Four	5. Five or more	6. None		
12. Sex partner (12 months)	1. Solely male	2. Male & female			
	3. Solely female	4. Nil			
13. Sex contacts (12 months)	1. Nil	2. S.A. only	3. Interstate		
	4. Overseas	5. (3&4)			
14. Steady partner	1. No	2. Yes	Duration		
Genital Examination	1. Yes	2. No	LPU:		
15. Urethral smear	1. Not done	2. <5p/hpf	3. GC		
	4. 5 – 9 p/hpf	5. 10+ p/hpf	6. Other		
16. Urethral culture	1. Not done	2. Negative	3. GC		
	4. Other				
17. Urethral chlamydia	1. Not done	2. Negative	3. Positive		Examination
M. Genitalium	1. Not done	2. Negative	3. Positive		
18. Throat culture	1. Not done	2. Negative	3. GC		
	4. Other	5. Chlamydia	6. GC & Chlamydia		
19. Rectal culture	1. Not done	2. Negative	3. GC		
	4. Other	5. Chlamydia	6. GC & Chlamydia		
Rectal Chlamydia	1. Not done	2. Negative	3. Positive		
20. Herpes culture	1. Not done	2. Negative	3. Type 1		
	4. Type 2	5. Detected			
21. Syphilis EIA	1. Not done	2. Non reactive	3. Prev reactive		
	4. Equivocal	5. Reactive			
22. Syphilis MHA	1. Not done	2. Non reactive	3. Weak reactive		
	4. 1:1 or more	Titre=			
23. Syphilis IFA	1. Not done	2. Non reactive	3. Prev reactive		
	4. Reactive minimal	5. Positive Igm	6. Positive IgG		
24. Hepatitis B	1. Not done	2. sAg-	3. sAb +		Assessment
	4. sAg+ eAg+	5. sAg+ eAg-	6. Other		
25. Hepatitis C	1. Not done	2. Negative	3. Prev reactive		
	4. Reactive	5. Indeterminate			
26. HIV serology	1. Not done	2. Negative	3. Prev reactive		
	4. Positive	5. Indeterminate			
27. Diagnosis	1. No Illness	2. HIV positive	3. GC		
4. Syphilis	5. Herpes	6. Chlamydia	7. NSU		
8. Warts	9. Trich	11. Crabs	12. Scabies		Treatment
13. Molluscum	14. B vag	15. Hep B Acute	16. Ur. Irritation		
17. Balanitis	19. Non STD Illness	20. Uncertain	21. Other STD		
22. PCC	23. Hep C Acute	24. nPEP	25. M. Gen		
28. Treatment	1. None	2. Penicillin	3. Tetracycline		
	4. Cryotherapy	5. Nitroimidazoles	6. Antifungals		
	7. Podophyllin	8. Vilicides	9. Macrolides		
	10. Cephalosporins	11. Other	12. Quinolones		
	13. Hep B Vaccine	14. Antivirals			follow up 1. None 2. M.O. 3. Results 4. Referral 5. Recall
					Time out

FIRST FOLLOW-UP VISIT Seen By 1. Doctor 2. Nurse

Time In Day Time Dr

36. Date 20

37. Main symptom 1. Worse 2. Unchanged 3. Improved 4. Resolved 5. Other

38. CC Test of Cure 1. Not done 2. Indicates cure 3. Indicates no cure 4. Other Date of Test: 20

39. Further follow-up 1. None 2. M.O. 3. Results 4. Referral

HIV result given: ___/___/ 20___ Signature

SECOND FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

THIRD FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

FOURTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. referral

FIFTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

SIXTH FOLLOW-UP VISIT DATE 20

Seen by .....

Time In Day Time Dr

Follow-up 1. None 2. M.O. 3. Results 4. Referral

COMPLETION OF EPISODE DATE COMPLETED 20

No. visits 1. One 2. Two 3. Three 4. Four 5. Five 6. Six 7. Seven

Status 1. Completed Survey 2. Did not attend (neg) 3. Absconded 4. Referred 5. Recall

Doctor 1. RMO 2. Reg/RMP 3. MP 4. SMP 5. Consultant 6. Clinical Nurse 8. Med Student 9. Other

FINAL CHECK

Episode No

Referred To: .....

Letter Sent: .....

Revised 2011

Appendix F: Additional related papers published during candidacy

1. Khaw C, **Li B**, Waddell R. Epidemiological treatment for chlamydia co-infection in men who have sex with men (MSM) with a presumptive diagnosis of urethral gonorrhoea in South Australia. ***Sexually transmitted infections.*** Dec 2012;88(8):580; **doi: 10.1136/sextrans-2012-050687. Epub 2012 Jul 6**.

2. Khaw C, **Li B**, Waddell R. Sexually transmissible infections and characteristics of men aged 60 years and over attending a public sexually transmitted diseases (STD) clinic in South Australia. ***Sexual health.*** Oct 2015;12(5):460-462; **doi: 10.1071/SH15016.**