UNDERSTANDING THE RELATIONSHIP BETWEEN HIV PRE-EXPOSURE PROPHYLAXIS, SEXUALLY TRANSMITTED INFECTIONS, AND ANTIMICROBIAL RESISTANCE

ADAM DALE NEWMAN WILLIAMS

A thesis submitted in fulfilment of the requirements for

the degree of Doctor of Philosophy in Medicine

Cardiff University, October 2023

SUMMARY

HIV pre-exposure prophylaxis (PrEP) prevents the acquisition of HIV. There are concerns around PrEP provision due to risk compensation (RC), a theory that suggests people become less careful when they feel safe. The argument suggests that using PrEP provision could lead to people engaging in higher-risk sexual behaviours, increasing other sexually transmitted infections (STIs), which would exacerbate antimicrobial resistance (AMR) through increased antimicrobial requirements. This PhD explores the influence of PrEP on sexual behaviour among men who have sex with men (MSM) in Wales, with a focus on the impact of the transmission of STIs and AMR. This was achieved using a mixed-methods design with insights from relevant literature.

Interviews were conducted with MSM to explore the relationship between PrEP, STIs, and AMR and to gain an understanding of behaviour changes after PrEP adoption. Anonymous sexual health records and AMR data were analysed to identify trends in PrEP and non-PrEP using MSM. The findings from these two studies, within the context of existing literature, informed the development of the conceptual framework, presenting the relationship between the variables. In response to the COVID-19 pandemic, a survey exploring sexual behaviour during lockdown was conducted with input from the interviews.

Results show that PrEP has had little to no statistical effect on STI rates, with rates reducing among most STIs since PrEP's introduction. The data available does not allow a detailed examination of AMR. Qualitative findings indicate a range of behaviours in response to PrEP uptake. A detailed account of RC is presented, identifying how the previous examinations may have been incomplete. COVID-19 restrictions were adhered to at the beginning of the pandemic, but over time, more people engaged in sexual behaviours with others despite social distancing measures still in force.

Behaviour change is complicated to measure, but what is known is that behaviour is often stable and change difficult, which RC fails to acknowledge. PrEP provision is necessary to protect all populations at risk of HIV. With STI AMR levels increasing, there is a need for greater focus on the identification and prevention of bacterial STIs. There is a need to change the discourse of concern regarding HIV and other STIs.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my supervisory team—Dr David Gillespie, Prof. Fiona Wood, Prof. Kerry Hood, Dr Kathryn Hughes, and Zoe Couzens—for their continuous support over the last 4 years. Their guidance, encouragement, and support have been invaluable in my completion of this thesis. My supervisory team has also helped me grow as a person and an academic, giving me skills to assist my future career. I have been incredibly lucky to have such a dedicated team supporting me.

I would like to give a special thanks to Dave. As my lead supervisor, he has always been available to meet and discuss with me. He has assisted in cultivating my abilities and ambitions, involving me in various projects, and actively seeking my views and opinions.

I would also like to acknowledge Zoe Couzens, my industry supervisor from Public Health Wales. From this partnership, I have gained multiple opportunities to work on projects, which have provided experience in developing myself as a researcher.

Cardiff University and the Centre for Trials Research have provided a secure and enjoyable working environment, allowing me to achieve my successes, and none of this would have been possible without the funding provided by KESS 2.

Finally, I would like to thank everyone who engaged with my research and supported its completion; this includes participants, clinicians, staff in Public Health Wales, and stakeholders.

PREFACE

As I sit down to write this preface, I am filled with a profound sense of gratitude and accomplishment. This PhD thesis represents the culmination of years of rigorous research, tireless dedication, and unwavering support from countless individuals who have played pivotal roles in my academic journey. I am deeply humbled to have reached this milestone, and I am excited to share the fruits of my labour with the academic community and beyond.

Originally, I did not intend to do a PhD after my master's in health psychology. However, a friend who learned of this studentship knew my interest in sexual behaviour and suggested I apply. I was interested in this thesis as I am a gay man myself and am familiar with PrEP, having been offered it previously and knowing many people using it. I was also familiar with the discourse around the language used to describe men who have sex with men (MSM), which I was interested in exploring.

I always found it interesting how simply being MSM led to one being automatically classified as sexually high-risk without any other information being required. The automatic labelling of all MSM as high-risk at a population level suggests a homogeneity among MSM that does not exist, with levels of risk ranging from high to low. While it is well documented that MSM have higher STI rates than our heterosexual counterparts, we also better engage with sexual health services and engage in various health protective measures, but this is overlooked by the research and medical community with a focus only on the negativity of risk. To me, it suggests a layover of historically stigmatising attitudes towards gay people, shame towards sexual activity, and fear induced by the HIV crisis, which leads to this labelling being deemed acceptable.

From my own experience of being a sexually active gay man while existing in a heterosexually normed world, I have a deep understanding of the vast differences with which communities engage in sexual behaviour. From reviewing the literature, I quickly became aware of how research on MSM did not include all MSM, as our community's intricacies and social dynamics were missing in multiple studies, from design to interpretation. It was interesting to hear the sentiment of "nothing about us without us," and while attending the AIDS 2022 conference, one of the panel members spoke of how this would not be fulfilled until the community was

leading projects about our community and not just included to advise. It was then that I realised that I fulfilled this role, and my experience allowed me to describe the intricacies of our social constructs, better reflecting the community. Throughout the thesis, I highlight areas of importance that have previously been missing from the literature.

The COVID-19 pandemic had a major impact on this thesis, occurring six months into the studentship and pausing my data collection and analysis for six months. However, I did not sit idly and took it as an opportunity to develop a new sub-study to explore behaviour during this period. It also provided me with a major opportunity in my work with Public Health Wales, running the evaluation of their National STI Postal Testing service and assisting in gaining its continued funding from the Welsh Government. Viewing the pandemic as an opportunity to engage in more work outside my thesis while progress was slowed, I was able to support the development of and secure the future of an essential service for Wales.

This thesis is intended to be a resource for a wide range of individuals who have an interest in or a connection to the fields of sexual health, risk compensation, and antimicrobial resistance, ranging from academics and policymakers to students and the public. The thesis aims to communicate complex ideas in a way that is accessible to a broader audience, with my artwork and visuals being a method for engaging multiple audiences.

PUBLICATIONS AND AWARDS

Publications from the thesis:

Publication linked to Chapter Three:

- Williams ADN, Wood F, Gillespie D, Couzens Z, Hughes K, Hood K. The relationship between HIV pre-exposure prophylaxis, sexually transmitted infections, and antimicrobial resistance: a qualitative interview study of men who have sex with men. BMC Public Health. 2022 Nov 29;22(1):2222. DOI: https://doi.org/10.1186/s12889-022-14645-0

Publication linked to Chapter Five:

- Williams, A, Gillespie, D, Couzens, Z. Wood F, Hughes K, Hood K. Changing sexual behaviours amongst MSM during the COVID-19 restrictions in Wales: a mixed methods study. BMC Public Health, 2022:22(396). DOI: https://doi.org/10.1186/s12889-022-12821-w

Publications from the partnership with Public Health Wales:

1. Channon, S., Williams ADN., Alvarado, CEA., Gillespie, D. Peer Support for People Living with HIV in Wales: Scoping and Feasibility, 2023 [Report]. Available from: https://www.cardiff.ac.uk/HIV-Peer-Support-Service-PHW.pdf
2. Williams, A. Public Perceptions of Sexual Health Services in Wales, 2021 [Report]. Available from: https://2021/public-perceptions-of-sh-services-in-wales.pdf
3. Williams, A. All Wales Postal Testing Evaluation, 2021 [Report]. Available from: https://postal-testing-report/2021.pdf
4. Williams, A. Fast Track Cardiff and Vale Getting to zero: Survey report, 2021 [Report]. Available from: https://2020/11/ftc-reportv.2.pdf

Blogs from the thesis:

1. Williams, A. World AIDS Day 2020: Bringing an End to HIV, 2020 [Blog]. Available from: https://centre-for-trials-research/world-aids-day-2020-bringing-an-end-to-hiv/
2. Williams, A. COVID Chronicles, 2020 [Blog and Audio]. Available from: https://kess2.ac.uk/covid-chronicles-adam-williams/

Awards from the thesis:

1. PGR Student of the Year, Cardiff University 2023
2. Research Images (Winner), KESS 2 award ceremony 2023
3. Art in Health (Europe Winner), STI & HIV World Congress 2023 (see below)
4. Best Scientific Poster, PRIME Conference 2022
5. LGBTQ+ Thesis of the Year, National Student Pride 2022
6. ART LAB winner (2nd), Creative Cardiff, 2021 (see below)
7. Images of Research (1st) Cardiff University, 2019 (see below)
8. Best oral presentation, 33rd Annual Cardiff Medical Research Symposium 2019

Thesis artwork:

ABBREVIATIONS

AMR	Antimicrobial resistance	**MG**	Mycoplasma genitalium
ART	Antiretroviral therapy	**MSM**	Men who have sex with men
BAME	Black, Asian, and Minority Ethnic	**NAAT**	Nucleic Acid Amplification Test
CAS	Condomless anal sex	**NHS**	National Health Service
GRASP	Gonococcal resistance to antimicrobials surveillance programme	**PEP**	Post-exposure prophylaxis
GUM	Genitourinary medicine	**PHW**	Public Health Wales
HB/UHB	Health board/University health board	**PIS**	Participant information sheet
HBM	Health belief model	**PrEP**	Pre-exposure prophylaxis
HCRW	Health and Care Research Wales	**RC**	Risk compensation
HEP	Hepatitis A/B/C	**RP**	Risk perception
HIV	Human immunodeficiency virus	**SHC**	Sexual health clinic
HPV	Human papilloma virus	**SMREC**	School of Medicine Research Ethics Committee
ITS	Interrupted time series	**STI/s**	Sexually transmitted infection/s
KESS	Knowledge Economy Skills Scholarship	**SWS**	Sexual health in Wales surveillance system
LGV	Lymphogranuloma venereum	**TA**	Thematic analysis

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

CHAPTER ONE
INTRODUCTION

My thesis, also known as the UPrEP study, is a study exploring the influence of HIV pre-exposure prophylaxis on sexual behaviour among men who have sex with men in Wales, with a focus on the impact of transmission of sexually transmitted infections and levels of antimicrobial resistance. This project uses a combination of qualitative and quantitative methods, with insights considered from relevant literature. This chapter presents an introduction to the study.

1.1 THE PROBLEM

HIV pre-exposure prophylaxis (PrEP) is a medication taken before sexual contact that prevents an individual from acquiring HIV even if exposed to the virus. Clinical trials have identified it as highly effective when taken as guided, and it is now recommended by the World Health Organisation.[1-3] Globally, PrEP has largely been promoted towards men who have sex with men (MSM), who have received it positively with increasing levels of uptake.[4] Since its introduction, PrEP has received mixed reviews from healthcare professionals, scientists, and policymakers due to concerns surrounding risk compensation. Risk compensation is a theory suggesting that people adjust their behaviour based on their perception of risk, with people becoming less careful when feeling safer. In terms of PrEP and sexual behaviour, the argument is that the use of PrEP to prevent HIV would result in people engaging in higher-risk sexual behaviours such as more condomless sex, group sex, and an increased number of partners.[5,6] Some fear that this potential behaviour change, particularly the reduction in condom use, may lead to an increase in the transmission of other sexually transmitted infections (STIs) among PrEP users and associated communities.[6] Some have extended this argument and fear that the increased transmission and diagnosis of STIs would exacerbate antimicrobial resistance (AMR) through the increased consumption of antimicrobials for treatment.[5]

There is currently no robust evidence to either refute or support the above theory linking PrEP use, risk compensation, STIs, and AMR. While there is some evidence of STIs increasing among PrEP cohorts, which has then been attributed to risk compensation[7-9], the interpretation of

these findings and hence their implications are limited by surveillance and selection biases, which may exaggerate the results. This project aims to provide a detailed understanding of PrEP use among MSM in Wales, exploring PrEP's relationship with STIs and AMR. Findings will provide health professionals, policymakers, and service users with high-quality evidence to inform decision-making about the future use of PrEP in Wales.

1.2 AIMS AND OBJECTIVES

The **aims** of this thesis are:

- To explore the relationship between HIV PrEP, STIs, and AMR in relation to potential risk compensation among MSM in Wales,
- To understand the impact PrEP provision has had on STIs and AMR among MSM.

To achieve the above aims, three main **objectives** were set:

1. Describe the longitudinal trends of STIs and AMR in Wales before and following the introduction of PrEP:
    - *Examining the number of infections, rates of testing, and positivity rates for STIs pre- and post-PrEP introduction,*
    - *Examining trends in the sensitivity of Neisseria Gonorrhoeae samples to various antimicrobials pre- and post-PrEP introduction.*
2. Describe the understanding, perceptions, and health beliefs of MSM about PrEP, STIs, and AMR:
    - *Knowledge and perceived impact of PrEP,*
    - *Factors contributing to condom use among MSM,*
    - *Knowledge and concerns surrounding STIs/AMR and prevention.*
3. Develop a conceptual framework that articulates the hypothesised causal relationships between PrEP use, STIs, and AMR.

The research period for this thesis occurred during the COVID-19 pandemic, with the variables being studied heavily impacted by its associated restrictions on behaviour, an additional aim and associated objectives were developed:

Aim: to understand the impact that the COVID-19 pandemic had on the relationships and variables studied within the thesis.

Objective: identify the extent to which the COVID-19 pandemic functioned as a contextual factor affecting the relationships described:

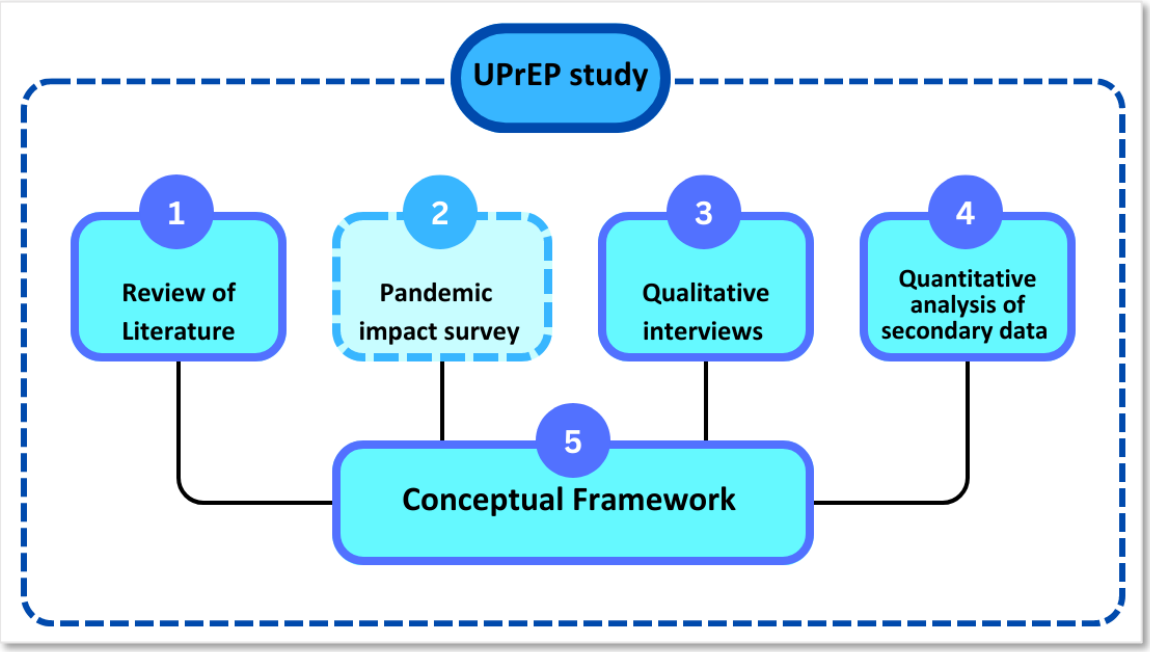
- *Impact on the variables and relationships described within the data,*
- *Identify any wider learning for future pandemic response.*

1.3 PROJECT ORGANISATION

To meet the aims and objectives, a mixed-methods design was adopted. The research combined quantitative and qualitative approaches into a single project. This mixture of methods provides a more comprehensive understanding of the aims, allowing intricate relationships to be explored in greater detail.[10] The combination of methodologies can also enhance rigour and improve results by providing a more comprehensive and complete understanding of how to achieve the aims and objectives.[11]

The thesis has five sections (see Figure 1.1) with the studies originally designed to be conducted consecutively, starting with the quantitative study, followed by a qualitative study, with the development of a conceptual model being an ongoing process. The conceptual model is developed from the literature and then reformulated to include findings from the quantitative and qualitative studies. Due to the COVID-19 pandemic, the order of the studies was altered, and a new study was added. For context, this PhD started in October 2019, with the COVID-19 pandemic occurring in March 2020, within 6 months of initiation. Public Health Wales (PHW), acting as an industry partner for the PhD, provided the STI and AMR surveillance data for the quantitative study. However, as PHW staff were redeployed to work on urgent pandemic-related work, they were unable to provide the data, resulting in a 6-month delay. PHW agreed that the data would be provided after the immediate pandemic response was dealt with, but it was unknown when this would be. The qualitative study was also delayed, but by adjusting the design to online data collection, I was able to begin this before the quantitative study. While waiting for these studies to start, I developed a sub-study to explore the impacts of COVID-19 on sexual behaviour. As all data collected would be affected by the pandemic and associated restrictions, it was important to understand the impact.

Figure 1.1 Structure of the UPrEP project.



1.4 APPROVAL AND GOVERNANCE

1.4.1 Ethical Approval and Sponsorship

Each study received full ethical approval from the appropriate source. Chapters 3 and 5 received approval from Cardiff University's School of Medicine Research Ethics Committee (Ref: SMREC 20.56, Ref: SMREC 20.21). Chapter Four received approval from the NHS Health Research Authority and Health and Care Research Wales, approving to undertake the research and to access and use of anonymised patient-level data (Ref: 20/HCRW/0026). Cardiff University sponsored all studies.

[See Appendix 1 for ethical approval letters]

1.4.2 PhD Studentship

The Knowledge Economy Skills Scholarship (KESS 2) provided funding for the three-year studentship. KESS 2 was a pan-Wales operation supported by European Social Funds through the Welsh Government. KESS 2 links companies and organisations with academic expertise in the higher education sector in Wales to undertake collaborative research projects. These industry partners partly fund the studentship based on the size of the company. As part of this studentship, PHW functioned as the industry partner and was thus able to aid in the design of the project to ensure that the direction of the project had an impact within the

context of sexual health in Wales. As per the terms of the studentship, I engaged in various projects with my industry partner throughout the PhD; these include:

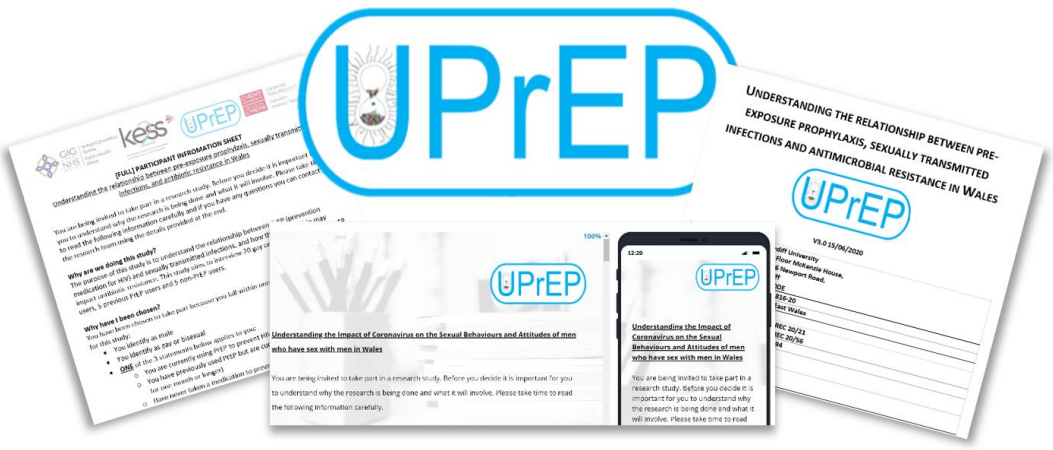
- An evaluation of the STI Postal Testing Service for Wales
- A survey study exploring public perceptions of sexual health services in Wales
- A scoping and feasibility study exploring the development of a national peer support service for people living with HIV in Wales

1.5 THE UPREP STUDY

In response to the introduction of HIV pre-exposure prophylaxis in Wales, the UPrEP study was developed to **U**nderstand **PrEP**'s relationship with sexually transmitted infections and antibiotic resistance. In the initial stages of the project, a study acronym and logo were designed using the study's winning entry to Images of Research 2019. The logo was used throughout on information sheets, advertisements, and relevant documents (see Figure 1.2).

This study is part of a portfolio of work within Cardiff University's Centre for Trials Research in the field of HIV and sexual health. Dr David Gillespie (supervisor of this studentship) is completing a fellowship exploring ways to improve adherence to PrEP. Additionally, the department is a partner of the Fast Track Cities initiative, supporting the Cardiff and Vale branch, and works closely with Public Health Wales. Two of the supervisors, Dr Kathyrn Hughes, and Prof. Fiona Wood, are employed within the Division of Population Medicine at Cardiff University and have a long-standing programme of work on clinical and behavioural aspects of common infections. This study was conducted in the context of multiple ongoing projects and initiatives related to HIV in Wales.

Figure 1.2 UPrEP logo used for study documents.



1.6 THESIS SYNOPSIS

This chapter has introduced the overall study:

- **CHAPTER TWO** describes the current evidence base in relation to PrEP, sexually transmitted infections, and antibiotic resistance.
- **CHAPTER THREE** outlines the methods and findings from the qualitative interviews conducted with MSM.
- **CHAPTER FOUR** presents the quantitative methods and analysis of the routine health data provided by Public Health Wales.
- **CHAPTER FIVE** describes changes in sexual behaviours in relation to the COVID-19 pandemic. With consideration to how these impacts have changed the situation for sexual health research.
- **CHAPTER SIX** outlines the conceptual framework of risk compensation, identifying the variables involved in the relationship between PrEP, STIs, and AMR, using literature and findings from previous chapters.
- **CHAPTER SEVEN** provides a summary and evaluation of the research findings and their importance in a wider context. The limitations of the project will be evaluated with a discussion of the implications of this project.

CHAPTER TWO
BACKGROUND

This chapter outlines the background information and current guidelines related to various sexually transmitted infections covered within this project and the growing problem of antimicrobial resistance. The situation of HIV pre-exposure prophylaxis (PrEP) in Wales is discussed, along with current recommendations and the theoretical domains of risk compensation. This review includes various sources of literature, including medical, psychological, sociological, and public health literature. The chapter concludes by identifying the gaps in the research.

The literature presented in this chapter was identified via a search at the initiation of the PhD, with articles being collected throughout the next three years, building a collection of scientific journals and reports used for the development of this chapter. The initial search terms included 'PrEP/HIV PrEP,' 'PrEP + STIs,' 'PrEP + antimicrobial resistance', and 'PrEP + risk compensation'. From the early papers identified, forward and backward citation searches were also conducted to develop a literature base.

[See Appendix 2 for the full list of search terms]

2.1 SEXUALLY TRANSMITTED INFECTIONS

Sexually transmitted infections (STIs) are a major public health concern, associated with a range of issues. While most STIs can be treated or managed if identified early, when left undiagnosed and untreated, STIs can cause a range of long-term health problems, from impacting fertility to cardiovascular and neurological damage. Along with the physical impacts, there is a stigma surrounding STIs, which can seriously impact the health and well-being of affected individuals.[12] There are numerous STIs, including very rare infections, but the focus for health agencies remains on the prevention of the most common STIs: gonorrhoea, chlamydia, syphilis, genital herpes, and genital warts, along with HIV and hepatitis. Each of these will be discussed, with Figure 2.1 presenting a summary of the infections. The testing, prevention, treatment, and burden of infection referred to below are Wales-specific.

2.1.1 Gonorrhoea

Infection and Symptomology

Gonorrhoea (*Neisseria gonorrhoeae*) is a bacterial STI transmitted through contact with infected genital fluids (discharge, semen, or vaginal fluid). The bacteria can infect the cervix, urethra, and rectum, as well as the throat and eyes. Symptoms of gonorrhoea include a thick green or yellow discharge from the vagina, penis, or rectum, pain when urinating, and bleeding between periods. It can lead to more serious long-term health problems if left untreated, such as pelvic inflammatory disease or infertility. In men, 90% present with symptoms, but it is suggested that only 50% of women present with symptoms.[13]

NOTE: *most previous work relating to STIs refers to symptomology and testing concerning men and women or male and female. However, this terminology is not inclusive of trans or non-binary individuals. There is a move to use more inclusive language focused on biology, i.e., penis or vagina and cervix, or male or female associated anatomy instead of assuming that all men have penises and women vaginas/cervixes. The terms men and women are used as the sources use this terminology.*

Testing, Treatment, and Prevention

Gonorrhoea can be identified through testing samples of discharge collected using a swab for the vagina, throat, and rectum, or with urine samples for people with a penis. This can be completed in genitourinary medicine (GUM) clinics using microscopy to identify intracellular gram-negative diplococci, or in microbiology laboratories through a positive culture or a nucleic acid amplification test (NAAT) for gonorrhoea bacteria. Pre-COVID, in Wales, the process involved microscopy of samples within GUM clinics, with additional samples sent to laboratories to be cultured and assessed for antimicrobial sensitivity.[14] The adoption of postal testing in response to the COVID-19 pandemic has resulted in individuals providing swab samples directly to a lab to be tested. In Wales, individuals identified as having a positive test for gonorrhoea are contacted by their local GUM clinics, informed of the result, and provided with an appointment to receive treatment where samples are collected for antimicrobial sensitivity testing.[15] Current treatment includes a single intramuscular injection of 1g of ceftriaxone. After receiving treatment, it is recommended the patient have

a follow-up test to ensure the infection has been cleared.[14] Prevention of gonorrhoea is usually achieved through barrier methods such as condoms and dental dams.[13]

Burden of infection

Public Health Wales runs the Sexual Health in Wales Surveillance Scheme and has previously produced quarterly reports presenting STI data in Wales. Their last quarterly report, published in July 2019, provided data up to July 2019 and indicated that new gonorrhoea infections have been increasing year on year, particularly among MSM.[16] The last full year of data available is from 2018, and by combining data from the four quarterly reports, the data show that MSM are the major risk group, accounting for 56% of all infections in 2018. This approach was also used for the following infections to identify risk groups, as annual reports were not available from the Public Health Wales archived files.[17-20] Gonorrhoea is currently under global surveillance due to prominent levels of multi-drug antibiotic resistance. This results in all positive gonorrhoea samples identified being routinely tested for antimicrobial sensitivities.[21] This topic is further expanded on in Section 2.2.

2.1.2 Chlamydia

Infection and Symptomology

Chlamydia (*Chlamydiae trachomatis)* is a bacterial STI commonly transmitted through contact with infected genital fluids. The bacteria can infect the cervix, urethra, and rectum, as well as the throat and eyes. Chlamydia is often transmitted due to a lack of awareness of the infection due to a lack of symptoms, as 80% of women and 50% of men do not show symptoms. Symptoms can include painful urination, unusual discharge from the infected site, testicular pain or abdominal pain, and vaginal bleeding. Chlamydia infections are usually uncomplicated and not a serious health problem. In rare circumstances, people can have complicated infections, and if left untreated, the infection can spread throughout the body and result in long-term health problems.[22]

Testing, Treatment, and Prevention

Testing for chlamydia occurs from samples taken from the throat, anus, vagina, or penis and detected using NAATs. Samples were previously collected in GUM clinics, but now can be collected independently using the postal testing service. Chlamydia samples are not routinely assessed for antimicrobial sensitivity.[23] The standard recommended treatment is the

antibiotic Doxycycline (200 mg, taken twice daily for 7 days). After receiving treatment, patients are recommended to have a follow-up test to ensure the infection has been cleared.[22] Prevention of chlamydia is usually achieved through barrier methods.[22]

Burden of infection

Chlamydia is the most common STI in the UK (including Wales), with one in ten of those tested finding positive results.[24] Those aged under 25 are the largest risk group for Chlamydia in Wales, with 70% of new infections being identified in this group in 2018.[17-20]

2.1.3 Syphilis

Infection and Symptomology

Syphilis *(Treponema pallidum)* is a bacterial infection that is transmitted through sexual contact with someone who is infected. Infection mainly occurs through contact with an infected sore. It is also transmitted through the sharing of needles used to inject drugs. Syphilis symptoms are not always obvious and disappear over time. There are various stages of syphilis, including primary, secondary, latent, and late/tertiary. At each stage, various symptoms can present before disappearing, but some people will present with no symptoms. If left untreated, syphilis can spread to other parts of the body and cause long-term health problems.[25]

Testing, Treatment, and Prevention

Diagnosing syphilis can be dependent on the symptoms with which the patient presents. Patients with sores or lesions can be identified through examination by a sexual health specialist, laboratory diagnosis, and serological tests. Syphilis is identified through serological testing, which requires a blood sample from patients.[26] Treatment for syphilis is usually a single intramuscular dose of the antibiotic benzathine penicillin. Late latent syphilis requires three doses of benzathine taken over the course of three weeks.[26] Syphilis can be prevented using barrier methods.[25]

Burden of infection

Syphilis was almost eradicated, but in recent years cases have been rising, with outbreaks occurring in specific groups such as MSM. In 2018, 61% of new infections were among MSM.[17-20] While case numbers remain small, they are closely monitored by PHW to ensure clusters are identified and treated in a timely manner.[27]

2.1.4 Human Immunodeficiency Virus (HIV)

Infection and Symptomology

HIV is a virus that damages the cells of the immune system, weakening their ability to fight everyday infections and disease. Ongoing infection without treatment can result in acquired immune deficiency syndrome (AIDS). This describes the various life-threatening infections and illnesses that can occur when the virus has severely damaged the immune system. HIV is found in bodily fluids, including semen, vaginal and anal fluids, blood, and breast milk. It can be transmitted through unprotected vaginal or anal sex, although it can be transmitted through the sharing of needles. It can also be transmitted through oral sex, but this is an exceedingly rare occurrence. Initial symptoms of HIV can be difficult to identify; it is a flu-like illness, usually occurring 2–6 weeks after infection and lasting for 7–14 days before symptoms disappear. As the virus slowly damages the immune system, more symptoms could appear, but these can vary and may only occur years after the infection. Annual testing for those at risk of HIV is recommended to avoid late diagnosis and reduce damage to the immune system.[28]

Testing, Treatment, and Prevention

HIV testing involves testing a sample of your blood or saliva for signs of the infection. If the first test suggests an HIV infection, a further blood test will be taken to confirm the result. If positive, people are referred to a specialist HIV clinic for more tests and a discussion about treatment options. HIV has no cure, but daily antiretroviral therapy (ART) can stop the virus from damaging the immune system, ensuring a long and healthy life. Those on effective ART have undetectable levels of HIV, which means they cannot transmit the virus to others.[28] As for prevention, emergency HIV prevention medicine (post-exposure prophylaxis; PEP) can inhibit infection if started within 72 hours of exposure. Additionally, individuals can use ART medications prophylactically, known as pre-exposure prophylaxis, or PrEP (further discussed in 2.3), along with barrier methods to prevent infection.[29]

Burden of infection

Up to 2019, over 100 people were being diagnosed with HIV every year in Wales, with more than half of new infections being amongst MSM (56% in 2018).[17-20] While these numbers are low, the Welsh Government has placed a focus on HIV to develop an HIV action plan for

Wales.[30] Additionally, Cardiff and the Vale of Glamorgan Councils have signed up for the Fast Track Cities initiative, which focuses on achieving the UNAIDS goal of ending HIV transmission by 2030.[31] This has resulted in renewed focus on HIV and ending its transmission. However, this goal suffers additional challenges due to the lack of surveillance and monitoring. There is no ongoing system in place to collate all new HIV infections identified across Wales, resulting in a lack of real-time data to assess the current HIV situation across Wales. Additionally, with no surveillance reports published for Wales since 2018, understanding of the COVID-19 impact on transmission and current rates of HIV is unknown.

***NOTE**: The HIV Action Plan has since been published (2022), and Public Health Wales has produced a new STI data report, but this was not the case at the time of conducting this literature review and was therefore not included. Additionally, the STI data report is for beyond 2020, with the data included in this thesis not going beyond 2019.*

2.1.5 Genital Warts

Infection and Symptomology

Human papilloma virus (HPV), commonly known as genital warts, is a viral STI caused by HPV types 6 and 11. The warts appear as small fleshy growths, bumps, or skin changes that appear on or around the genital or anal regions and are usually painless. It is transmitted through skin-to-skin contact and does not require penetrative intercourse to be transmitted.[32]

Testing, Treatment, and Prevention

Genital warts are identified by examination by a sexual health clinician. There is no cure for genital warts, but warts can be removed, although they can return throughout a person's lifetime. Treatment depends on the location of the warts but can include a cream or liquid topical treatment, cryotherapy, or even surgery. However, treatment does not work for everyone. Barrier methods can assist in preventing transmission, but depending on where the wart is located, this is not always possible. HPV vaccines can assist in preventing genital warts.[33]

Burden of infection

Genital warts are the most common viral STI, with approximately 6,000 first episodes diagnosed each year in Wales.[32] Those aged under 25 are the leading risk group, with 60% of infections attributed to this group in 2018.[17-20]

2.1.6 Genital Herpes

Infection and Symptomology

Genital herpes is a minor, long-term condition caused by the herpes simplex virus type 2. It is highly contagious and transmits through skin-to-skin contact, such as during various sexual contacts, not requiring penetrative intercourse to spread. The virus remains dormant until activated; these triggers vary but are often related to lifestyle factors. When active, the virus causes outbreaks of sores or blisters on the genitals and surrounding areas. Symptoms might not appear for weeks or even years after infection with the herpes virus. There is also the herpes simplex virus type 1, which classically causes 'cold sores', but this is not considered genital herpes, although it can also cause genital sores.[34]

Testing, Treatment, and Prevention

Testing involves having a swab taken from a blister to be tested via culture or NAAT; however, this can only be done if blisters are visible, and as mentioned, people can have the virus unknowingly for years. There is no cure, but symptoms are controlled by antiviral medicines such as acyclovir when flare-ups occur. Creams can also be used to assist with pain management. Flare-ups usually settle by themselves and do not always require treatment. Barrier methods can assist in preventing transmission, but depending on where the blister is located, this is not always possible.[35]

Burden of infection

Genital herpes (type 2) is extremely common, with 10% of people carrying the virus. Most are unaware due to presenting none or mild symptoms.[34] The number of first diagnosis episodes is increasing year on year in Wales, with more cases identified in males. Those aged under 25 make up the majority of identified cases (52% of cases).[17-20]

2.1.7 Hepatitis

Infection and Symptomology

Hepatitis (HEP-) A, B, and C can be sexually transmitted, but the focus will be on strains B and C as there are very few cases of HEP-A in Wales (only 1 case in 2018).[17-20] The HEP-B virus is an infection of the liver, usually transmitted through contaminated blood or body fluids via sexual intercourse or needle sharing. Infection can be 'acute' (a short-term illness) or 'chronic' (becoming a long-term illness where the virus remains in the body). Chronic HEP-B often requires long-term treatment and regular monitoring to check for liver problems. Many people with HEP-B do not present with symptoms; those who do show flu-like symptoms and jaundice (yellowing of the eyes and skin).[36,37] HEP-C is a bloodborne virus most commonly transmitted through drug use in the UK. It can be transmitted through sexual intercourse, but this is rare. It can cause both acute (usually asymptomatic) and chronic infections. Between 15 and 45% of those infected with HEP-C spontaneously clear the virus within 6 months of infection without any treatment; the remaining develop a chronic infection.[38,39]

Testing, Treatment, and Prevention

Hepatitis testing is done via a blood sample, with these being cultured or using NAAT. If the first test suggests infection, a further blood test will be taken to confirm the result. For HEP-B, treatment depends on the length of the infection. If detected early, emergency treatment can help prevent infection. For acute HEP-B, treatment will only be used to relieve symptoms while the body fights off the infection. For infections lasting over 6 months (chronic HEP-B), antiviral medicines will be used to keep the virus under control and reduce the risk of liver damage.[37] HEP-C is treated with antiviral medicines (sofosbuvir and daclatasvir), taken over several weeks, that stop the virus from multiplying.[39] Hepatitis can be prevented using barrier methods, with vaccines available to prevent HEP-B.[36,38]

Burden of infection

The number of new infections for hepatitis is small in Wales, but certain groups are at increased risk. This includes people originally from high-risk countries, people who inject drugs, and people who have unprotected sex with multiple sexual partners. Wales has an estimated 12,000–14,000 people with HEP-C, most of whom are undiagnosed.[38] In 2018, there were 27 new cases of HEP-B and 48 cases of HEP-C.[17-20]

Figure 2.1 Summary of the most common sexually transmitted infections.

	Infection	Symptoms	Transmission	Testing	Treatment	Risk Group	Cases in Wales (2018)
GONORRHEOA	Bacterial/ Curable	Discharge	Bodily fluids	Swabs/Urine sample	Antibiotics	MSM	2,650
CHLAMYDIA	Bacterial/ Curable	Discharge	Bodily fluids	Swabs/Urine sample	Antibiotics	Under 25s	13,097
SYPHILIS	Bacterial/ Curable	Painless skin lesions	Skin-to-skin	Blood sample	Antibiotics	MSM	465
HIV	Viral/ Manageable	Flu-like symptoms	Bodily fluids	Blood sample	Antiretroviral medications	MSM	141
GENITAL WARTS	Viral/ Manageable	Painless skin lesions	Skin-to-skin	Swabs/Urine sample	Wart removal	Under 25s	4572
GENITAL HERPES	Viral/ Manageable	Painful skin lesions	Skin-to-skin	Swabs/Urine sample	Antiviral medicines	Under 25s	2976
HEPATITIS B/C	Viral/ Manageable	Flu-like symptoms	Bodily fluids	Blood sample	Symptom-specific medications	MSM	27/48

2.1.8 Uncommon STIs

Above I have discussed the most common infections but there are less common STIs. Due to these infections being rare in the UK, they are not routinely screened. These infections may be mentioned throughout the thesis but are not a focus due to limited routine data collection.

- Lymphogranuloma venereum (LGV) is a type of chlamydia bacteria that attacks the lymph nodes. It is rare among heterosexuals, largely being found among MSM. It is mostly transmitted through unprotected sexual contact. Infections are treated with antibiotics.[40] Following a positive chlamydia test, if symptoms suggest an LGV infection, clinicians will organise further testing to make a diagnosis.[41] New infections of LGV each year remain low, and in Wales, 10 infections were identified in 2018, the highest level to date.[17-20]
- *Mycoplasma genitalium (*MG) is a bacterial STI mostly transmitted through unprotected sexual contact. MG infections often do not present any symptoms with the infection clearing naturally. Testing only occurs if a patient shows symptoms, and the common infections have been ruled out. When identified, it is treated with antibiotics.[42] In Wales, there is no data on MG infections, but a study exploring prevalence among 1000 participants across three sexual health clinics in Wales reported that prevalence is low.[43] Antibiotic resistance is also a growing concern for MG.[43]
- *Trichomonas vaginalis* is a STI passed on during unprotected sex. It is more common in females. Infections can be passed to males, but these are rare, and most infections are asymptomatic. Testing only occurs if a patient shows symptoms and other infections have been ruled out; treatment is with antibiotics.[44]
- Shigella, or dysentery, is very infectious, affecting the gut and causing diarrhoea, stomach cramps, and fever. It is caused by bacteria found in faeces, and sex involving anal contact or contact with faeces is the main transmission route. In most cases, the infection clears within a week, but some people will require intravenous antibiotic treatment. Since September 2021, there has been a detectable rise in cases of extremely antibiotic-resistant Shigella infections in the UK, mostly among MSM.[45]
- Molluscum contagiosum, scabies, and pubic lice are all conditions affecting the skin and transmitted through skin-to-skin contact, which can be transmitted during sexual

intercourse, but this is not the only form of transmission. All can be treated with various creams, although molluscum contagiosum can clear itself without treatment.[46]

2.1.9 Summary

There are various STIs, most being easily treated if diagnosed promptly (chlamydia, gonorrhoea, syphilis genital warts, and genital herpes). However, STIs such as HIV, syphilis, and hepatitis, pose a more serious threat to health especially if not identified and treated quickly. Treatment for many STIs includes some form of antimicrobial, either antibiotics or antivirals. However, the use of these drugs is becoming limited for certain infections due to antimicrobial resistance, leaving fewer treatment options available.

2.2 ANTIMICROBIAL RESISTANCE

Antimicrobials are medicines used to treat and prevent infections in humans, plants, and animals. It is an umbrella term that encompasses antibiotics, antivirals, antifungals, and antiparasitic medications.[47] For the purposes of this research, I will only be referring to antimicrobials in the context of antibiotics and antivirals.

Since his discovery in 1947, Alexander Fleming warned that the misuse of antimicrobials would inevitably lead to resistance and the loss of their effectiveness.[48] This is now occurring, with many antimicrobials no longer being effective for the treatment of certain infections.[48] Antimicrobial resistance (AMR) occurs when infecting microbes (bacteria, viruses, fungi, and parasites) change and adapt to antimicrobials used as treatment, resulting in the microbe no longer responding to those treatments. This leads to antimicrobial medicines being ineffective, with infections becoming difficult or impossible to treat. Microbes that develop AMR are often referred to as “superbugs.”[47]

2.2.1 Causes of AMR

Antimicrobial resistance is a natural occurrence through genetic change but is exacerbated by the overuse and misuse of antimicrobials. The scarcity with which new classes of antimicrobials are identified and developed makes the situation harder to deal with. Previous research has linked the overuse of antimicrobials to the emergence and dissemination of resistant bacteria and viruses.[49, 50] When it comes to overuse, there are differences between antibiotics and antivirals:

- For antivirals, these medications often need to be taken daily for prolonged periods of time by someone with a viral infection, such as HIV or hepatitis. These medications prevent the virus from replicating and harming the body. Unfortunately, the ongoing viral replication and prolonged exposure to the medication lead to the natural selection of resistant strains of the virus developing and becoming dominant, leading medications to become ineffective. This has resulted in viral infections often being managed with multiple drug combinations.[51]
- For antibiotics, overuse is linked to a lack of regulation and the use of antibiotic drugs when not required. This is a major problem globally, where in certain countries there is little regulation and antibiotics are easily accessible and cheap, promoting overuse. Extensive use within agriculture also exacerbates the problem.[52]

***NOTE**: Here we focus on the use in humans, but overuse and misuse of antimicrobials are also extremely prevalent within animal care, along with overexposure to the environment, which are large drivers of antimicrobial resistance and can reduce efficacy for use in humans.*

The UK has greater regulation of antimicrobials; however, studies continue to show overprescription of antibiotics, especially in primary care.[53,54] This overuse is often related to the provision of antibiotics for viral infections, which provide little therapeutic value and can increase the possibilities for the development of antibiotic resistance, particularly if low levels of antibiotics are provided.[49] Some also argue that patients misusing antibiotics by not following prescribed guidelines, such as stopping use before recommended, sharing medications, or saving antibiotics for future use, may be contributing to antibiotic resistance.[55]

With the current number of antibiotics becoming less effective, there is a dire need for new classes of antimicrobials, especially antibiotics. However, development is complex, costly, slow, and faces regulatory obstacles.[47] The major influence is that antibiotics are not a wise economic investment. Excessive cost is involved in development, but medications are often used only for short periods as they are curative, and due to the inevitable resistance, their use would be limited both in terms of effectiveness and provision to avoid resistance developing.[49] For these reasons, 15 of the 18 largest pharmaceutical companies have

abandoned their work on antibiotics.[56] Despite warnings from scientists regarding antimicrobial resistance, these medications continue to be overprescribed worldwide.

2.2.2 Consequences of AMR

Antimicrobial resistance is classified as a major public health threat in the 21st century. Antimicrobials treat infections and have made it possible to perform organ transplants, cancer treatments, therapies to modify the immune system, and other complicated surgical procedures. In a future of widespread AMR, infection complications from medical intervention would become frequent and increase fatalities. The UK Government Review on Antimicrobial Resistance predicted that AMR could lead to ten million deaths per year by 2050.[57] The first study to develop comprehensive estimates of the AMR burden estimated that there were five million (3·62–6·57) deaths associated with bacterial AMR in 2019. These deaths by AMR had a higher prevalence in lower-resource countries. However, data from these countries had lower quality, so estimates are likely to be lower than the reality.[58] This highlights that AMR is a current problem with severe consequences for health. Due to the threat of AMR, the global community has made a concerted effort to enhance antimicrobial stewardship. This refers to the systematic effort to measure and improve antibiotic prescriptions by clinicians, following up-to-date evidence-based guidance, and educating patients to improve their use. Improving prescribing and use is critical to effectively treating infections, protecting patients from unnecessary antibiotic use, and combating antibiotic resistance.[57] Preventing AMR is essential to ensuring the continued usability of antimicrobials.

2.2.3 AMR in STIs

Gonorrhoea

Antibiotic-resistant gonorrhoea is acknowledged as a global threat to public health, and in response, monitoring of antimicrobial resistance is ongoing worldwide. England and Wales have the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), which started in 2000. Currently, gonorrhoea is the only STI routinely tested for antimicrobial sensitivities in England and Wales. In Wales, monitoring of AMR comprises culturing isolates, testing of cures, and the maintenance of comprehensive surveillance. This is to ensure the detection of emerging trends and maintain the effectiveness of first-line treatments for

gonorrhoea.[21] However, widespread gonorrhoea resistance has reduced treatment options. Since the 1970s, antibiotic-resistant strains of gonorrhoea have rapidly emerged to multiple classes of antibiotics, including sulphonamides, penicillin's, tetracyclines, macrolides, fluoroquinolones, and cephalosporins, with multi-drug resistance becoming a new threat.

Figure 2.2 presents a timeline of the introduction of various antibiotics to be used as treatments for gonorrhoea and the subsequent identification of resistance. This figure was developed from various sources.[59,60] Across the world, ceftriaxone (an extended-spectrum cephalosporin) is the only remaining treatment option for gonorrhoea and must be provided in injectable form at a higher dose of 1g.[14,47] While ceftriaxone-resistant cases of gonorrhoea were rare in the UK, from December 2021 to February 2022, there have been six cases of multi-drug-resistant gonorrhoea (including ceftriaxone) identified. What adds to the concern is that the cases do not appear to be related and are not associated with travel to Asia-Pacific regions where ceftriaxone resistance is more prevalent. This suggests that the transmission of ceftriaxone-resistant strains of gonorrhoea may have become endemic.[61]

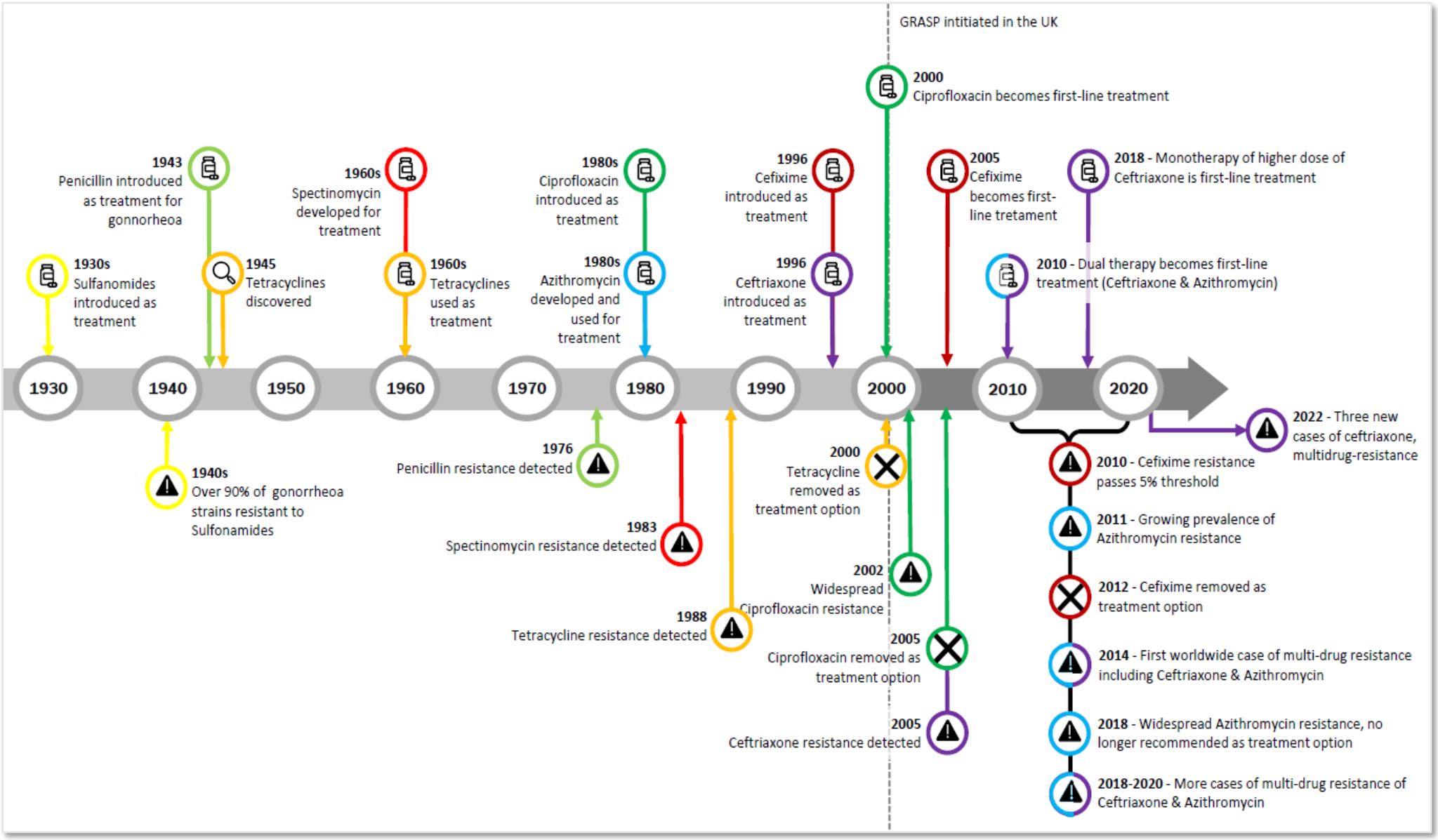
Chlamydia

While chlamydia is the most reported bacterial STI worldwide, it has shown little evidence of developing resistance. When resistant isolates are identified, they often display low survivability or lose resistance during transmission, suggesting the transmission of resistance strains is less likely to occur. However, this does not mean that widespread resistance could not develop.[62-63] A vaccine is currently being developed, which is in a phase 1 clinical trial, and hopes are that it can be developed before a potential growth in resistance occurs.[64]

Syphilis

The current treatment for syphilis remains penicillin, and to date, there have been no documented cases of penicillin resistance in syphilis strains. However, due to allergies to penicillin's, other classes of antibiotics such as tetracyclines and macrolides have been used as treatments. This has now resulted in widespread macrolide resistance in syphilis across Europe, Australia, China, the USA, and Canada. There is currently no alternative medical intervention for syphilis and little monitoring of resistance outside of research purposes, providing a setting for the growing emergence of syphilis resistance.[62]

Figure 2.2 Timeline of antibiotic use and resistance for gonorrhoea.



NB. NG = *Neisseria Gonorrhoeae.* GRASP = gonococcal resistance to antimicrobials surveillance programme. All points in this timeline (guidelines/ resistance) relate to the UK.

Human Immunodeficiency Virus

The development of antiretroviral therapy (ART) for treating HIV, has saved many lives. However, the increased use is accompanied by the emergence of drug resistance, with levels increasing in recent years. If not prevented, drug resistance will turn back the clock and result in increasing numbers of HIV infections and HIV-associated health problems.

When ART is taken successfully, it has the effect of suppressing the viral load, preventing the virus from replicating, damaging the body, and being transmitted, small levels of HIV drug resistance is expected as it is a natural occurrence. Resistance can be identified before treatment begins. The World Health Organisation identified that up to 10% of adults starting HIV treatment present with drug resistance to first-line treatment, with a higher prevalence among children under 18 months and those newly diagnosed. HIV infection among those taking PrEP is rare. However, among those using PrEP who do seroconvert, drug resistance is common, as these are often breakthrough infections. The dual combination medications used for PrEP are not currently used as treatment, but acquiring resistance to them (e.g., through PrEP use) risks knocking out a class of HIV treatment options regardless.[65] With new cases of HIV infection reducing, the introduction of various prevention medications, and the boost in potential for an HIV vaccine based on COVID-19 vaccine technology, there is hope for infections to be largely reduced before antiviral resistance renders medications ineffective.[66] Potential resistance is monitored by HIV specialists and the Antiviral Unit, hosted by Public Health England, now the UK Health Security Agency.[67]

Genital Herpes

The antiviral treatment of herpes simplex virus infections has been ongoing for over two decades, with minimal drug resistance identified among immunocompetent patients. Resistance is identified at higher levels within immunocompromised patients, and this does create clinical difficulties, but even in this population, there is little evidence of increasing resistance despite the increasing antiviral usage.[68] The development of resistance is monitored by physicians, but there is no governing surveillance system by public health bodies in the UK, although some of this may fall within the remit of the Antiviral Unit.

Hepatitis B and C

Resistance to medications used to treat hepatitis can occur over the course of treatment (similarly to HIV), which presents challenges in prolonged treatment. One study identified that after one year of treatment for hepatitis B, 14–32% of patients carried resistant variants, increasing to 80% after four years, resulting in the need for altering medication regimes.[69] Similar growths in resistance are also identified for hepatitis C, as daily exposure to antivirals provides a favourable setting for the development of resistance. The transmission of hepatitis is not common or a major threat.[70] Again, hepatitis does not have a dedicated surveillance system but can be monitored through physicians and the Antiviral Unit.

2.2.4 Pandemic Impact

Before the COVID-19 pandemic, the world was making progress on antimicrobial stewardship, but this was undermined by the COVID-19 pandemic. During the initial days of the pandemic, with no treatment options and suspicions of bacterial co-infection, patients with the COVID-19 virus were often provided various antibiotics as treatment.[71, 72] Research has since identified that the prevalence of bacterial co-infection was very low at 3.5%; this rose to 14.3% for secondary infections in patients hospitalised with COVID-19, with antibiotics providing little support.[72] A rapid review and meta-analysis of antibiotic prescribing in COVID-19 patients found three-quarters of patients received antibiotics, way above estimates of potential bacterial co-infection. This suggests COVID-19 patients have become a population with high levels of unnecessary antibiotic use.[72] This overuse of antimicrobials increases the possibility of AMR developing, coupled with healthcare workforces being strained globally and reduced surveillance capacity for antimicrobial-resistant organisms, which has led to concerns that AMR will become the lasting consequence of the COVID-19 pandemic.[73,74] However, as attendance at primary care reduced over the pandemic period, there may have been less antimicrobial exposure for the general population (non-hospitalised COVID-19 patients), potentially reducing the overall burden of AMR.[72-74]

2.2.5 AMR Summary

Antimicrobial resistance is a current threat to health, resulting in millions of fatalities globally. Resistance among STIs is an escalating problem that will increase potential treatment failure. The situation for gonorrhoea is far more severe, with ceftriaxone one of the only remaining

antibiotics available and growing multi-drug resistance. Any variable that may influence an increase in gonorrhoea resistance needs to be understood.

2.3 HIV PRE-EXPOSURE PROPHYLAXIS

Due to the severity of HIV and its impact during the 1980s and 1990s, extensive research was focused on treatment and prevention. Currently, HIV is considered a chronic condition managed by daily antiretroviral therapy, and when medications are taken correctly, it prevents the virus from being transmitted from those living with HIV to others. These medications have been successfully used to prevent HIV infection among HIV-negative individuals.[28.29] The U.S. Food and Drug Administration approved HIV PrEP for use as a preventative medication in 2012 after evidence of its safe and effective use in preventing HIV.[75] HIV PrEP contains two medicines, emtricitabine and tenofovir disoproxil fumarate, these medications prevent the virus from replicating in the body, preventing an individual from acquiring HIV even if exposed to the virus, by any mode of transmission.[76] PrEP was available for purchase online in the UK from 2012 but was not adopted by the NHS until 2017.

2.3.1 PrEP Regimes

PrEP is now a recommended priority by the World Health Organisation in populations with an HIV incidence of at least 3 per 100 person-years.[3] Clinical guidelines for PrEP use in men or trans women recommend one of two options. It can be taken daily (one tablet daily), resulting in a constant level of the drug in the body to block HIV.[1-2] It should be noted that for receptive anal sex, the medication needs to be taken for seven days before maximum protection is achieved. The second way, known as ‘event-based’ dosing, is two tablets taken 24 hours before sex and a single tablet taken 24 and 48 hours after sex.[1-2] Recently, organisations such as the Terrence Higgins Trust have been promoting the use of alternative regimens of PrEP, referred to as ‘Ts and Ss’ and ‘Holiday PrEP’.[81] The ‘Ts and Ss’ approach suggests taking four pills weekly on Tuesdays, Thursdays, Saturdays, and Sundays, based on evidence from the IPrEX trial.[2] Alternatively, ‘Holiday PrEP’ suggests taking a set amount of PrEP before, during, and after a planned sexually active period. For example, daily use for seven days before a holiday, daily during the holiday, and for seven days after returning home. Evidence supporting this approach was recently published in a non-randomised observational clinical intervention.[82] But these two methods are not recommended under clinical

guidance. It is important to know that these methods are only promoted for use by people with penises, as people with vaginas will need to take PrEP for at least 21 days before gaining adequate levels of protection. This is due to the biological structure of the vagina, with it taking longer for the medication to permeate the tissue to provide protection.[83]

2.3.2 Provision of PrEP in Wales

Following work undertaken by Public Health Wales (PHW) in 2016/2017 (including an Independent HIV Expert Group and the All-Wales Medicines Strategy Group), the Welsh Cabinet Secretary for Health announced an all-Wales trial period to provide the drug Truvada® (emtricitabine/tenofovir disoproxil fumarate) prophylactically to all those who would benefit from the preventative treatment. [77,84] From July 2017, PrEP was offered freely through integrated sexual health clinics within Wales on a three-year trial basis before the Welsh Government decided if PrEP would continue to be provided. Provisions were dependent on meeting a set of eligibility criteria.[90] In June 2020, at the conclusion of the PrEP trial, the Minister for Health and Social Services announced that PrEP would become part of routine NHS care within sexual health clinics and provided to all people where clinically appropriate.[85] Since the summer of 2018, NHS services have stopped providing Gilead's brand of PrEP Truvada® as generic brands of emtricitabine and tenofovir disoproxil fumarate became available for use. The current generic brand used is 'Teva' and can be acquired at a significantly lower cost than Truvada, aiding in the decision to continue its provision in Wales.[86] Those prescribed PrEP can receive courses of 30, 60, or 90 tablets at a time, with 90 tablets (3-month daily supply) being the most frequent prescription.[83] To receive PrEP in Wales through the NHS, individuals must meet one of the following eligibility criteria:

- MSM who have had a HIV negative test on the day of starting PrEP and had another HIV negative test in the preceding year and report condomless intercourse in the past 3 months with a likelihood of condomless intercourse in the next 3 months,
- Have partner living with HIV is not known to be virally suppressed, and condomless intercourse is anticipated before treatment of the HIV-positive partner takes effect,
- HIV-negative persons who are at a similar risk of HIV acquisition as those above.[86]

When an individual first requests to start PrEP, they are invited to a consultation with a clinician in a sexual health clinic. The clinician checks that they meet the eligibility criteria and

completes the clinical evaluation; this involves taking a history and completing recommended tests, most importantly an initial HIV test to ensure the individual is HIV negative before initiating PrEP. Counselling is provided at the initiation consultation to ensure individuals are aware that PrEP only prevents HIV and has no effect on other STIs. Reviewing the potential side effects and explaining its effectiveness is determined by appropriate use. After initiation, all individuals must receive quarterly testing for HIV, with MSM also receiving an STI screen quarterly as per guidelines. Non-MSM PrEP users are screened for STIs "when appropriate". Ongoing monitoring of adherence, renal functioning, and bone density is also conducted. Prescriptions are collected from in-house sexual health clinic pharmacies. Full details are available from the PrEP operational guidelines if required.[84]

PrEP use in Wales

The latest data regarding uptake of PrEP in Wales from PHW covers the period of July 2017 to March 2019.[87] There was meant to be a final report from the three-year pilot of PrEP, which ended in July 2020, and while its provision has been continued, there has been no report of PrEP data due to the impact of the COVID-19 pandemic. It is unknown how well the available data (from 2019) reflects the current situation of PrEP use in Wales. From the last report (July 2017–March 2019), 1,627 people were identified as eligible for PrEP in Wales by clinicians. Of these, 1009 (62%) initiated PrEP, 218 (28%) were in the process of accessing PrEP, 385 (24%) declined its use, and 15 (2%) were unable to initiate for medical reasons. Of those prescribed PrEP, 99% (998/1009) were male, with 96% (961/998) reporting to be MSM. Ages ranged from 16 to 77, with a median age of 32 years. The majority of those using PrEP in Wales (93%) have been prescribed a daily regimen.[87]

Adherence

From the PrEP report (July 2017–March 2019) mentioned above[87], adherence to PrEP appeared to be low, with only half of users who initiate PrEP continuing its use (523/1009). Ten percent (98/1009) were reported to have stopped PrEP, with 34% (343/1009) identified as 'lost to follow-up' (i.e., not seen in clinic for over 2 months since their last prescription should have finished or there is no information).[87] A recent article reporting the experiences of MSM when initiating, implementing, and persisting with HIV PrEP in Wales presented that the use of PrEP tends to fluctuate. At times when people's sexual activities would reduce or they would enter a monogamous relationship, their perceived risk of HIV

was low, leading some to temporarily pause their PrEP use. In situations where risk would rise, there would be a re-establishing of PrEP use.[88] Despite this fluctuation in systematic use, assessments of risk episodes by clinic staff identified that 97% of all or most risk episodes were covered by PrEP, suggesting that people are able to correctly assess risk and adhere to the medication when required.[87] Fluctuating adherence to PrEP would not be identified by NHS systems, and so the 34% 'lost to follow-up' may be due to people's prescriptions not having finished due to treatment pauses, and the current figure may be different.

STI monitoring

In Wales, of those provided PrEP, none have been diagnosed with HIV, although eight new diagnoses of HIV were identified among those wishing to initiate PrEP. Of the 1009 people who initiated PrEP, nearly a quarter (23.9%, 242/1009) were diagnosed with an STI after starting PrEP, equating to 380 infections identified: 176 (46%) cases of gonorrhoea, 149 (39%) cases of chlamydia, 34 (9%) cases of syphilis (18 early latent, 10 primaries, and 6 secondary); 11 (3%) first episodes of warts; six (2%) first episodes of herpes; and three LGV (1%) diagnoses.[87, 89] When comparing the incidence of STIs among PrEP cohorts from Wales to the IMPACT trial in England, it shows that the PrEP cohort in Wales had half the STI incidence, 23.9% compared to 47.5%.[87, 89] STI incidence figures among PrEP cohorts within previous studies identified similar results to the IMPACT trial, including incidences of 57%, 41%, and 52% identified at follow-up.[1,2,8] This may suggest that Wales' STI incidence among PrEP cohorts is lower than most previous studies; more research is required to explore this further and provide potential explanations for this difference.

The impact of COVID-19

The introduction of the COVID-19 restriction measures in March 2020 resulted in changes to the provision of PrEP, both to initiation and follow-up. There are currently no published reports of changes that occurred, but from conversations with Dr Darren Cousens, consultant in sexual health and PrEP lead for Wales, it was explained that the pandemic and associated restrictions resulted in the move from a face-to-face senior clinician model with fixed appointments booked in advance to a patient-initiated follow-up model. It was reported that 50% of appointments booked three months in advance within the old model were not attended, and excess demand was channelled into a waiting list at the start of the pandemic, resulting in an 18-month backlog. Changing the pathway resulted in the completion of the

waiting list within three months. All clinical staff members were trained to deliver PrEP as part of their routine consultations, i.e., if someone is in for treatment of their rectal gonorrhoea, they were given PrEP on that day rather than referred to a separate service with the inevitable wait. Additionally, there has been a recent move to a bi-annual follow-up consultation (instead of quarterly) as HIV and STI testing can be organised personally through PHW's postal testing service rather than having to come through a clinical service.

2.4 RISK COMPENSATION

During the development and introduction of HIV PrEP over the last decade, the notion of risk compensation has permeated the scientific literature, becoming a prominent concern and argument for blocking the provision of PrEP. The theory of risk compensation (RC) developed as an economic theory and has grown in popularity, now being applied to various areas including health behaviours and risk. The theory of RC suggests that through adopting a protective measure, an individual's risk perception (how an individual identifies their risk of a certain outcome occurring in relation to their behaviour[90]) will decrease, and this can result in increased risk-taking behaviour due to perceived protection. However, the protective measures are often specific to a single element of danger and have a limited impact on additional risk behaviours adopted.[91] A recent example is the use of face coverings to protect against COVID-19. The wearing of a face covering or mask would act as a protective behaviour, but in response to the perceived protection, some would then not follow the social distancing measures or mix with multiple people or households, increasing their risk of being exposed to COVID-19.[92] For the case of PrEP, the argument suggests that the protection the medication provides from HIV could result in intentional reduced use of condoms, increasing numbers of sexual partners, and engagement in high-risk sexual situations such as group sex parties or chem sex, with these behaviours resulting in increased transmission of other STIs.[5, 93-95] A qualitative study in which interviews were conducted with various health professionals and academics identified a common fear of RC, particularly that PrEP would result in an increase in STIs such as gonorrhoea and chlamydia. Interviewees theorised that PrEP would lead to reduced condom use, particularly among MSM, due to altered risk perceptions. Some took this a step further, theorising that the subsequent increase in STIs due to PrEP use could exacerbate the growing AMR problem, particularly for gonorrhoea.[5] Other studies have identified that concerns by healthcare practitioners can result in a

reluctance to prescribe PrEP, and policymakers might not support its implementation.[94] These concerns may explain the guidelines for PrEP provision being a risk-based criteria, being provided only to those MSM who report already engaging in condomless sex instead of being openly available to anyone wishing to receive its protection. Attempting to avoid people starting PrEP and subsequently engaging in condomless sex through the RC mechanism.

The discussion of RC has focused on individual RC, but some researchers have presented the notion of community-level RC. There is little work examining this, but the theory implies that those not using PrEP within the MSM community will intentionally reduce their condom use levels due to a perception that since others are using PrEP, there is less risk of HIV among the community. This was first noted in an observational study from San Francisco (one of the first places to adopt PrEP), which identified a reduction in consistent condom use among HIV-negative MSM, both PrEP and non-PrEP users. They suggested that certain men may have removed their focus on condom use due to the assumption that sexual partners will be using PrEP.[96] This idea of community-level RC was further considered by Holt and Murphy, who presented the idea of 'prevention optimism'. Using previous work from HIV treatment optimism, they suggested that among the MSM community, there is a belief that the risk of HIV infection is lowered due to the increasing use of PrEP by others, making it safer to engage in condomless sex. The authors identified that this area of work is currently not explored in research around RC, focusing solely on those using PrEP and ignoring the non-users in the community. They argue that future work exploring PrEP use in MSM should include a focus on those not using PrEP to understand community impact, with a need for qualitative work to understand the nuances of behavioural responses to PrEP provision.[97]

2.4.1 A Theoretical Link

Due to these concerns, studies examining PrEP have incorporated elements of risk compensation into their outcomes. However, as RC is not directly observable, it is usually explored through other observed variables, viewed as outcomes of potential RC. One of the main variables used to identify RC is STI diagnosis.[1,2] Behavioural measures used include self-reported condom use, numbers of sexual partners, sex with HIV-positive or HIV-unknown partners, changes to sexual positioning during anal intercourse (insertive or receptive), and other risk behaviours such as group sex and chemsex.[1,2,7-9] Within the literature, previous research focuses heavily on exploring the existence of a causal relationship between PrEP and

RC, with no evidence effectively identifying a causal link.[93,96, 98-99] An early review of the clinical trials conducted in 2015 concluded that, up to that point, there was no evidence of RC occurring within the randomised controlled trials reviewed.[99] However, research participants' behaviours are likely to be affected by the possibility of receiving the placebo, potentially reducing risk behaviours and therefore not presenting an accurate behavioural response to PrEP use. A systematic review and meta-analysis of open-label studies was conducted in 2017. The review identified that PrEP use was associated with increased STI diagnoses among MSM, with this being used to evidence the potential occurrence of RC.[96] Identifying evidence of a potential causal relationship relating to RC is complex due to the nature of RC itself, and without a tailored longitudinal clinical trial, this is unlikely to be identified. While associations do not prove causation, instead of exploring the existence of RC, understanding the potential magnitude of RC would progress the research area.

2.4.2 Challenges and Limitations in Research

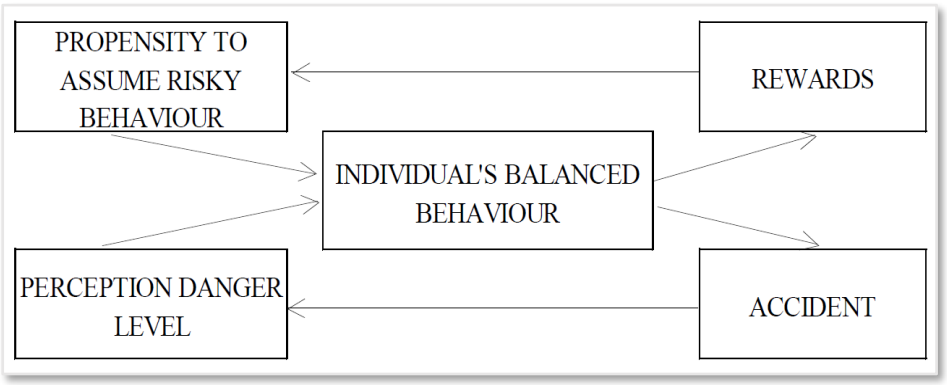
Measuring risk compensation

RC is challenging to identify and measure because it is not directly observable and encompasses various latent concepts. The original model was developed by Gerald Wilde and updated by John Adams (1996),[100-101] see Figure 2.3. Certain studies have adapted the model to their specific research areas. However, there is no agreed-upon universal model of what behaviours to measure or the best methods in relation to RC. This has resulted in a lack of consistency among the literature as to what is required to explore RC. Even where there is consistency in behaviour measured, such as condom use, the various methods used to measure this behaviour have led to difficulties drawing conclusions from comparisons.

A limitation of the current literature measuring RC is the restrained data collection in relation to behavioural measures. In most studies, both clinical trials and observational, a single baseline measure of behaviour is collected, with these behaviours collected at set time points during the study period, with comparisons identified from the difference from baseline.[1,2 97,99,100] The problem is that behaviour may fluctuate throughout the study period; this will also occur outside of the study period as people's behaviours, especially sexual behaviours, may fluctuate based on situations, experiences, and even seasonal effects. Therefore, a single baseline measurement does not provide an accurate representation of a person's behaviour. This means that the changes identified may be due to a common fluctuation and not the

influence of PrEP. To identify a change during an intervention, longitudinal behavioural measures need to be collected prior to baseline to provide an accurate reflection of existing behaviour.

Figure 2.3 Risk Compensation model adapted by Adams (1996).



Source: Image from Cembalo, Cicia & Vernau (2009) [101].

Biases in the measurement of risk compensation

Exploring RC in relation to PrEP is difficult, and previous studies have suffered from multiple challenges, with studies unable to prove causality. Studies that have identified increases in STI diagnoses among MSM using PrEP compared to those not using PrEP can be partly attributed to biases within the data and analysis. The first of these is selection bias: to receive PrEP, individuals must be deemed at higher risk of contracting HIV; this results in the cohorts of PrEP users having a higher risk profile than their comparison group. This affects the results, as studies identify that PrEP users report more condomless sex before initiating PrEP and have more previous STI diagnoses.[1,96,102] Secondly, there is surveillance bias: those using PrEP are required to have an STI screen every three months.[7,96,103] This results in PrEP cohorts testing more frequently and therefore being more likely to have an STI diagnosed. The bias occurs in multiple ways: PrEP users may otherwise test for STIs less frequently if not for mandatory screening; testing levels will likely be different from comparison cohorts used for analysis; PrEP users are screened rather than only testing when symptomatic. Studies that adjust for STI testing frequency often report reduced to no effect size between PrEP and comparison cohorts in relation to new STI diagnoses.[1,9] One extensive, open-label intervention study in Australia monitored STI incidence in PrEP users from 1 year pre-enrolment to follow-up (mean 1.1 years). The initial findings identified a 40% increase in STI rates associated with PrEP. After adjusting for pre-PrEP testing frequency, the magnitude of

the increase dropped to 10%, presenting the dramatic impact that not adjusting for testing can have on findings.[104] A failure to account for these biases in the analysis severely impacts the validity of inferences and does not present a true picture of the impact of PrEP.

Longitudinal trends

Research exploring PrEP-associated RC is often limited by time constraints. A limited number of PrEP studies explore STI diagnoses up to 1-year pre- and 1-year post-PrEP's introduction, with most examining behaviours cross-sectionally at baseline and then at follow-up points.[1,2,7-9] While 2 years would be classified as a longitudinal study, the changes identified within studies may be part of the existing trends in diagnoses, separate from PrEP. There is a lack of evidence examining PrEP within the context of the ongoing trends in STI rates. A quasi-experimental study conducted in the United States examined STI rates from 2000 to 2017 in relation to the introduction and utilisation of PrEP.[104] They found that following PrEP implementation, there was an increase in syphilis and gonorrhoea rates and a reduction in chlamydia rates. While this study had the strength of being able to identify existing trends, it was severely limited by their study not directly examining PrEP users but simply using PrEP implementation rates, weakening their ability to draw conclusions related to PrEP impact. Numerous factors could explain the rise in syphilis and gonorrhoea rates. The increase in infections was presented starting from the initial date of 2012 and could be explained by numerous reasons, such as the general reduction in condom use over the time-period, an increase in STI testing among the population, and increases in sexual liberty, resulting in more sexual partners and opportunities to be infected. This study's timeline began in 2012, when PrEP was approved by the FDA, so it is unknown if the increasing trend is part of a longer-term trend or if the increase in infections started after PrEP was introduced, and if it did start afterwards, to what extent PrEP was influencing the increase.

2.5 GAP IN THE RESEARCH

Understanding the relationship between PrEP, STIs, and AMR and the potential role of RC is important for improving the provision of PrEP and for STIs and AMR. The introduction of PrEP is likely to have had an impact on STIs to some degree, and it is important to understand what the impact may be. From thoughtful consideration of impact, we can then respond appropriately and improve the provision of PrEP, maximising its beneficial properties and

addressing any potential negatives. The relationship with AMR is currently only theoretical, and without understanding the influence on STIs, we are unable to predict the subsequent influence on AMR. Due to the serious threat that AMR imposes, it is essential to understand any potential influencing factors to improve the collected knowledge of factors related to AMR if we are to prevent future treatment failure.

The lack of consistency around RC measurement leaves an inability for comparison, limiting firm conclusions. The identification and accurate measurement of all variables related to RC are required for future studies to identify the extent of its impact. Previous studies have examined the variables within the confines of 1-3 years. However, an understanding of the trends in STI rates among the population examined is required to assess PrEP's impact more accurately. Identified increases in STIs from previous research are limited by not examining the findings within the context of pre-existing trends. Identifying deviations from existing STI trends in response to PrEP utilisation among those adopting it, compared to those who do not, would provide stronger evidence. The literature is also lacking in providing the views and experiences of those within communities who have adopted PrEP. A detailed understanding is required from those using PrEP, including their reasons for using PrEP, their awareness of PrEP, their attitudes towards STIs, and their thoughts on the notion of RC. External opinions from experts may not be reflected by the lived experiences of those using PrEP.

Only by understanding the impact on STIs can we begin to understand the link to AMR. Increased STI testing, identification, and treatment would logically lead to an increase in the development of AMR. PrEP also provides protective measures, such as increased surveillance through quarterly screening. Therefore, a balance may need to be considered around risks and protective measures. But first, the relationship needs to be established.

2.6 CHAPTER SUMMARY

This chapter has provided a summary of sexually transmitted infections, focusing on transmission, treatment, and the current situation within Wales, along with antimicrobial resistance and the development and provision of PrEP in Wales. The current literature is presented relating to risk compensation, identifying the state of evidence relating to risk compensation. The chapter concludes by identifying the gaps in the research. The next sections will present the research conducted to address the gaps.

CHAPTER THREE
A QUALITATIVE EXPLORATION OF THE RELATIONSHIP BETWEEN PREP, STIS AND AMR

This chapter focuses on the qualitative project within the PhD, exploring the knowledge and concerns of both PrEP and non-PrEP users relating to PrEP, STIs, and AMR. The theoretical perspectives and methods employed are described, with justifications provided for the methods and sampling approaches used. Recruitment methods and procedures are described before a summary of the data collection method and analysis is summarised, including a brief discussion.

3.1 PHILOSOPHICAL PERSPECTIVES

The overall thesis mixed-methods approach requires a pragmatic paradigm that combines multiple stances (i.e., positivist and constructivist/interpretivist perspectives). Therefore, all the philosophical dimensions of this study combine the two, broad, contrasting positions of positivism for the quantitative elements and constructivism for the qualitative work.

3.1.1 Epistemology

This relates to the theory of knowledge, where researchers must consider what is knowable and worth knowing.[105] Epistemology is more widely considered within qualitative research, as methods of data collection and analysis are more subjective. Most quantitative research encompasses a realist or positivist paradigm, which assumes that reality is stable, and events exist whether researched or not. Positivism is centred on three beliefs: that research is empirical, there is a unity of method (procedures for testing are the same), and inquiries are value-free (knowledge is not bound by subjective viewpoints).[106]

Qualitative research does not fit well within the positivist paradigm, as research examining human behaviour is complex, unpredictable, and heavily influenced by social dynamics. Popular epistemological standpoints in qualitative research are constructivism and interpretivism. Constructivism assumes that reality is a social construct, built through historical, political, and social processes. It is accepted that, under varying circumstances,

varied beliefs and behaviours can co-exist. While interpretivism is used to address how each person interprets the world rather than knowing the reality of the world, seeking subjective meanings of experiences.[107]

3.1.2 Ontology

Ontology refers to the study of being and existence. Again, positivist, constructionist, and interpretivist paradigms are considered within the context of the nature of reality and being. Positivist notions are linked to realism, suggesting that there is a single objective reality. This contrasts with the latter two paradigms that fall under relativism, assuming there is not a single objective reality but multiple constructed ones.

3.1.3 Theoretical Stance

Coming from a background in psychology, I am familiar with debates between quantitative and qualitative methods and ideologies. For this project, it became clear that before potential interventions could be developed, an understanding of the relationship between PrEP, STIs, and sexual behaviour was required. To achieve this project's aims, an interpretive or constructive view of individual actions is required, along with an examination of how associated beliefs, concerns, and culture may influence these actions. It is understood that behaviour needs to be interpreted within the boundaries of the MSM culture towards sex and sexual relations.

3.2 STUDY AIMS

This study aimed to use a qualitative approach to:

- Gain an understanding of knowledge and concerns around PrEP use, contracting a sexually transmitted infection, and contributing to AMR.
- Explore attitudes towards condom use among groups of MSM and develop a typology of behaviour.
- Explore intervention opportunities for reducing STI transmission and improving awareness of AMR.

3.3 QUALITATIVE DATA COLLECTION

Qualitative research is focused on gaining an understanding of the world from an individual's perspective and allows in-depth exploration into topics that would be hard to research using quantitative methods. The use of qualitative research methods has been expanding within health-related disciplines, and they are now promoted as essential for the development and implementation of health interventions.[108] The research questions related to this study aim to discover answers that cannot be directly observed, including motives behind decisions and potential contradictions among attitudes and behaviours. Therefore, qualitative methods were most appropriate as participants were provided with the opportunity to give accounts for their actions and beliefs, allowing the researcher to gain a deep understanding of participants' knowledge, attitudes, and behaviours.

Semi-structured interviews were determined to be the most appropriate method for data collection. Interviews were chosen over focus groups as the project explores sexual behaviours, which participants may not wish to discuss as explicitly within a group setting as with a single interviewer. A focus group setting has the potential for social desirability bias to play a larger role as individuals may omit or alter their sexual experiences and encounters to follow the group consensus. It was believed that interviews would bypass the influence of others, limiting social desirability bias as much as possible, and that the anonymity interviews provide would allow a more honest description of sexual encounters and opinions. Additionally, there were unforeseen benefits to interviews as virtual focus groups were found to lose the group dynamics and spontaneity that are essential for focus group data collection.[109]

3.3.1 Qualitative Interviews

Within qualitative research, interviews are reported as the most common method of data collection.[110] Qualitative interviews allow researchers to address the 'why' questions with a focus on experiences. The flexible and open nature of interviews allows for adaptation throughout the data collection process when new topics may be uncovered. This can allow researchers to gain a focus on the areas that truly need exploration, not just their preconceived notions.

3.3.2 Interview Structure

There are varying combinations of types and styles of interviews available, which should be decided based on the specific needs of the study. Within the team, we determined that semi-structured interviews would be most suitable. This would allow predetermined questions to be set while allowing the flexibility for participants to provide their own account of their beliefs on a topic and expand on what is important to them. Within this interview style, an interview schedule can be developed to provide a guide to topics for discussion, but participant responses set the order and focus of questions.

As for the type of interview, it was originally decided that one-on-one, in-person interviews would be best due to the potentially sensitive nature of discussing sexual activities and sexual health history. The advantage of this method for interviews is that rapport can be more easily developed through responses to verbal and non-verbal communications. In response to the COVID-19 pandemic, certain elements of this had to change. With in-person interviews not viable, video-mediated interviews were chosen. Using the platform Zoom, interviews could still be conducted in person with video, allowing for non-verbal communications to be observed. While adding the benefits of remote data collection, including time efficiency as well as financial and environmental benefits, interviews could be conducted across Wales without the need for travel.[109] Some research also suggests that when discussing sensitive topics such as sexual behaviour, video-meditated interviews provide a 'protective barrier' that increases comfort.[111]

3.3.3 Sampling

In this study, purposive and snowball sampling methods were employed. A purposeful strategy assumes that certain groups of individuals may have a unique, different, or important perspective on the phenomenon, and their presence in the sample should be ensured.[106] This allows for a range of views and insights to be acquired. Within the realms of the current study, a minimum quota was set for the three required groups (PrEP users, previous PrEP users, and non-PrEP users). This was paired with snowballing, where participants were asked to refer other potential participants.[112] Snowball sampling can be an 'informal' method used to reach a target population where trust is required to initiate contact with stigmatised populations, such as MSM.[113] The sample methods used will be viewed as biased from a

positivist perspective for not allowing researchers to make claims about generalisability, but this is not required within qualitative research.[113]

Within the sample collected, there was a criterion that participants within the three groups relating to PrEP use. The ideal sample consists of ten participants currently using PrEP to prevent HIV, five who had previously used PrEP but stopped (no use within the previous four weeks), and five who have never used PrEP.

3.4 METHODS

3.4.1 Ethical Approval

Full ethical approval was received from Cardiff's School of Medicine Research Ethics Committee (Ref: SMREC 20.21).

[See Appendix 1.2 for the ethical approval letter]

3.4.2 Inclusion Criteria

Individuals were eligible to take part if they identified as men who had sex with other men, were aged 18 years or older, and were currently living in Wales. Individuals were excluded if they could not give consent, were unable to converse in English, or did not have access to an electronic device that enabled teleconferencing. Telephone interviews were not considered appropriate as the face-to-face element was important for building rapport when discussing topics around sexual behaviour.

3.4.3 Recruitment

Participants were recruited using three approaches:

- **General promotion:** Advertisements were posted on the social media websites Facebook and Twitter. Facebook groups specifically for LGBTQ+ individuals and Twitter posts were used to post the advertisement, inviting eligible males to get in touch if interested. Individuals were directed to a study email address to show their interest. Eligible men were sent the participant information sheet (PIS) and consent form.
- **Approached through Grindr profile:** Messages were sent to potentially eligible individuals relaying the advertisement and again asked to indicate their interest through contact via the study email. Eligible participants were sent the PIS and

consent sheet. Grindr is a location-based social networking and online dating application for gay, bi, trans, and queer people.

- **Snowball sampling:** Participants were also invited to participate through invites from those who had already participated. These individuals contacted the lead investigator via the study email, and those eligible were sent the PIS and consent form.

[See Appendix 3.1 & 3.2 for Participant Information Sheet and Consent Form]

3.4.4 Interview Process

Interview schedule

The interview schedule was developed before participant recruitment and modified between interviews. The initial draft was developed from an examination of the literature in relation to the study's aims, reviewed by the research team, and modified accordingly. Questions were focused around the main topic areas to first gain an understanding of the participant's knowledge and then allowing the participant to guide the interviewer into their experiences. The schedule was used as a template to flow through the topics but could be adapted for each interview depending on the direction the participant took the conversation. As new topics emerged through the progression of interviews, the schedule was updated to reflect these, allowing evolution throughout data collection.

[See Appendix 3.3 for the Interview Schedule]

Interview procedure

Once the consent form had been received, the date and time for the interview were confirmed. Individuals received invites along with a Zoom link that could be saved into electronic diaries, and automatic reminders were sent one hour before the arranged time. Before the interview, brief demographic information was collected, including age, sexuality, location in Wales, ethnicity, highest education level, and relationship status.

Participants were advised to allow between 30 and 60 minutes for the interview and asked to ensure there was a constant signal and use a device that enabled Zoom. Participants were provided an opportunity to ask questions and discuss concerns before the recording began. Participants were reminded that anything they reported would be confidential and that they did not have to answer any questions they did not feel comfortable answering:

"Please remember that everything you say to me will be kept strictly confidential. If you find any of the topics or questions difficult to discuss, please let me know. You can decline to answer any questions."

At the end of each interview, participants were provided another opportunity to ask questions. Participants were thanked before the call ended. All participants received a £20 Amazon e-voucher as compensation for their time.

All interviews were audio-recorded for transcription and played during analysis for better immersion. Brief field notes were made during the interview that provided a resource for reflection during analysis. Appropriate adjustments to the interview schedule were made both during interviews and as data collection progressed, based on responses from participants. The field notes were referred to during the analysis. All interviews were conducted using Zoom, and recordings were saved to Cardiff University's secure drive. Only the audio recordings were saved, and they were all stored in password-protected files following Cardiff University's data storage guidelines. Interview recordings were transcribed verbatim by a professional transcription service approved by Cardiff University (Victoria Pink Transcription).

3.5 REFLEXIVE THEMATIC ANALYSIS

Thematic analysis (TA) is a common method of analysis within qualitative research, first introduced by Braun and Clarke in 2006.[114] However, their more recent writing explains that there has been a misinterpretation in the use of the method and emphasises the need for reflectiveness within TA. They explain how TA, including reflectiveness, can be used to "describe the 'lived experiences' of particular social groups" or "examine the 'factors' that influence, underpin, or contextualise particular processes or phenomena".[115] This analysis method suits the needs of the project to achieve the aims of exploring sexual behaviour and knowledge among men who have sex with men.

3.5.1 Data Familiarisation

To become fully immersed in the data, I reviewed each of the transcriptions while listening to the recordings to correct any mistakes and fill in missed words or phrases. Each transcript was read with reflective notes. To ensure full immersion, initial coding was conducted while listening to the recording.

3.5.2 Coding

Coding was supported by NVivo 12 (a qualitative data analysis computer software package produced by QSR International), which was used to store and manage all data. Code and themes were developed in NVivo and stored as nodes. The initial codes reflected the interview topics, such as “knowledge” and “impact on condoms.” Certain codes were introduced based on common references by multiple participants, i.e., “mental health.” A group of codes was also created, referenced as “base,” which included demographic information and items relevant to the methodologies. From the initial themes, time was taken away from the coding to allow for reflection on the initial codes. This produced rich and complex themes, as suggested by Braun and Clarke (2021), for practising reflexive TA.[116]

Alternative perspectives

To improve validity, the framework was developed with two members of the research team. From the initial five interviews, two were double-coded by supervisors FW and DG. Each analyst developed a series of codes and themes, and then all sets were compared and discussed together. Following this exercise, the coding framework was amended, clarifying a code or code description further where necessary. Although codes could be added throughout the analysis as more participants were interviewed.

Accuracy

To assess coding accuracy, 10% of the transcripts were also coded by FW using the finalised coding framework. The transcripts coded by FW were compared to the coding I completed and reviewed for similarities and differences before being discussed. Some researchers recommend evaluating intercoder reliability using Cohen’s kappa. However, this is a controversial topic within the qualitative research community.[117] As this project follows the Braun and Clarke method for TA, a consistency statistic was not calculated, as they view it as contradicting the interpretative nature of qualitative research.[118]

3.5.3 Coding Framework

Within NVivo, a coding framework can be developed to define each code and theme. For example, the main code PrEP contained sub-codes on “Knowledge,” “Impact on condoms” and “Stigma.” The framework was developed from initial interviews, adapted throughout the analysis, and better-defined during the review.

[See Appendix 3.4 for Coding Framework]

3.5.4 Sample Size

The sample size was informed by 'information power', which suggests that the more relevant and in-depth data a sample holds for a study, the smaller the sample needs to be.[119] The narrow aims of the interviews, participants belonging to specified target groups, and strong dialogue between participants and the interviewer led the research team to conclude that the sample size was sufficient at twenty participants. At this point, there was a sense of data saturation.

3.5.5 Research Team and Reflexivity

I conducted all the interviews; I have extensive training in qualitative research from the completion of a BSc and MSc in the field of psychology. I am a white gay cisgender man, aged 25 at the time of data collection. I have no lived experience of taking PrEP but have been offered it at a previous clinic appointment and regularly tested for STIs. While younger than many of the interviewees, I am familiar with the culture of sexual behaviour between MSM and the importance of apps such as Grindr and Scruff. As my familiarity with the population being examined may have impacted my interpretation, the double coding of transcripts by team members DG (principal research fellow, heterosexual) and FW (professor of medical sociology, heterosexual) provided greater assurance to the accuracy of coding and provided alternative perspectives.

3.6 RESULTS

This section will explore the themes identified in the interviews. Quotes have been chosen that illustrate the theme, with alternate perspectives provided to demonstrate opposing positions. After each quote, a participant identifier has been included (e.g., PP01), along with whether the interviewee was "using PrEP", "stopped" or "no PrEP." Interviewer dialogue is presented by "I," with "P" representing participant dialogue. Themes are visually presented in a thematic map, see Figure 3.1.

***NOTE**: Findings from this chapter have been published in BMC Public Health. This article is available from; https://doi.org/10.1186/s12889-022-14645-0*

3.6.1 Participant Characteristics

Twenty participants were interviewed face-to-face via Zoom in the seven months between September 2020 and February 2021. All participants were cisgender men with ages ranging from 19 to 53 years. Most participants reported being white British and gay (both 17/20, 85%) and single (14/20, 70%). Of those in a relationship, two-thirds reported an open relationship. The sample was educated, with 75% (15/20) having achieved an undergraduate degree or higher. Participants mostly lived in Southeast Wales (16/20, 80%), mainly in Cardiff, see Table 3.1.

As per the inclusion criteria, participants reported either currently using PrEP (11/20, 55%), had previously used PrEP but stopped (3/20, 15%), or never used PrEP (6/20, 30%). Of those using PrEP, only one reported using event-based dosing, while the rest adopted daily dosing. All PrEP users received their PrEP free of charge from integrated NHS GUM clinics. Reasons for stopping PrEP included experiencing prolonged side effects and ceasing sexual activity due to the COVID-19 pandemic and associated restrictions. Two participants reported starting PrEP after the onset of the COVID-19 pandemic.

Table 3.1 Participant Characteristics from Interviews.

PID	Using PrEP?	Age	Sexuality	Ethnicity	Highest Education	Relationship Status	Region of Wales
P01	No	29	Gay	White British	UG	Single	Southeast
P02	No	53	Bisexual	White British	UG	Single	North
P03	Yes (daily)	23	Pansexual	White British	PG	Relationship	Southeast
P04	Yes (daily)	51	Gay	White British	PG	Relationship	Southeast
P05	Yes (daily)	25	Gay	White British	UG	Relationship (open)	Southeast
P06	No	30	Gay	White British	PG	Single	Southeast
P07	No	22	Gay	White British	PG	Single	North
P08	Stopped	48	Gay	White British	PG	Relationship (open)	Southwest
P09	No	22	Gay	South Asian	A-levels	Single	Southeast
P10	Yes (daily)	21	Gay	White British	PG	Single	Southeast
P11	No	19	Gay	White British	A-levels	Single	Southeast
P12	Yes (daily)	27	Gay	White British	UG	Relationship (open)	Southeast
P13	Yes (daily)	32	Gay	White British	PG	Single	Southeast
P14	Stopped	42	Gay	White British	PG	Single	Southeast
P15	Stopped	23	Gay	Mixed British	A-levels	Single	Southeast
P16	Yes (daily)	20	Gay	White British	A-levels	Single	Southeast
P17	Yes (event)	53	Gay	White British	UG	Single	North
P18	Yes (daily)	22	Pansexual	White British	A-levels	Single	Southeast
P19	Yes (daily)	38	Gay	White British	PG	Civil partnership (open)	Southeast
P20	Yes (daily)	23	Gay	White European	UG	Single	Southeast

NB. UG = undergraduate degree, PG = postgraduate degree

3.6.2 Knowledge and Awareness

Knowledge of PrEP

Knowledge of PrEP was proficient among all participants, with accurate and detailed accounts being provided. Reports included facts about two dosing options (daily, or event-based) and that protection only occurs when taken correctly. Some participants referred to the rates of effectiveness of the medication when taken correctly, which was a fair estimation of the findings produced by the PROUD study and the IPERGAY trial.[1-2] This indicates an elevated level of knowledge among some participants about PrEP. A key point to mention is the clarity with which participants were aware that PrEP only protected against HIV and not any other STIs.

> *"I would describe PrEP as a medication that can be taken daily or on an incidental basis which can help prevent contracting HIV." P05 (using PrEP)*

Awareness and knowledge of PrEP were largely reported to come from clinics through discussion with nurses as well as through social discussion among MSM. Social media was believed to have an influence on awareness of PrEP, promoting positive information about its use but also propagating PrEP-associated stigma. These were reported to take the form of attacks on the character of those using PrEP, with reports of *"Truvada whore" (P07, No PrEP)* and *"PrEP is for tarts that can't say no." (P17, using PrEP).*

> *"…particularly in social media, in terms of stigmatisation or to use the phrase, slut shaming, that it can be misrepresented as a free-to-pass ticket to do what you want. Which is not actually about the drug at all, it's about the perception of the drug and its users. Or misperception." P04 (using PrEP)*

Despite some participants experiencing stigma, PrEP was viewed as having a positive influence in reducing HIV stigma as it promoted a better understanding and removed the fear of engaging in intercourse with HIV-positive individuals.

> *"And I just think it... it also opens up the conversation about HIV more generally." P05 (using PrEP)*

Attitudes and Opinions of PrEP

Opinions around PrEP among participants were universally positive towards the medication. Largely centred on the various ways that PrEP provided a sense of freedom to both the individual and others, PrEP was valued for its ability to provide "peace of mind" and alleviate the fear of contracting HIV, allowing individuals to engage in the type of sexual intercourse they desired (e.g., condomless). As well as presenting the societal benefits of reducing HIV transmission within the community.

> *"The biggest benefit is having that freedom to be able to have sex with somebody without the fear of there being a barrier, as in condoms." P02 (No PrEP)*

> *"I think I'd always found that sexual health was quite a stressful thing, and… the thought of contracting something as serious as HIV, say, when there is an option to, you know, reduce that chance and reduce the chance of it spreading further around the community, is just a good option to take". P03 (using PrEP)*

The freedom from fear provided by PrEP was described as having mental health benefits in reducing the stress previously associated with sex and, for some, easing the internal battle between wanting the pleasure of condomless sex and the fear of HIV.

> *"It's changed my attitude towards sex. There's less fear. There's less fear about that. And it… it just cuts through all the stigma. It cuts through the fear of HIV tests. It cuts through the fear of a condom splitting. It is… it truly feels like it has revolutionised how I feel about sex." P13 (using PrEP)*

Participants who used PrEP also believed it initiated or *"broadens up a conversation about sexual health with partners." (P05, using PrEP).* On the other hand, non-PrEP users voiced opinions that PrEP shut down these conversations, as being on PrEP was seen to nullify the requirement for a discussion around condom use and sexual health:

> *"I think people seem to be kind of less inclined to have that conversation about sexual health and more inclined to have that conversation; are you on PrEP or not?" P02 (no PrEP)*

Both those who used and did not use PrEP agreed that its use would improve engagement with sexual health, as the requirement of regular HIV and STI testing ensured regular return

visits for check-ups. The health monitoring that goes alongside PrEP provision was also perceived as positive for general health maintenance.

> *"…you must have contact with a clinician every three months or so. And I think that in terms of testing, in terms of sexual health promotion, in terms of just general wellbeing, and even mental health comes into it, you are being almost monitored. So, you are kind of... you're not going to slip through under the net." P07 (no PrEP)*

Health monitoring is an appealing factor for those not using PrEP as a reason to start.

> *"…they routinely check your health. So, I almost saw it as a way of, I guess, getting frequent check-ups so you're more aware of your sexual health as well as your overall health." P01 (no PrEP)*

Many of the benefits of PrEP described above coincided with the reasons conveyed for choosing to use PrEP, relating to the autonomy PrEP provided participants.

Knowledge of STIs

Overall, there was a high awareness of STIs described by participants, with HIV, chlamydia, gonorrhoea, and syphilis being commonly referenced. Genital warts, genital herpes, and hepatitis B were less commonly discussed, and where they were mentioned, less detail was provided compared to HIV, chlamydia, and gonorrhoea. Some participants included details of the transmissibility and even epidemiological trends of STIs, representing their advanced knowledge.

> *"You know, I've seen in my clinic that gonorrhoea is on the... on the up. Syphilis of all things is apparently on the up as well." P05 (using PrEP)*

Many described their knowledge as originating from personal concerns about having contracted an STI. In response, they would search the internet for information relating to symptoms of various STIs to self-diagnose.

> *"Finding out myself on the internet. Usually, if I was worried, I'd caught something. If I got… if someone told me, they had something or… or if I'd been tested and it was positive." P14 (stopped)*

Clinics were described as a constant source of information, including leaflets given by nurses and posters displayed. Participants described their knowledge as fair to high, but an interesting comparison arose from those who viewed their knowledge as low, with statements suggesting that despite their knowledge being poor, it was "probably better than most straight men" (P09, no PrEP). The comparison to heterosexual men suggests that it is assumed that knowledge around sexual health is naturally higher among MSM. Knowledge was often referenced as coming from having to teach themselves and proactively seek information due to "not having LGBT sexual education in school" (P09).

Some of the suggestions for interventions to reduce STI transmission focused on the need for more education. However, participants generally felt that STI education would come from an educational setting, not a health one, with emphasis placed on sexual health education needing to be provided early on in people's lives. It was perceived to be more effective to inform people before or at the start of their sexual exploration, rather than after sexual practices become ingrained.

> *"I think education has got to be the biggest thing. It seems like, […], you turn 16, 17, 18 whatever, […] you move away, go to university, you come to terms with everything at once, and no one's told you about any of the risks about STIs." P03 (using PrEP)*

> *"I think it's about teaching gay men. Well, I think in the beginning, in schools, about the kind of… young gay men about that they're… they don't… they can have a relationship. It's not just about going out and having sex with somebody. I think when you teach them about that and you teach them about their value, then you… then you… then the campaign is not as needed as much." P02(no PrEP)*

Other suggestions for reducing STI transmission were centred around increasing STI testing and condom use. This was based on the belief that condom use, increased testing, and treatment would reduce the number of infections circulating within the population. Additionally, there was a desire for normalising sexual health and testing through campaigning, and particularly grassroots-level work was a focus for some participants. One participant suggested STI advocates would be useful, as has been implemented with HIV advocates, as this intervention would help to remove the veil of secrecy and shame around

having a STI. All these suggestions were driving the point that stigma needs to be targeted to improve testing and eventual treatment, making the community safer.

> *"Well, it would just be going back to taking preventative measures. Either, you know, going back to using condoms with, you know, unknown partners where you don't know what their risk factors are. And, you know, when you go to get tests done, if something does come back positive, then, you know, finishing the course of antibiotics prior to engaging in any more encounters." P06 (no PrEP)*

> *"So, I think there is an increase in testing, not in HIV or syphilis or things like that, but in gonorrhoea and chlamydia. But I think that should be for all people. I think that should be available not just to PrEP users, but because most of the people I know who've ever gotten chlamydia have all been women. So, I think just more testing for the more common stuff would definitely help lower transmission." P18 (using PrEP)*

> *"…trying to remove the stigma of getting tested. Like in the media there should be more transparency about getting tested. Like in TV shows, if you normalise getting tested, and if you normalise someone, for example, getting chlamydia and then getting rid of it in the next episode or whatever, it can really normalise stuff like that in the same way that people with HIV and AIDS have been... the stigma has been reduced because of media." P10 (using PrEP)*

Additionally, grassroots work and campaigning were viewed as essential to showing that sexual health is linked with mental and physical health and is not a separate element. The current health system treating sexual, mental, and physical health separately is believed to result in people viewing parts of their health independently from each other and not understanding they are linked. Improvements in mental health were believed to positively influence a person's sexual behaviours and health.

> *"…working in like sexual health or working separately to mental health, mental health working separately to HIV testing, and all those things. And I think unless you kind of do everything together, like, have the conversation around STIs, HIV, use PrEP, use condoms, then I don't think an individual thing is going to be the be all and end all." P02 (no PrEP)*

Some acknowledged that information campaigns may have a limited impact and that teaching and improving people's self-esteem and self-value would have a far better influence on sexual practices.

> *"I think when you teach them about that and you teach them about their value, then you… then you… then the campaign is not as needed as much." P02 (no PrEP)*

AMR awareness

First, it is important to note that the questions from the interviewer referred to "antimicrobial or antibiotic resistance" but participants only used the word "antibiotic resistance". This may indicate a lack of understanding of the term 'antimicrobial', but this was unclear. Varying degrees of knowledge were identified, ranging from no awareness to a detailed understanding of that of a person studying a science at the degree level. Overall, there was a basic understanding of antibiotic resistance: the microbe (bacteria or virus) develops resistance to antibiotics. However, there were some reports of the individual, body, or community becoming resistant to the antibiotics, but these were few. Participants were aware of factors that could contribute to antibiotic resistance, such as failure to complete a course (although this is heavily debated in scientific literature; Llewelyn et al., 2017[120]) and the overuse of antibiotics.

> *"It's where antibiotics find that they can resist the antibiotic... Sorry, germs, viruses, whatever the organism is, gain resistance by having been subjected to antibiotics of a certain type. But not enough to kill it to the point where it survives, then recovers, and then is able to multiply again, but then has learned that actually, we're going to learn to defend against that thing that nearly wiped us out. So incorrect use of antibiotics, not taking it for long enough, not taking it at the correct times and dosages." P01 (No PrEP)*

> *"I: Are you aware of the term antimicrobial or antibiotic resistance?*
> *P: God, no. No. I don't know what that is." P15 (stopped)*

Interestingly, although many participants understood AMR, this did not often correspond with an awareness of AMR relating to STIs. Certain participants voiced surprise after being made aware of the current global issue surrounding antibiotic-resistant gonorrhoea by the interviewer.

I: "…and for gonorrhoea, it's one of the best infections for developing resistance, and currently there is only one antibiotic left to treat it."

P: "Jesus. Oh wow, I didn't know that." P15 (stopped)

Of those who were aware, references to "super gonorrhoea" were often made early in the conversation. The term "super gonorrhoea" has become a popular reference within the media and refers to drug-resistant strains of gonorrhoea with high-level resistance to the recommended treatment options at the time (ceftriaxone and azithromycin) as well as many other antibiotics.[47,55] One comment about antibiotic-resistant gonorrhoea provided an interesting insight, highlighting the perception that AMR infections, at least for gonorrhoea, are more of a problem within "gay populations", which is currently not the case.

"I know that gonorrhoea is one of those illnesses that is becoming too resistant to some forms of treatment. And I also understand that areas with bigger gay populations, particularly London, Manchester, and Brighton, tend to have or seem to tend to have bigger outbreaks of resistant gonorrhoea." P13 (using PrEP)

Participants believed that the awareness of AMR among the public was poor. Some explain that when the public is made aware of AMR, it is not in relation to STIs.

"I can't remember. But something was along the same lines in a general term. And… and doctors were saying don't prescribe this unless it's absolutely necessary because antibiotic resistance is coming in. But in terms of STI-specific. I would say no." P12 (using PrEP)

Many participants suggested that improving awareness would be important, with a focus on the consequences of contracting a multi-drug-resistant infection:

"I'd probably say that there needs to be less emphasis on actually catching super gonorrhoea and more emphasis on what happens after." P18 (using PrEP)

When it came to the format of potential campaigns, participants were direct in stating that fear should not be a focus. In comparison to the HIV/AIDS campaigns of the 1980s, they expressed concern that if fear was used to alter behaviour, it may have negative effects. These could include individuals avoiding getting tested for fear of the result and trying to ignore the problem.

"…you don't want to make it like a scaremongering campaign. You don't want to frighten people into not wanting to go to the clinic or not wanting to sort of face up to these sorts of things." P03 (using PrEP)

Some participants conveyed that even if provided with information relating to AMR STIs, there are some people (including themselves) who would accept the risk and continue to engage in condomless sex. Presenting that the problem of antibiotic resistant STIs would need to become more prominent and a direct threat to them before they would consider altering their behaviour. No remarks were made relating to concerns about the potential for transmission of resistant bacteria to others. Suggesting that either it is not something considered, or, they are unaware that it is something they should consider or be concerned about.

"This is where I'm going to be very cynical. I doubt that many things could. Unless that person has come up against a person or their own experience of that. I've… I don't think that, from the people that I know and the conversations I've had, people would heed many warnings." P01 (no PrEP)

3.6.3 Sexual Behaviour

Discussions around sexual behaviour presented a range of attitudes towards condom use. Many participants reporting STI testing being an essential part of many participants' sexual health practices. Sexual practices such as condom use were explained to be heavily influenced by mental health and fear of HIV. With some participants engaging in sexual behaviour as a coping mechanism for low mood, then experiencing anxiety after due to fear of HIV.

Sexual health practices

There were mixed views about condom use. Those not using PrEP viewed condoms as essential on a personal and societal level, with safety and protection being paramount. Despite their own views of the importance of condoms, it was held that other MSM did not see condoms as important, presenting an 'irresponsible other'[121]:

"I think it's very important. It should be very important, and it should be more widely adopted, that people have sex with protection, irrespective of if they're on PrEP or not, because of things like chlamydia, gonorrhoea, etcetera. However, do I think that gay men think it's important? No." P01 (no PrEP)

Of those using PrEP, it was commonly explained that while they would use condoms, they were also comfortable not using condoms, particularly since starting PrEP. But the importance of condoms was still paramount.

> *"I do think they're important for… I certainly, when I wasn't on PrEP, was using condoms and was significant… and was choosing partners based on their attitudes to condoms. I think PrEP has changed my thoughts on it. …I think I'm willing to use condoms less, but I know that others may not." P13 (using PrEP)*

Even those participants who did not use condoms, still highlighted the benefits within a societal context for safety and reducing transmission: *"It doesn't mean I like them, but I think they're important" (P12, using PrEP).* Some identified that their own personal preference for condomless sex was counterproductive to the safety and protection of wider society.

> *"I would say they're important for somebody who wants... you know, who doesn't want to contract or... you know, really reduce their risk of catching anything. But for me, I would consider that probably the least important because I know that there are treatment options available." P06 (no PrEP)*

As PrEP provided protection from HIV, the occasional STI seemed an acceptable "trade-off", with chlamydia and gonorrhoea being viewed as *"occupational hazards" (P13, using PrEP).*

In relation to condoms, certain participants suggested that times are changing with the potential for new forms of protection to emerge. From discussions, it was clear that for many who use PrEP, condoms were only used for protection from HIV, and once PrEP fulfilled that role, the use of condoms became redundant.

> *"Generally, they use condoms because the biggest worry tends to be HIV. And so, when you take out the HIV by being on PrEP, you remove... you remove the thought of HIV, and then people are more likely to have condomless sex..." P10 (using PrEP)*

"Getting tested regularly, especially young LGBT+ people" (P10, using PrEP) was essential for many participants and a major element of sexual health maintenance, as well as the culture of MSM. The frequency of testing was explained to be related to levels of sexual activity, with the average frequency being 3-6 months, but at times of increased activity, testing would

increase to compensate for potential exposure. Again, there were references to comparisons with heterosexual counterparts, where testing was suggested to be rare.

> *"I don't know of many men—straight men my age—who would still be going to sexual health clinics. And speaking with my friendship circle of gay men, it tends to be that we're getting checked every three to six months. And that isn't something that, I think, tends to be replicated with my straight friends." P13 (using PrEP)*

There was a perception that while the general population is uncomfortable talking about sex, gay men are perceived to not experience the same embarrassment, with there being an openness to discussing sexual health.

> *"Gay men are quite open about talking about STIs, sexual health, sex." (P02, no PrEP)*

Risk perception

Where risk perception was alluded to, it was apparent that many were able to appropriately acknowledge their personal levels of risk. Those who did not report engaging in risky sexual behaviour perceived themselves as low risk. In contrast, those who reported higher risk sexual encounters had an awareness of the risks they were taking.

> *"I probably engage in quite risky behaviour in not using condoms, so using PrEP probably would be more of a benefit to me." P06 (no PrEP)*

> *"And then I'd also say just... like just to educate myself just because I did use to be fairly like promiscuous. So, I did look up these things just to know... just to kind of get to grips with what's out there." P18 (using PrEP)*

As is the nature of human behaviour, comparisons to others played a significant role in these discussions. Of those who reported actively engaging in condomless sex, knowing it was a risky behaviour, many made downward social comparisons, likely a defence mechanism for their self-esteem. For example:

> *"The sort of sex that I have tends to avoid the most risky… I'm not someone who's going to go and have sex in a park. I'm not going to go and have… I'm not going to be someone who goes to chem-sex sessions where those treatment resistant gonorrhoea are more prevalent." P13 (using PrEP)*

From the quote above, we see that there is a perception that the location of sex affects the level of risk of infection. However, condomless sex with casual partners, regardless of location, carries a risk, and only with the use of injectable drugs would a chemsex party increase the odds of infection. Participants presented themselves as being separate from other MSM, who they view as having a higher risk of infection due to the situation in which the sex is occurring. Whereas sex with a new casual partner in a park or in a house will carry the same level of risk with regards to infection. This presents a level of judgement towards those engaging in sex in unconventional scenarios with a view of them being at higher risk.

Fear

Fear was described as a major influence on behaviour. Participants expressed prominent levels of fear towards HIV, to the point of extreme anxiety in some cases:

> *"I think I'd always found that sexual health was quite a stressful thing, and… I don't know, the thought of contracting something as serious as HIV." P03 (using PrEP)*

Fear was also suggested to be common among all gay men due to the shared history of the devastating impact HIV and AIDS had on the gay community in the 1980s and 1990s.

> *"I think there is a worry about other STIs, but not as much as HIV or AIDS. Especially as the history of HIV and AIDS in the LGBT+ community and the potential impacts of AIDS." P10 (using PrEP)*

Despite HIV no longer being the death sentence it once was, with effective treatment options available, the descriptions of fear suggest the campaigns of the 1980s have transcended down the generations. Consequently, those born after the epidemic stage of HIV were still fearing a disease that, within their lifetime, has been a treatable (although not curable) condition. Interestingly, everyone explained that they knew HIV was treatable yet still reported elevated levels of concern and fear in some cases.

> *"I think, you know, you have the HIV scare almost every single time, because it's just a kind of a part of the institution... you know, a historic institutional trauma that we as gay people have to live with." P05 (using PrEP)*

From the conversations, it was clear that the longevity and incurability of HIV are what lead to the heightened concern. With fear of HIV leading many to attempt to consistently use

condoms pre-PrEP and on occasions where they did slip, this explained the onset of severe mental distress in response. While not as openly discussed by participants, the stigma associated with HIV has an influence on creating the high anxieties around potentially contracting the disease. The anxieties may also stem from having to explain to all future partners about the condition and the fear of passing on the infection.

The fear of HIV overshadowed concern for all other possible STIs. Many participants reported a far lower concern for gonorrhoea and chlamydia than HIV. It was stated that they would try to avoid contracting these STIs if possible, but the ability to attend a clinic, receive treatment, and have the infection cleared quickly resulted in a lack of concern.

> *"Like things like HIV, and I think it's herpes that are like, once you get it, you can't get rid of it. I think for a lot of people, the permanence of an STI is what affects how concerned they are about it, because, …like if you get chlamydia, you go on antibiotics for like a couple of days to a week, and like it's cleared up like that. But like if you get HIV, it's a constant thing that you have to think about, not just for your health but for other people's health." P09 (no PrEP)*

Syphilis was perceived to be the most concerning of the bacterial infections but did not receive the same level of concern shown to HIV by many. Although some with a heightened understanding of HIV did allude to an increasing concern for syphilis over HIV due to the seriousness and unpleasantness of syphilis symptoms and the fact that HIV can be managed.

> *"I've worked in HIV on and off for years, I kind of… my fear is STIs. Because the last thing I want to do is get syphilis. The last thing I want to… and the last thing I want to do is because… one because it sounds awful, and it sounds… and it's supposed to be painful. Anal syphilis is supposed to be really painful as well. All those things, I don't want to get. So actually, my fear is more around STIs than it is around HIV, because I know HIV is manageable." P02 (no PrEP)*

Influence of mental health

Participants emphasised how their own mental health could influence their sexual health behaviours. References were made to how sex can be used as a coping mechanism for many MSM, where sex could be used to alleviate feelings of depression and loneliness. During these low moments in their lives, individuals would engage in higher risk sexual encounters than

normal, potentially lowering boundaries, such as relinquishing the use of condoms, just to engage in a physical act of pleasure.

> *"But the one thing I am very conscious of is that when my mood is bad, I will have more risky sex. And I'm less able to ask for a condom, want a condom, don't care if I have a condom or not when my mood is particularly bad." P13 (using PrEP)*

An interesting point raised was that in struggles around self-worth, some people may disregard the risk to their own health due to a sense of not needing to care about themselves.

> *"I've spoken to some people who are a lot worse off than I am in terms of how they perceive themselves, and they almost are engaging in very unsafe sexual practices, not with the intention but knowing that there is a very credible risk to their sexual health but disregarding it because of their low self-esteem and because they don't really feel that they need to be considerate of their own health." P01 (no PrEP)*

For some participants, this was used as an argument for why information campaigns may not work, as it was believed that those in a poor mental state would be less likely to change sexual practices as the risk behaviours may be a consequence of a coping mechanism.

> *"I think when you teach them about that and you teach them about their value, then you… then you… then the campaign is not as needed as much." P02 (no PrEP)*

3.6.4 Risk Compensation

Participants were clear that they believed PrEP would result in a reduction in condom use for many users. The perceived reduction was expected to lead to an increase in infections such as chlamydia and gonorrhoea. This was viewed as an acceptable trade-off for ending HIV transmission. There were few considerations about how this might impact AMR.

PrEP and condoms

Overall, the perception of PrEP was that, for many, it meant that they would no longer need to use condoms as they were safe from HIV. The reasons being that the removal of the risk of HIV resulted in the freedom to engage in condomless sex without caution. However, this was how participants thought others would behave, based on friends' or acquaintances' experiences.

"…the kind of guys going onto the PrEP, guys that have been on the PrEP for a long time, they do think, I'm taking this one medication invincible, I don't now need to use condoms now. And they almost forget about everything that was said in that initial meeting when they were given PrEP, saying that, you know, you're only going to be protected against one... one STI, you're only protected against HIV." P07 (no PrEP)

"I don't know many people who use PrEP and condoms." P14 (stopped)

For those who used PrEP, many referred to other people thinking they did not need to use condoms despite reporting similar behaviours; they never grouped themselves with this group of "others". These views on PrEP users may be influenced by PrEP stigma, as mentioned previously, with influences from social media creating a perception of how PrEP users behave. Those using PrEP may want to separate themselves from this view despite engaging in similar behaviour. Of those using PrEP, there were some who stated outright that they did not like using condoms and would not have used condoms previously, so PrEP was providing them with a protection that they previously did not have.

"I was having condomless sex before PrEP. I think it will now continue to be after PrEP as well." P05 (using PrEP)

However, most participants who reported a personal reduction in condom use described it as being associated with the onset of PrEP use due to the protection it provided from HIV. On further exploration with these participants, it became clear that the reduction occurred mostly with casual partners who they frequently engaged in sexual contact with.

"…with partners I know and trust and who are on PrEP then I don't necessarily have to use condoms, but for new partners who I don't trust and haven't got, you know, information about their sexual status, then I do use condoms." P05(using PrEP)

Many specifically reported how they would still always use condoms with new sexual partners for self-protection. Despite other STIs not having the same level of concern or fear as HIV, people still do not want to contract one, even if it can be easily treated.

"I'd say yes, it has [reduced condom use]. With partners that I'm more regular with, who are... and I'd probably say yes with partners I'm more regular with. With other... with more random hook-ups, I wouldn't say as much." P18 (using PrEP)

"P: I just had a friend with benefits staying here for nine days… no, seven days, and I took PrEP the whole time and didn't use a condom once. So, if it hadn't been for PrEP, we'd have used condoms every time."

I: What about a new or random encounter?

P: Then it would definitely… I would use condoms. "P17 (using PrEP)

This context of how PrEP affects condom behaviour is important to understand.

Impact (on STIs and AMR)

All participants theorised that there was a relationship between PrEP and STIs, with PrEP leading to an increase in STIs, particularly chlamydia and gonorrhoea. The increase was perceived to be due to the reduction in condom use among PrEP users, which would lead to an increased transmission of other infections.

"So… if I was to try and draw any correlation between it in my head it's that, you know, before PrEP, I never had any STIs. After having a couple of years of PrEP, and most of the gay men I know being on PrEP as well, STIs seem to come from left, right and centre. So, the correlation I would draw in my head is that PrEP has meant that chlamydia and gonorrhoea have spread a lot faster around Cardiff." P03 (using PrEP)

Some did recognise that STIs were rising before PrEP due to a reduction in condom use among MSM, but that PrEP may have exacerbated an already growing issue.

"I wouldn't be surprised if rates of other STIs go up. Because of the people who think that they can have a free pass. However, I wouldn't be surprised if they're already rather high because of the naivety of some gay men and the issues regarding the relationship with sex in the gay community." P01 (no PrEP)

However, some participants expressed hope that the regular testing required by PrEP users would detect and potentially counteract any potential increase in STIs. This is because these STIs would be identified and treated sooner, thus reducing the spread of infection.

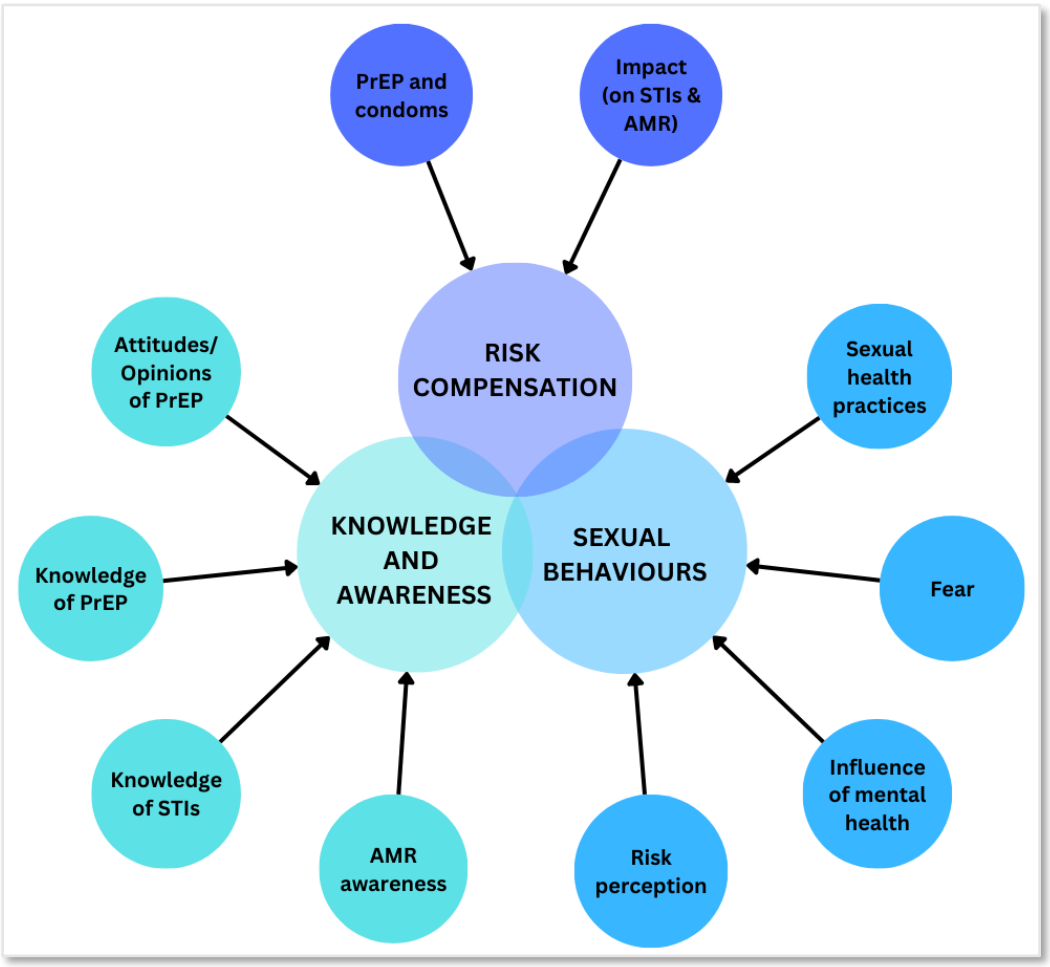
Despite the belief that there would likely be a rise in STIs, none of the participants viewed PrEP as having a negative impact. Some participants explained that this was an acceptable risk for the elimination of HIV, trading off the risks of increasing STIs for the numerous benefits

of ending HIV transmission. This argument appears logical since fear of HIV was explained by many to surpass all other infections.

> *"I just hope that regular testing picks it up, but I would not be surprised if there was an increase in particularly the bacterial… the very easy to transmit bacterial infections such as chlamydia and gonorrhoea. But then again, they were always very easy to spread through oral sex, through rimming, through just touching someone's penis, you can pick it up. I don't know about syphilis. I mean, I wouldn't be surprised if that also increased. But I would imagine it would… it could only go up with PrEP usage. But that feels like, if that is manageable, that feels like a small price to pay for the possibility of eradicating HIV, which is by far the most deadly, the most expensive for the NHS to treat, the most impactful on life." P13 (using PrEP)*

Participants had less certainty around how the potential rise in STIs due to PrEP may then influence AMR. Few associated the rise in STIs with potentially driving antibiotic resistance.

Figure 3.1 Thematic Map of codes identified from data.



3.7 INTERPRETATION

Participants' knowledge and concerns surrounding PrEP and STIs appeared to heavily influence their attitudes and behaviours relating to condom use. Of those aware of increasing antimicrobial resistance, their current understanding of the low levels reported in the UK resulted in little influence on behaviour. Interventions suggested by participants to tackle rising STI rates focused heavily on education and improving testing, believing a test-and-treat model would make the most impact.

3.7.1 Beliefs and Behaviour

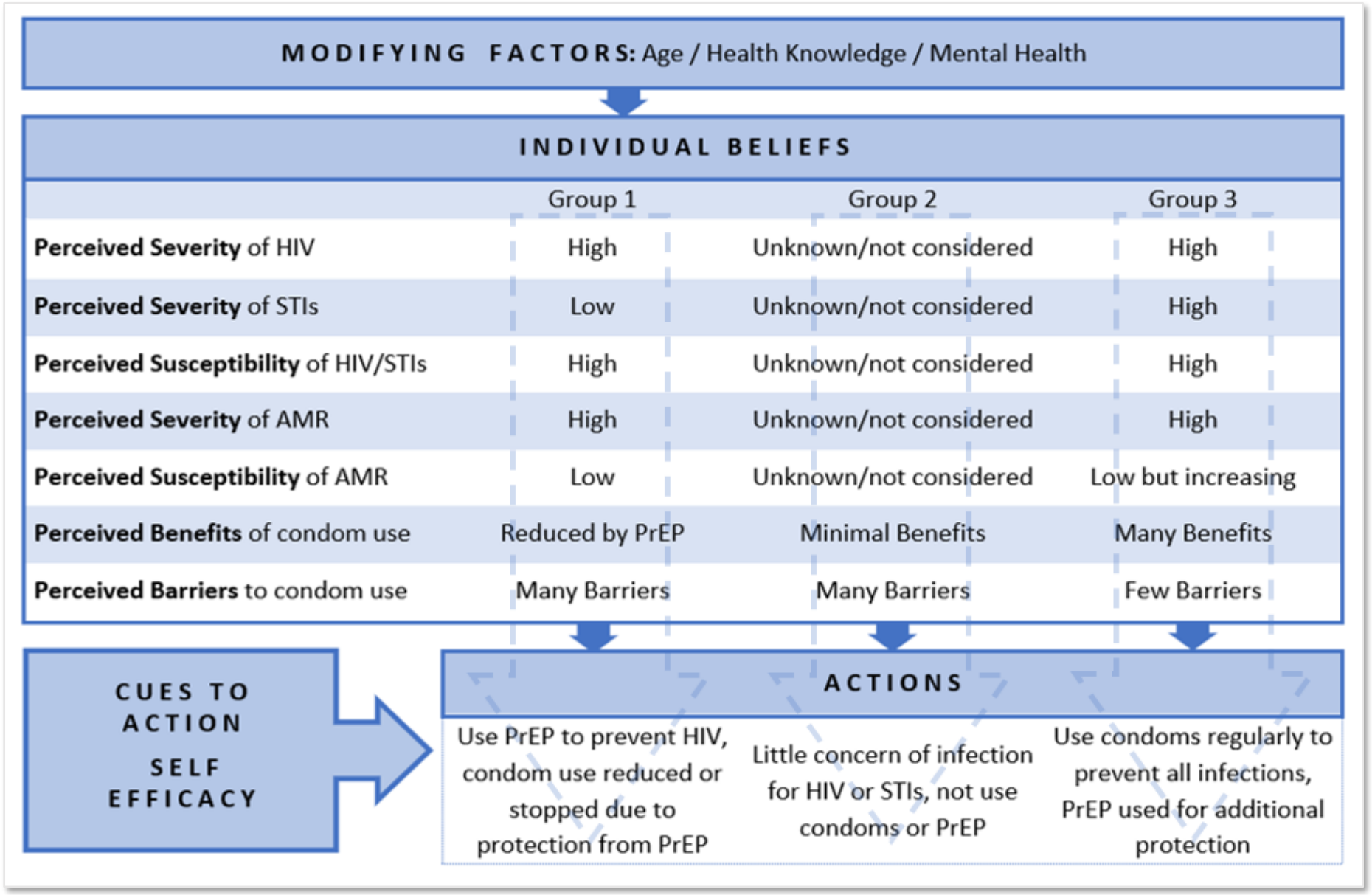
From exploring the participants' knowledge, concerns, and attitudes surrounding HIV/STIs and antibiotic resistance, as well as exploring behaviours relating to PrEP and condom use, a typology of three distinct groups were identified:

- Group 1: Use PrEP with limited to no use of condoms.
- Group 2: Do not use PrEP or condoms.
- Group 3: Use PrEP and condoms.

These groups differed based on beliefs surrounding HIV/STIs, which influenced reported behaviours, in keeping with the health belief model (HBM). The HBM has been widely used to explore health behaviours, including sexual risk behaviours.[122] The key variables of the model include severity and susceptibility to potential illness, benefits of preventative actions, barriers to actions, and self-efficacy. Modifying factors should also be considered when applying the HBM.[123]

Within the model, as shown in Figure 3.2, perceived severity and susceptibility were split between HIV and general STIs, as participants explained that HIV is perceived as separate from other STIs such as chlamydia or gonorrhoea. The differing beliefs relating to HIV and STIs would result in different actions. Perceived severity and susceptibility of antimicrobial-resistant infections were included in the model, although similar attitudes were held across all groups. The perceived benefits and barriers of condom use form the latter elements of the model and are particularly important in determining the behaviour. Decisions of whether to use condoms are also affected by alternative motivations, described as "cues to action" and "self-efficacy" within the HBM.[123]

Figure 3.2. Health Belief Model of MSM behaviours relating to condom and PrEP use.



The HBM presents multiple dimensions of people's actions and decisions. Each of the groups is discussed with explanations of the perceptions relating to individual beliefs:

Group 1: are identified by their use of PrEP and limited use of condoms. This group perceived HIV to be more serious than general STIs (chlamydia or gonorrhoea), reported barriers to using condoms, and believed that the benefits of condoms were reduced by the availability of PrEP. PrEP provides protection from HIV, which is the major concern of most, so with this risk mitigated, the need for condoms reduces, resulting in a reduction in the use of condoms.

Group 2: have little concern for infection and did not consider the severity of HIV or STIs, viewed minimal benefits to using condoms, and numerous barriers such as an inability to engage in sexual contact while using condoms due to personal and/or partner dislikes, resulting in condoms being infrequently used during sexual encounters. PrEP use among this group would be a positive step forward due to the high-level threat they face from infection. Few participants fell within this group. However, it should not be assumed that individuals with these views are a minority within the general population, as a typical group 2 individual might be less likely to engage with research due to their lack of consideration for the topic.

Group 3: perceive HIV and STIs to have equal severity, acknowledge the benefits of condoms and identify few barriers, and would regularly use condoms to prevent all infections. Of those among this group who did take PrEP, it functioned as an additional level of protection. These individuals took a pragmatic view, knowing that there may be situations where condoms would not be used (such as oral sex, getting caught in the heat of the moment, or sex with recurring casual partners), and so PrEP provided them with a safety net for such occasions.

Participants mainly presented characteristics of Groups 1 and 3. However, these beliefs and behaviours are not set, and people are likely to switch between them based on varying experiences. There were many situations where their beliefs and behaviours would slide towards the lack of concern presented in Group 2, often influenced by a low mood.

Of those with an understanding of AMR infections (and this did not include everyone within the groups identified), it was portrayed that the severity of an AMR infection was concerning. However, the perceived risk of acquiring a resistant infection was low among most participants, as it was viewed as a future problem and not something they needed to concern

themselves with currently. While among some, it was suggested that their concern was increasing, it was not currently at a level that would affect actions and behaviours.

As presented in the model, the individual beliefs are influenced by modifying factors. From the findings of the interviews, the major modifying factors were health knowledge and mental health. As might be expected, those who knew about multiple STIs and details of HIV tended to perceive both as equally risky to health, resulting in protection being paramount. However, some participants with extensive knowledge explained how they would weigh the risks of infection with the protection provided by PrEP and accept the potential for infection with chlamydia, gonorrhoea, and syphilis. The ability to be easily treated for these infections resulted in them not viewing the risk as equal to HIV, which, even though manageable, is still a lifelong condition. Limited knowledge presented a split in how it affected perceived severity and susceptibility. Some participants who lacked knowledge of STIs would then not consider the dangers of unprotected sex. However, there were others who, conscious of their lack of understanding, would be overly cautious to prevent infection, influenced by fear. This emphasises the influence that knowledge has on individual beliefs and is thus important to explore. The varying behaviours related to levels of knowledge are likely to represent the varying constructs of knowledge. Stoutenborough and Vedlitz argue that there are different constructions of knowledge, and these differences result in differing perceptions of risk and thus differing behaviours.[124] This can explain why individuals with high and low levels of knowledge will have differing perceptions of risk.

Another modifying factor is mental health, presented as a far stronger influencing factor than knowledge. Times of adverse mental health were considered too strongly affect perceptions and risk behaviours. Despite usually perceiving a high level of severity and susceptibility towards infection, during times of mental distress, some participants felt that these concerns would be pushed aside or ignored to simply enjoy the moment of passion. Participants often reported using the sexual experience to relieve their negative feelings and emotions. The link between risky behaviour and poor mental health is not novel, and many previous studies have highlighted this, particularly among MSM.[125-128] Literature documents a higher prevalence of mental health issues among the LGBTQ+ population,[129-130] which may be linked to the higher levels of risky behaviour and higher rates of STIs identified among MSM. Condom use behaviours were not solely decided by beliefs or perceptions, with self-efficacy

playing a significant role. Previous research has identified that self-efficacy is a strong predictor of intended and actual condom use.[131] Findings from the interviews highlight that partner preference for condom use can have a considerable influence, and this can alter the individual's self-efficacy for using a condom. Even when an individual may want to use a condom, their determination will waiver based on the partner's preference. PrEP provided a solution, as the use of PrEP was not something negotiated with partners, being taken regardless of partners. Additionally, cues to action have an impact. Fear was presented as a potential cue to action, but it was largely reported as occurring after the encounter. The anxiety and fear experienced after a sexual encounter is a cue to action for future behaviours. However, the literature presents inconsistencies in cues to action predicting condom use.[132-133]

It is worth noting that the typology from the model is not binary, with every individual sticking to their specific group; rather, the typology should allow that knowledge, mental health, and self-efficacy will influence people's beliefs and change the outcome of action. Every individual interviewed could appear within each of the groups throughout their life depending on circumstances, which may explain why condoms and PrEP use have low adherence among MSM.[134-135] The plethora of factors influencing these actions can continuously change. Likely, other groups are not included, as the typologies reflect the participants interviewed, and it is possible that these groups would be expanded if more people were interviewed.

This HBM can assist in the development of future public health interventions. MSM is a broad group and not homogenous, the model provides a typology with group 2 being the group requiring attention. With this group in mind, any intervention can be developed specifically for groups of higher need than the usual suspects who are repeatedly exposed to generic MSM interventions.

3.7.2 Interventions

Individuals within the study described interventions they thought might be helpful to reduce STIs. These centred around improving knowledge, increasing testing, condom, and PrEP use, as well as reducing stigma. All suggestions implied that improved knowledge would lead to a reduction in STIs. Their suggestions assume that the public has poor knowledge of sexual health, and improving their understanding would result in a better ability to assess their risks

and make better health choices, presenting a knowledge deficit model.[136] However, many previous public health interventions have shown that improved health literacy does not always equate to improved health behaviours. Using smoking as an example, most people in the UK are now aware that smoking is bad for their health, but some continue to engage in the behaviour. This idea of knowledge-changing behaviour assumes that people are rational actors, whereas, in reality, most people engage in behaviours in the moment without consciously doing a risk assessment. This was evident in some participants when they proposed that improved knowledge would lead to better condom adherence. Their own condom use was inconsistent, despite having a good understanding of infections and an awareness of the risks of condomless sex.

Many participants believed that improved access to testing with a holistic approach to having a healthy sexual life had the potential to reduce rates of transmission. Their logic was based on the premise that regular testing would identify positive cases before potential transmission to others. However, participants were mindful that stigma and shame can surround STI testing for some people. It was pointed out that improved knowledge could reduce stigma around STIs, and participants therefore felt it important to start open conversations around sexual health in schools. The ideas of improving education of sexual health were not directly for the outcome of improved condom usage (many explaining that personal preference would win out over knowledge), but for the benefits knowledge would have on areas such as testing and stigma. Meta-analyses of previous interventions have found that education can be successful in reducing stigma for various conditions.[137-138] However, evidence is mixed with a natural experiment in Uganda concluding that additional education within formal schooling had no causal effect on reducing stigma towards HIV.[139] The holistic approach suggested would encompass sexual health, mental health (which was previously identified as having an important influence on behaviour), and physical health, helping an individual to think of their body and mind as a single entity. While holistic approaches to health are becoming more popular, the integration of sexual health is more complicated. A systematic review and meta-ethnography conducted to examine the discussions mental health nurses have with their clients relating to sexual health issues highlighted some difficulties.[140] The study found that many nurses had difficulties broaching the subject of sexual health, with personal values often impacting professional

practice. While this is just one example and only relates to mental health nurses, it shows some of the difficulties in developing an integrated approach encompassing sexual health.

AMR awareness was perceived as poor among the general population. An interesting point raised is that any intervention should focus on the consequences for people and make it relatable rather than attempt to provide a scientific understanding of AMR. However, as previously mentioned, education-based interventions for changing behaviours have their limitations in effectiveness.

3.7.3 Strengths and Limitations

There are some key strengths and limitations relating to certain aspects of this section of the project. These include the sample, the researcher, and the impact of COVID-19.

Within the sample, one limitation was that well-educated individuals dominated. Therefore, the level of knowledge is unlikely to reflect the understanding and concerns of MSM across Wales. The nature of volunteering to participate creates its own bias, as samples are filled by those with an interest in or investment in the topic area. This is evidenced in the current sample of those who reported employment or interest in sexual health, explaining some of the heightened understanding, particularly around antimicrobial-resistant infections. It is difficult to assume what a generic level of knowledge would be and then be able to target those individuals to interview. One observation from conducting the interviews was that those who did present with a lower understanding of sexual health matters provided less discussion and detail, even when probed. The study's focus on knowledge and awareness may be a reason for the heightened engagement of those educated in this area and those with limited understanding not participating. Future recruitment for studies with a focus on knowledge should place emphasis on engaging with a wide range of participants regardless of their perceived awareness, with this made clear in recruitment materials.

The sample was also dominated by white individuals, which limits the scope of the findings. Glitter Cymru (a group supporting Black, Asian, and Minority Ethnic LGBTQ+ people in Wales) were engaged to help promote the study, but this had little impact. Previous research finds similar challenges engaging Black, Asian, and Minority Ethnic groups (BAME) in research relating to sexuality and sexual health unless those groups are the key focus.[141-142] Better ethnic diversity within research is a goal for all researchers to work towards. The strengths of

the sample were that it included a diverse age range, with participants relating to all experiences of PrEP.

It is well documented in qualitative research that the researcher will bring their own bias to the projects and interviews.[143] In this case, the lead interviewer being a gay male likely led to an unconscious bias in the probing and interpretations made. There is the possibility that a gay male researcher resulted in participants needing to provide less explanation around certain topics. In contrast, a heterosexual researcher may have pulled out more detail due to a lack of cultural knowledge. However, having a shared social experience may be a strength in developing rapport with participants. Before one interview began, a participant queried my sexuality as the interviewer and was relieved when I reported that I was gay. Upon questioning this response, the participant indicated that they could discuss their sexual encounters more openly due to a perceived understanding that another gay male would have relating to how sexual encounters occur (via apps such as Grindr).

While the COVID-19 pandemic had the limitation of delaying interviews and slowing the progress of the project, there were some benefits to the pandemic in terms of data collection. The move to virtual interviews and the acceptance of virtual interviewing as a robust method of data collection within the research community had the benefits of reducing cost, energy, and time. Interviews could be conducted without the need for excessive planning or travel for either party. This change sped up the process of interviews, and so multiple interviews were able to be conducted in one day with people across Wales. This was a major strength, as it provided the ability to catch up on the time lost. Additionally, the use of virtual interviews can make the participants more comfortable when discussing sensitive topics such as sexual behaviour, as discussed in the methods section.[111]

3.8 CHAPTER SUMMARY

This chapter has explored the understanding and concerns of MSM towards PrEP, STIs, and AMR using qualitative methods. A description of the methodology was provided, detailing data collection and analysis. Findings were presented with a discussion of health beliefs and behaviours. Findings from this chapter will be combined with data from other chapters and further discussed in the development of the conceptual framework (Chapter 6) and final discussion (Chapter 7).

CHAPTER FOUR
AN EPIDEMIOLOGICAL EXAMINATION OF THE IMPACT OF PREP ON STIS AND AMR

This chapter aims to explore the relationship between the introduction of PrEP, STIs, and AMR in Wales. This will be done using a quantitative approach with routine health data. An explanation of the nature of the data and how they were obtained is followed by my analysis strategy for the purposes of this study. After outlining the analysis, the results are presented, and a compared with the current literature. The chapter concludes with a discussion of the strengths and limitations of this study.

4.1 DATA CONTEXT

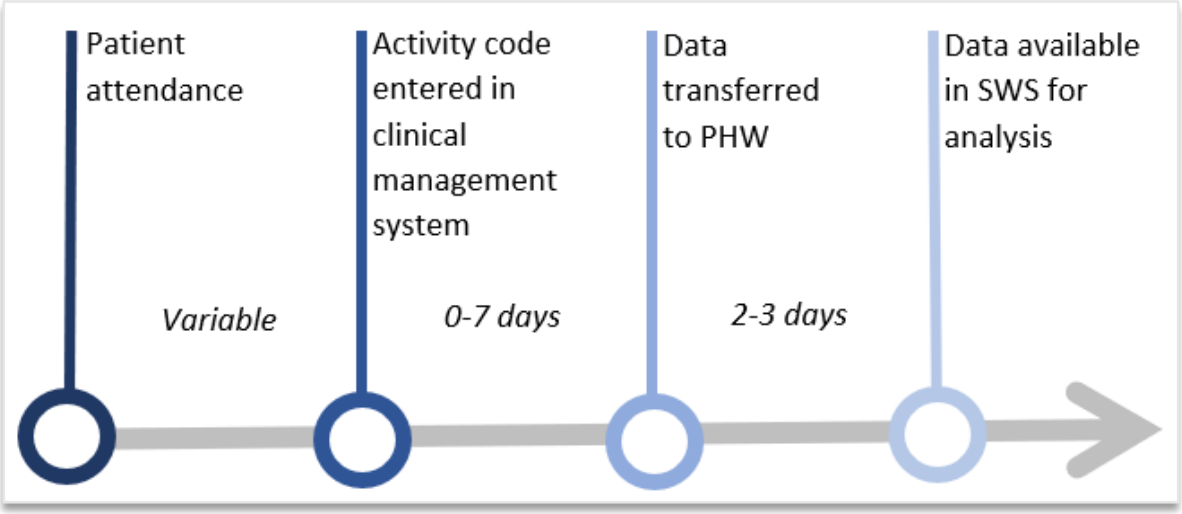
4.1.1 Sexual Health in Wales Surveillance System

Sexual health in Wales is governed and monitored by Public Health Wales (PHW), with data from sexual health clinics monitored through the Sexual Health in Wales Surveillance System (SWS). The SWS collects clinical data relating to STI testing and results from sexual health clinic service user systems across Wales and combines them to form the National Dataset for Sexual Health in Wales. Consultations, testing, and treatment for STIs can occur in NHS services outside of sexual health clinics, such as GP surgeries and hospitals, but this data is not included in SWS. Service user data is recorded as codes for the primary purpose of service user management and should include service user demographic details and clinical or risk factor data collected during service user consultations. Administrative staff usually collects the demographic details of service users, with clinical coding and the collection of risk factor information usually conducted by clinical staff. All sexual health services are requested to submit weekly updates of all service user attendances to their clinical management systems. Records are meant to be updated with the appropriate consultation codes on the systems as soon as possible, no later than six weeks after the relevant attendances. Activity codes indicate the purpose of the attendance and highlight the outcomes; in this case, activity codes relate to various STI testing, treatment, health advice, and any preventative interventions (PrEP, vaccines). These data are then extracted and submitted to PHW weekly, usually on

Fridays. Following receipt of data, the PHW informatics department will upload the datasets to the SWS, making them available to the Communicable Disease Surveillance Centre for data analysts to clean for analysis.[144] Figure 4.1 (below) presents a visual representation of the ideal data flow and timelines of the SWS.

Since the introduction of PrEP in July 2017, data has been collected within sexual health clinics that provided PrEP and integrated within the existing SWS. Activity around PrEP is captured through a series of 33 codes that cover eligibility, outcome of offer, reasons for declining or stopping, frequency and number of doses, adherence, and coverage of risk episodes.[144] Further details of the SWS and coding structure can be found here.

Figure 4.1 Data flow diagram of the Sexual Health in Wales Surveillance System.



Note. *Since the introduction of the postal testing service in response to the COVID-19 pandemic, the data flow process has changed. However, as the data analysed in this study was collected before the pandemic, the old process remains applicable. PHW has not produced any updated documents on how the integration of the postal testing service has altered the data management systems, so the new process is currently unclear.*

4.1.2 Gonococcal Resistance to Antimicrobials Surveillance Programme

As previously explained in Chapter 2.2.3, gonorrhoea is currently the only STI which is routinely tested for antimicrobial sensitivities in England and Wales. This is covered by the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP). Under the GRASP protocol, specimens for culture (urethral, endocervical, neovaginal, anorectal and pharyngeal swabs) should be taken alongside nucleic acid amplification tests from people suspected clinically of having gonorrhoea and from sexual contacts. Cultures of gonorrhoea are sent from sexual health clinics to their associated laboratories for antimicrobial susceptibility testing. Susceptibilities to eight different antimicrobials should be tested (azithromycin, cefixime, ceftriaxone, ciprofloxacin, doxycycline, penicillin, spectinomycin, and tetracycline), chosen for their previous use as therapy for gonorrhoea or use in the treatment of other bacterial STIs.[21] Findings are recorded as cultures:

- (S) susceptible, standard dosing regimen: meaning standard dosing of the antibiotic would have a high likelihood of successfully treating the infection.
- (I) susceptible, increased exposure: this means that there is a high likelihood of therapeutic success if the antibiotic agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
- (R) resistant: this means that there is a high likelihood of treatment failure even if a higher dosing regimen is adopted. While isolates may be identified as resistant, it is not a guaranteed treatment failure, so cases may be identified as resistant, but the treatment may still be successful.

These current descriptions were introduced in 2019 by the European Committee on Antimicrobial Sensitivity Testing (EUCAST).[21] On review of the previous guidelines on the EUCAST website, it seems the major change is that (I) used to be referred to as intermediate, with the breakpoint of MIC 0.5 mg/L for N. gonorrhoeae azithromycin resistance being replaced with an 'epidemiological cut-off' of 1.0 mg/L [145]. However, for continuity in reporting, GRASP retains the historic reference point. [21]

All results are uploaded to DataStore by lab technicians for access by PHW and forwarded to GRASP.[21] PHW do not produce any reports of Wales only AMR data, with all Welsh data being integrated within the UK GRASP report. Full procedures for antimicrobial susceptibility testing can be found here.

4.2 STUDY AIMS

The aim of this study was to explore the impact the introduction of PrEP has on STIs and AMR in Wales. This was achieved through the following objectives:

- Describing the trends in:
    - STI testing,
    - positive cases of STIs,
    - positivity rates for STIs.
- Estimate changes in STI infections prior to and following the introduction of PrEP.
- Identifying the trends in antibiotic resistance of gonorrhoea samples in relation to the introduction of PrEP.

4.3 METHODS

This study was a retrospective observational analysis of routinely collected sexual health data from sexual health clinics across Wales. All data were provided by PHW and included STI testing and result data from the SWS, with antimicrobial sensitivity data provided from GRASP.

4.3.1 Study Population

The population examined was exclusively MSM, with datasets including only male sexual health service user records coded as MSM. For all datasets, all available cases that were identified as MSM were analysed. Service users were identified based on their consultation code (MSM) entered at the time of consultation. All available test and clinic data linked to a consultation were included; the STI data included records from January 2007 to February 2021, with the AMR data ranging from January 2012 to February 2021.

4.3.2 Ethical Approval

Full NHS ethical approval was received for the use of the data, as explained in Chapter 1.4. The data received from PHW were pseudo-anonymised using clinic numbers as identifiers. Data retention and storage was conducted following Cardiff University's data protection and retention policy.

[See Appendix 1.3 for ethical approval letter]

4.3.3 Data Management

Data access delays

Delays ran throughout the course of this study due to the onset of the COVID-19 pandemic. First, delays occurred in the NHS ethics process as the study was not considered a high priority as it was not a COVID-related study. Once NHS approvals were received, discussions started with relevant PHW data managers to negotiate the data extraction and sharing processes. However, as staff within PHW had been seconded from their principal areas of work to focus on tracking and analysing COVID-19 associated data, there was not enough capacity within PHW to extract and send the required data, resulting in a 9-month delay in receiving data.

Data extraction

After receiving ethical approval, service user data were requested from PHW. Non-identifiable data variables were requested from the SWS national dataset and GRASP DataStore. For STI data, two datasets were provided, one with the data of individuals with positive STI results and the other with individuals with negative STI results. The SWS data management system does not have service user records as a single file, so an additional dataset for PrEP data was provided, which would need to be matched to the other records. This third dataset included only PrEP-related coding information with a clinic identifier (ID) to assist matching. This information was extracted and filtered by a PHW data manager, but duplicates were not removed.

The antimicrobial resistance testing data were provided in a single file. These data were extracted from the regional DataStore systems by data managers within PHW. The required variables were extracted and filtered before being provided for analysis. Within DataStore, duplicate isolates were removed from analysis. Isolates were deemed duplicates if the same organism with the same antibiogram (overall profile of antimicrobial susceptibility testing result) was grown from the same sample type within 91 days. This process removes potential skews from duplicate testing.[21] This dataset included simple demographic information with results from the susceptibility testing for azithromycin, ceftriaxone, cefixime, ciprofloxacin, doxycycline, penicillin, spectinomycin, and tetracycline. All four datasets can be viewed in Figure 4.2.

[See Appendix 4 for full list of variables included in each dataset]

Data quality

For all datasets, coding was employed with the aim of ensuring that data were standardised across all services in Wales. However, this relies on the correct coding being adopted by clinicians, administrative staff, and lab staff. There is little evidence assessing the accuracy of the coding by staff members, but a recent evaluation of the postal testing service has identified that there are some challenges in ensuring that correct coding is completed within the data sent from clinics to PHW[146].

The data provided only included testing and diagnoses identified through sexual health clinics; data for any STIs tested/diagnosed within other settings, such as general practices, hospitals, or prisons, were not provided. A recent PHW report [2023] presented that STI testing and identification in GPs or other medical settings (outside sexual health clinics) are less common for men than women, with an average of 5246 males (including all sexualities) being tested in these settings each year from 2013 to 2019.[147] Unfortunately, as data were not separated by sexuality, it is unknown how many of the males in the dataset were MSM.

Other quality issues in the STI dataset are that after receiving treatment for chlamydia, gonorrhoea, or syphilis, follow-up testing is recommended to confirm that the infection has been cleared; usually two weeks after diagnosis. This results in two testing reports being linked to a single consultation. While tests coded as “follow-up” were removed, if they were not coded to indicate this, then they may have been included within the sample.

Within this dataset, the variable sexuality is a reference to who the individuals are engaging in sex with and not a true reflection of self-identified sexuality. This variable only included 3 categories: heterosexual (only engaged in sex with the opposite sex), homosexual (only engaged in sex with the same sex), or bisexual (engaged in sex with both sexes). Therefore, a man identifying as heterosexual who engages in sex with other men would be coded as bisexual, regardless of their identified sexuality. This inaccurate use of the term sexuality is problematic and does not allow for stratification via sexuality. The data requested was for all MSM, and so it only included gay and bisexual categories.

In 2012/2013, the EUCAST antimicrobial susceptibility testing methodology was implemented across the laboratories in Wales to remove issues around methodological variability. This removed variability in how samples are tested, but it is important to note that laboratories

do not have a set testing regime for which antibiotics are tested.[21] While the GRASP protocol suggests testing susceptibilities to eight different antimicrobials, some laboratories only test susceptibilities to certain antibiotics. For example, one laboratory may only test certain antibiotics when an organism presents with resistance to first-line drugs, whereas others will test against all agents routinely.[21] Full details of EUCAST can be found at https://www.eucast.org.

Data cleaning

From the various datasets provided, extensive cleaning was required to produce two datasets, one for the STI testing and result data and one for the AMR data, both including a variable related to PrEP use. Figure 4.2 presents the dataset flow diagram.

STI dataset: Data were initially checked against the criteria of being MSM, and the positive and negative STI datasets were merged using clinic IDs. In this STI dataset, an additional variable for PrEP use was added based on matching clinic IDs. There were 202,250 individual consultations identified, equating to 13,960 service user records. All consultations were within the date range of January 2007 to February 2021. The STI dataset included duplicate columns, these were created from merging various clinic datasets to form a dataset by PHW, these were reviewed, and duplicates deleted. Codes were reviewed, and matters relating to consultations other than STI testing, and results were removed (PrEP interest/ initiation/ consultations, vaccines, treatment, other), leaving 105,957 consultations. Records pertaining to a single consultation were identified and aggregated into one 'case' to represent all information related to a unique consultation. Upon review, there were very few cases and tests of STIs pre-2012 within the PrEP cohort. Rather than reflecting a true picture, this is due to the limited number of patient records with data for pre-2012. As 2007–2011 had limited data available for PrEP users, this data was excluded from the analysis, which removed 513 service user records. Data from January 2020 up to February 2021 were removed as they would not be comparable to other years due to the influence of the COVID-19 pandemic, this removed 1653 service user records.

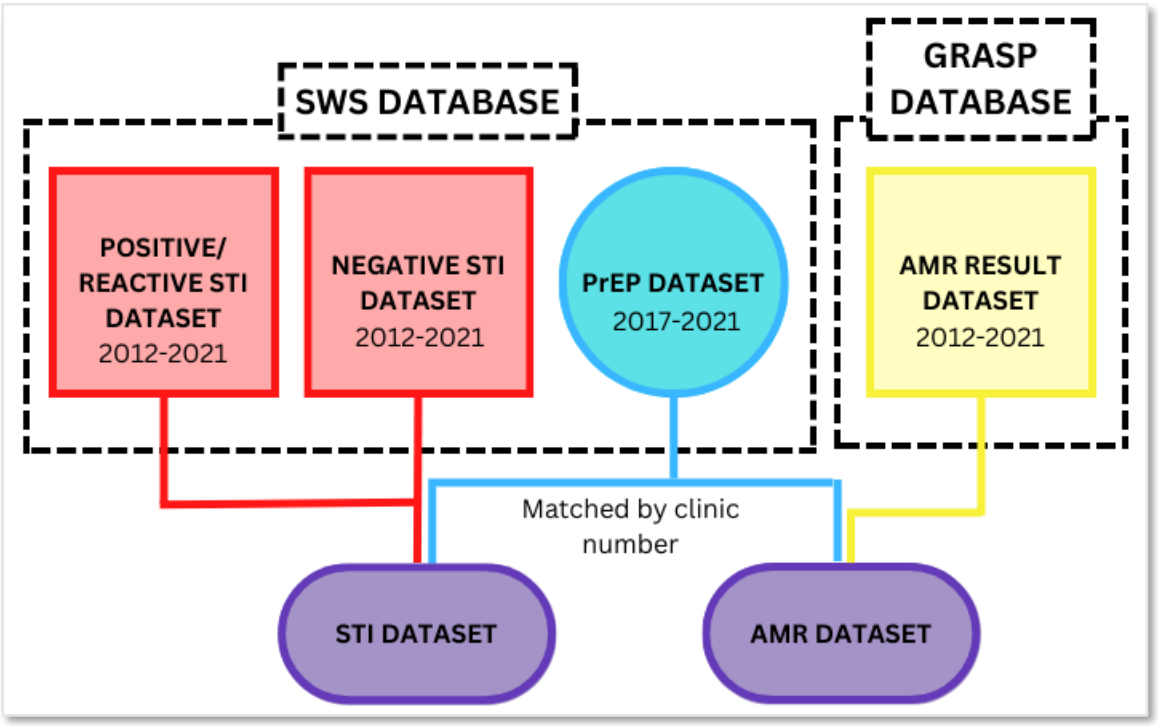
In some cases, extracting the individual tests from the codes provided was necessary. This was because many codes were grouping various tests together, such as "chlamydia and gonorrhoea testing," "3-site testing," and "full sexual health screening, including HIV antibody

testing." Testing data were calculated per quarter, with the number of tests calculated from coding frequency. For example, the tests for chlamydia would be derived from the frequency of multiple codes such as “chlamydia and gonorrhoea testing,” “full sexual health screening” and “chlamydia-only testing.” The extrapolated testing per quarter was combined to form a result for the year. The final dataset to be analysed included 62,464 consultations, equating to 11,415 service user records.

AMR dataset: The data provided included all lab samples received from sexual health clinics for MSM in Wales, which included cases ranging from 2012 to early 2021. Data from 2020 and early 2021 were removed as they would not be comparable to other years due to the influence of the COVID-19 pandemic. My intent was to use the clinic ID numbers to match the SWS dataset. However, the clinic ID variable within the AMR dataset was not dependable, with the variable including a mixture of alternative numbers and surnames that did not match the SWS IDs. This resulted in an inability to match all records accurately. A variable related to PrEP use was created using the clinic IDs available. As mentioned, not all cases had accurate IDs; therefore, the PrEP use variable only reflects those able to be matched and so may not be a true reflection of all PrEP users. A new variable was created that matched clinic IDs and formed a variable to indicate PrEP use. On inspection of the data, the PrEP cohort had only four data points identified in 2012 and a single in 2013. These were removed from the analysis, leaving data for the years 2014 to 2019.

Due to the nature of the data management system, matching for both datasets were not exact. Each time PHW receives a new dataset from clinics, these data are simply added to the end of the existing file, creating layers of information. This could be solved by matching clinic IDs; however, service users do not receive a single clinic ID that can be used across clinics but a clinic ID that is only applicable within a specific location. Therefore, people could attend multiple clinics and have multiple clinic IDs. Additionally, there is no national ID system, so different people in different clinics can have the same ID. I matched the data by month and year of birth to help exclude some of the overlapping, but duplication is still possible. People may appear in the data multiple times if they attended different clinics over the eight years of data presented. There is no way to identify the impact, so the data will have an interdependence of observations that cannot be accounted for, meaning there is a risk that the standard errors (and hence any confidence intervals and p-values) are artificially narrow.

Figure 4.2 Data flow diagram of the datasets to be analysed.



4.3.4 Analysis

A statistical analysis plan was developed based on the study objectives and the types of data available. However, on inspection of the data provided, it became apparent that certain analyses planned would not be able to be completed as incorrect assumptions regarding the data had been made.

Primary analysis

I aimed to:

- Describe the STI testing rates for MSM.
- Describe the longitudinal trends in STI cases.
- Describe the longitudinal trends in positivity rates for STIs.
- Investigate the impact of the introduction of PrEP in Wales on STI rates.
- Describe the longitudinal trends in resistance for gonorrhoea samples.

The original intention was to conduct an interrupted time series analysis to identify potential changes in rates of antimicrobial sensitivities after the introduction of PrEP. However, due to the limited data available for the PrEP cohort, this analysis was not possible to complete; therefore, descriptive analysis alone was conducted for the AMR data.

Descriptive statistics

Univariate analyses were conducted to describe service user characteristics, including age, sexuality, ethnicity, and health board. These are described using means, percentages, and ranges. STI testing and positive infections, along with positivity rates, were presented as frequencies, with graphs used where appropriate. Positivity rates for STIs were calculated using positive tests and the total number of tests for each period (year and quarter). The definition used to describe a new consultation was any testing or positive result identified after 14 days of a previous test or infection. Using this definition, I have assumed that any consultation after 14 days (from the previous consultation) indicates a new episode.

The trend analysis includes an individual focus on chlamydia, gonorrhoea, and syphilis while also examining all STIs (including chlamydia, gonorrhoea, syphilis, HIV, genital herpes, genital warts, LGV, HEP B, and C). This was decided as genital herpes and genital warts are often diagnosed via visual inspection without testing being conducted, meaning there is limited testing data to develop an accurate positivity rate. Up to 2019, no PrEP user had been diagnosed with HIV, so comparisons between PrEP and non-PrEP users were not possible. Finally, LGV and the various strains of hepatitis have very few cases (under 50 cases over eight years); these were excluded from individual inspection.

Interrupted time series analysis

Time series analysis is a method of analysing multiple data points recorded at consistent intervals over a set period. This can show how outcomes change over time and whether these changes differ depending on the group. This approach requires extensive data points (more than eight) for reliable results and to ensure that any trends or patterns discovered are not outliers and can account for biases such as seasonal variance.[148] In an interrupted time series (ITS), the design involves comparing longitudinal trends before and after an intervention is introduced. This includes a series of observations pre- and post-intervention points to establish the trend. The assumption is that the level and trend in the outcome among those exposed to the intervention would not change if the intervention did not occur, strengthened by the inclusion of a control group. Essentially, there is a trend before the intervention, and it is assumed (the counterfactual assumption) that the trend would have continued in the future (often represented visually as a dashed line). Observed data points are used to establish an observed line, or a level and trend, for the post-intervention period.

The observed data points are compared to the counterfactual to identify if there was a change in the level and/or a change in the trend of the outcome after the intervention.[149]

An ITS analysis was conducted on consultation rates over eight years of data from 2012 to 2019, being segmented into quarterly periods. For this ITS, the approach I adopted involved fitting a generalised least squares regression line to each segment of the independent variable (PrEP use), time, assuming a linear relationship between time and the outcome within each segment [150]. The following linear regression model was specified to estimate the level and trend in the STI rate before PrEP was introduced and the changes in level and trend following the provision of PrEP in comparison to non-PrEP users:

$$STI\_rate_i = \beta_{0\,i} + \beta_1\, time_i + \beta_2\, PrEP\_use_i + \beta_3\, PrEP\_period_i + \beta_4\, time_i * PrEP\_use_i * PrEP\_period_i + \varepsilon$$

Intervention status was PrEP_period (pre- or post-PrEP), group was PrEP_use (1=yes, 0=no), and time (time in quarters from the start of the observation period to the last point in the time series, 32). I modelled the outcome (STI rate), taking the values 0 occurring before PrEP was available and 1 after PrEP provision, which was implemented at time point 23 in the series. Time, after PrEP is provided, is a continuous and linear variable recording the number of quarters after the intervention. In this model:

- β0 = STI rate for non-PrEP users prior to the introduction of PrEP is the baseline STI rate for non-PrEP users.
- β1 = time trend of STI rates in non-PrEP users prior to PrEP's introduction.
- β2 = STI rate for PrEP users prior to PrEP's introduction.
- β3 = average STI rate in non-PrEP users after PrEP's introduction.
- β4 = time trend of STI rate in PrEP users after PrEP's introduction.
- ε represents the random error term.

There are characteristics of a time series that can lead to biased results; these include autocorrelation and seasonality.[150] Autocorrelation refers to there being a relationship between data points over time. To explore autocorrelation, I first ran a Durbin-Watson statistic[151], followed by plotting autocorrelation (ACF) and partial autocorrelation functions (PCF). Examining the partial autocorrelation function for the dataset confirmed that no adjustment for seasonality was required. To allow for autocorrelation in the data, the

segmented regression described was fitted using R's "gls" function from the "nlme"package.[149] This package allows for the regression model to be estimated under the condition of autocorrelation. For explanations and examples related to elements around conducting an interrupted time series (autocorrelation, partial autocorrelation, seasonality), you can access the following sources: 149, 152.

Data were cleaned and analysed in IBM SPSS Statistics 27 with the interrupted time series being conducted in RStudio with graphical outputs developed and presented using a mixture of RStudio and Microsoft Excel.[153-155]

4.4 RESULTS

Results from the two datasets will be presented sequentially, with the first providing the findings from the STI dataset. The findings from the AMR dataset start at 4.5.7. PrEP users are defined as those currently using or going to use PrEP (for the years before PrEP was provided).

4.4.1 STI Demographics

There were 62,464 consultations, equating to 11,415 service user records from 2012 to 2019. From the records, 10.1% (1153/11415) were identified as having initiated PrEP.

[See Appendix 4.4 for a table of demographic information.]

Age (at first consultation)

For all MSM, the mean age was 33 years, ranging from 13 to 86. The age group 18–25 held the largest population of service users (34.9%, 3980/11415), followed by the 26–34 age group (28.7%, 3278/11415). Fifteen percent were aged between 35 and 44 (1763/11415), 11% were aged 45–54 (1261/11415), and those aged under 18, 55–64 and over 65 each accounted for less than five percent of the sample. The PrEP cohort had a slightly higher mean age of 34 years, with a third of the group being aged 26–34 (33%, 381/1153), 27% aged 18–25 (314/1153), 20% within the 35–44 category (232/1153), and the rest like the overall group. The non-PrEP cohort age groupings were reflected by all MSM (being much of the group).

Sexuality

Within the full sample, 80.2% of service users were identified as homosexual (9155/11415), with 19.8% being coded as bisexual. Within the PrEP cohort, there was a higher number of

service users identifying as homosexual (1005/1153, 87.2%). The non-PrEP cohort presented similar levels to the full sample (homosexual: 79.5%, 8158/10262).

Ethnicity

For the full sample, two-thirds of the service users were white British (65%, 7418/11415), 13.5% reported to be other white (1539/11415), and 5.4% were white Irish (618/11415). For the remaining ethnic identities, each had varying percentages, all less than 1% of the sample. Ethnicity was not reported for 11% (1259/11415) of the sample; this was the only demographic variable not stated as a category. The PrEP cohort had a slightly lower percentage of White British (62.8%, 718/1153) and a higher proportion of other White identities (19.2%, 221/1152). Black, Asian, mixed, and other ethnicities all had higher percentages than the combined sample but remained below 1%. Ethnicity was not reported for 6.9% (80/1153). The non-PrEP cohort had a near-exact match following the whole sample, with 11.5% not having ethnicity reported (1179/11415).

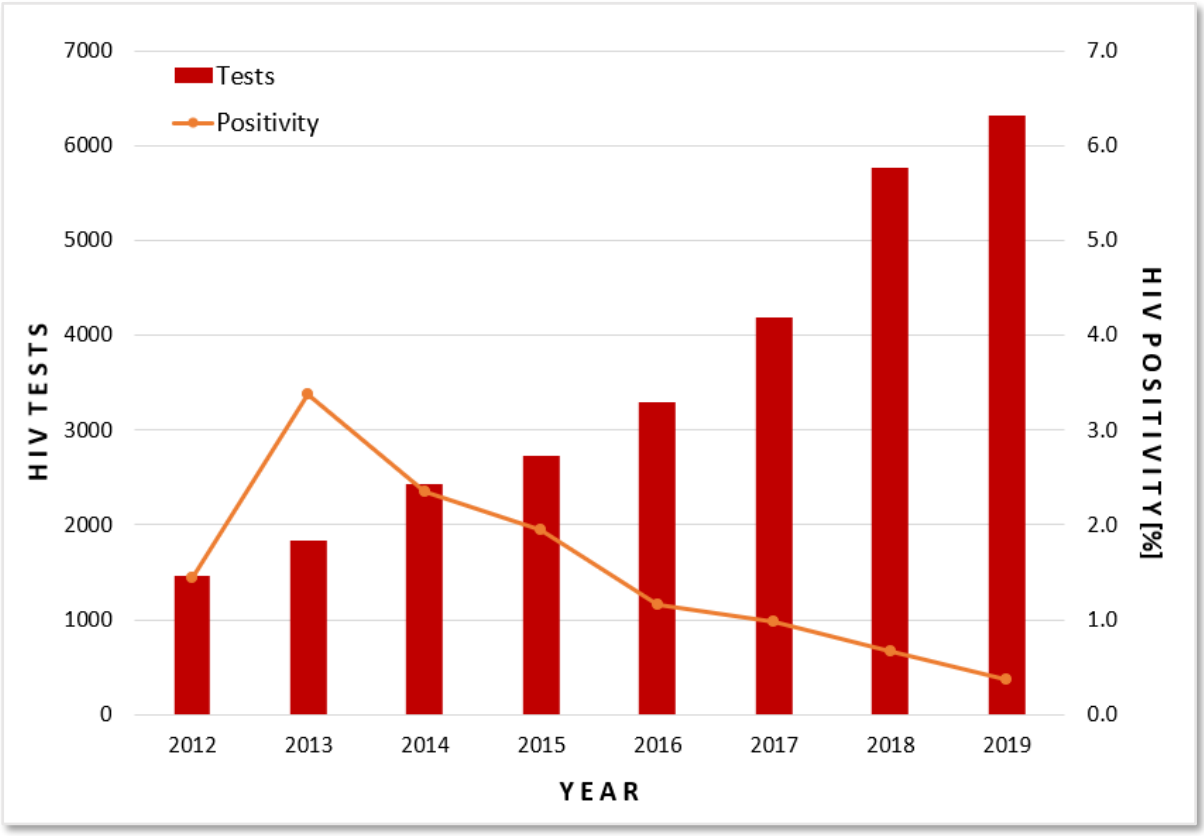
Health board

Most consultations were recorded within the Cardiff and Vale University Health Board (UHB) (39.5%, 4521/11415); compared to other health boards, 21.6% were recorded within the Aneurin Bevan Health Board (HB) (2467/11415). Nearly 15% of the data were reported from Betsi Cadwaladr HB (1640/11415), 10.5% from Swansea Bay UHB (1193/11415), 7.4% from Hywel Dda HB (843/11415), and 6.5% from Cwm Taf HB (744/11415), with 16 service users attending a clinic within Powys Teaching HB (0.1%). The non-PrEP cohort health board data was almost identical to the overall, while the PrEP cohort had higher representation in Aneurin Bevan (24%, 277/1153) and Swansea Bay (16%, 184/1153), while each other HB had a lower percentage with no service users in Hywel Dda.

4.4.2 HIV Testing and Positivity

When considering PrEP impact, it is important to remember that PrEP is provided to reduce HIV transmission. Figure 4.3 shows that testing has been increasing each year by relatively consistent increments, with larger increases being found from 2017 to 2018. After the 2013 peak of a 3.3% positivity rate, HIV infections have continued to be on a downward trend. Since 2017 and the introduction of PrEP, we have seen a stable decrease in the positivity rate, with 2019 having the lowest-ever rate of 0.5% and the highest number of HIV tests at 6323.

Figure 4.3 Yearly trends in HIV testing and positivity among all MSM in Wales.



NB. Left-hand axis corresponds to bars with the line graph having its axis on the right.

4.4.3 STI Testing

Figure 4.4 presents the data on the yearly number of STI tests conducted with a breakdown of the percentage of STI tests between PrEP and non-PrEP users. The figure illustrates that there have been year-on-year increases in STI testing among MSM since 2012. It combines all STI testing, including chlamydia, gonorrhoea, syphilis, HIV, LGV, genital herpes, genital warts, and hepatitis A/B/C. Between 2012 and 2016, there was an average increase of around 2000 tests per year, larger increases in the number of tests provided since 2017, with 30,927 tests being conducted in 2019. The percentage split between those using PrEP and those not using PrEP, indicates that PrEP users test more, with PrEP users accounting for 28% of all STI testing in 2018 (7573/26873) and 2019 (8648/30927), despite PrEP users only forming 9% of the sample. This increase in STI testing among PrEP users after 2017 was expected, as individuals provided with PrEP within the NHS are required to have quarterly STI testing.

Data around testing frequency demonstrates that the majority of MSM receive STI testing multiple times a year (see Figure 4.5). From 2013 to 2016, around 60% of the PrEP cohort

attended a sexual health clinic for STI testing at least twice a year, with the number testing over four times per year doubling in 2017 and increasing further in 2018 and 2019. In comparison, the non-PrEP cohort presented a gradual increase in the frequency of testing year-on-year since 2012. Increases in testing frequency per year may indicate that people increase the frequency of their testing over time. The PrEP cohort presented a more stable pattern of testing frequency from 2013 to 2016, although there were gradual increases to more frequent testing. With the introduction of PrEP in 2017, there has been a near doubling in those testing more than four times per year, with increases in testing three or more times per year from 2017 to 2019. A requirement of PrEP is quarterly STI screening, which could equate to testing four times per year. Some may expect this frequency to increase from 2017, but not everyone initiated PrEP at this point, and the annual testing period would be spread over years, and a few will start in January to have all periods covered in a single year.

Figure 4.4 Number of STI tests by year with percentage breakdown by cohort.

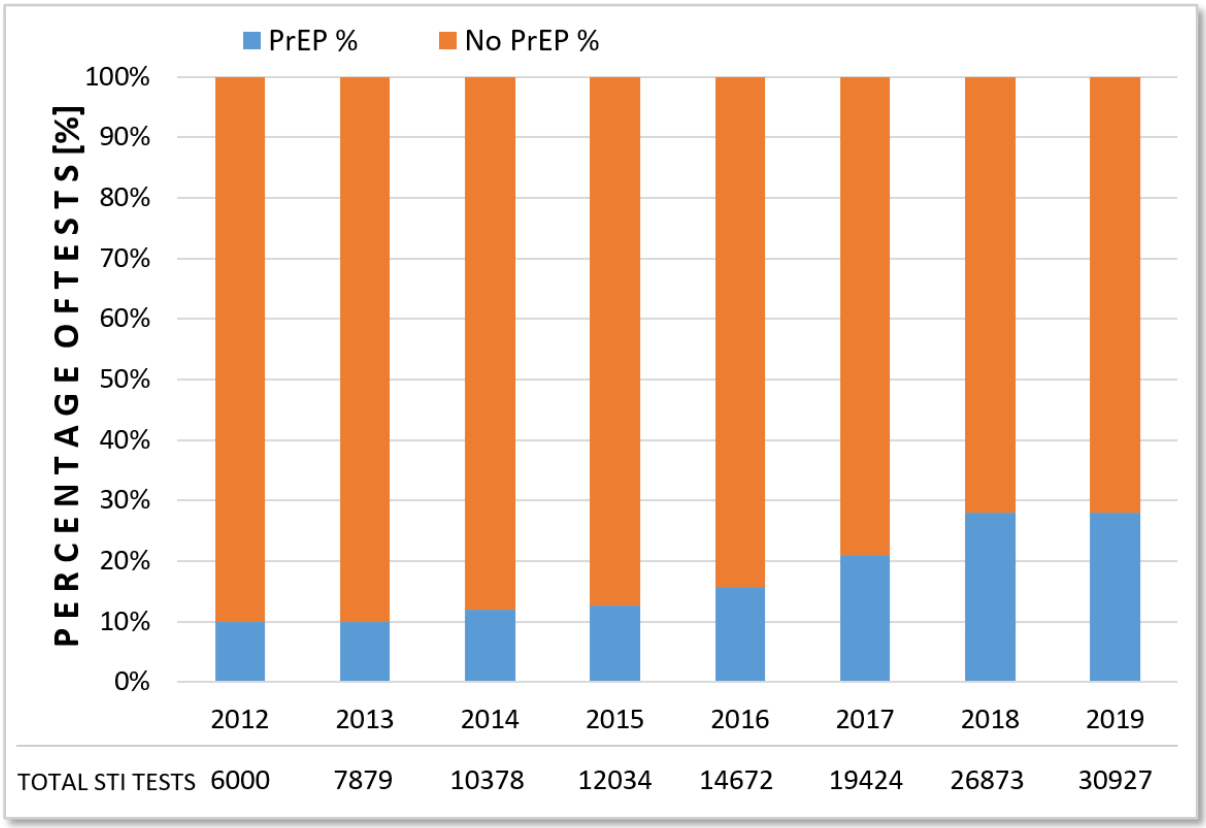
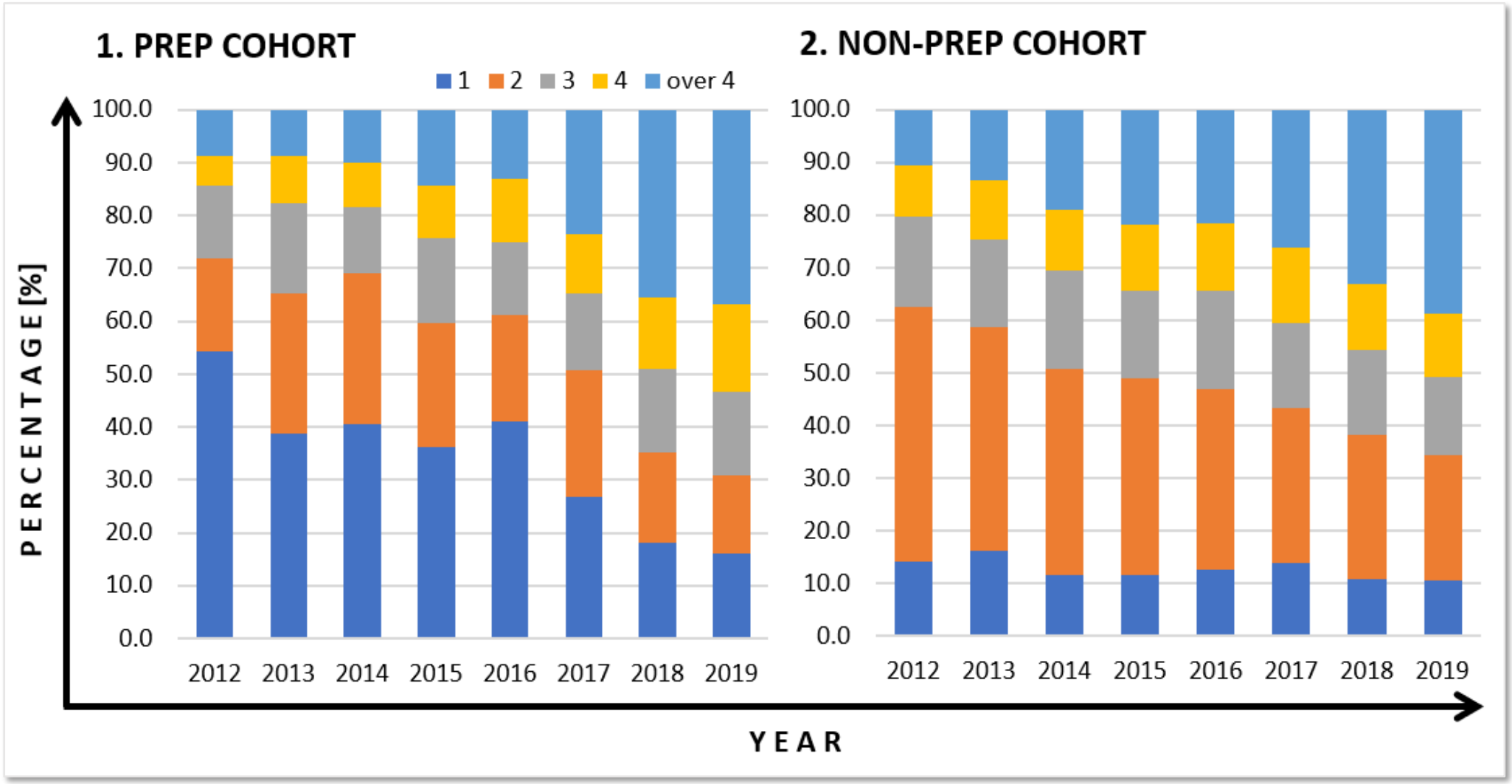


Figure 4.5 Frequency of STI testing per year.



4.4.4 STI Frequency

Table 4.1 (below) shows the number of positive STI tests for all MSM between 2012 and 2019, and the rate refers to the number of positive tests divided by the number of people in the group. There were 7893 positive diagnoses; gonorrhoea was the most common infection (3168 cases), followed by chlamydia (2461 cases) and syphilis (854 cases). The frequency of STIs was higher among the PrEP cohort for all STIs (except HEP C and HIV, of which no cases were identified). The frequency of chlamydia and gonorrhoea was three times higher among the PrEP cohort compared to the non-PrEP cohort, twice as high for syphilis, and overall, the PrEP cohort STI frequency was 2.5 times higher.

Table 4.1 Overall STI frequency among MSM (2012-2019)

	All MSM [N=11415]		No PrEP cohort [N=10262]		PrEP cohort [N=1153]		Rate ratio [PrEP/No PrEP]
	Freq	Rate	Freq	Rate	Freq	Rate	
Chlamydia	2461	0.22	1819	0.18	642	0.56	3.14
Gonorrhoea	3168	0.28	2385	0.23	783	0.68	2.92
Syphilis	854	0.07	683	0.07	171	0.15	2.23
Genital warts	794	0.07	693	0.07	101	0.09	1.30
Genital herpes	277	0.02	229	0.02	48	0.04	1.87
Hep B	26	<0.01	24	<0.01	<5	<0.01	0.74
Hep C	37	<0.01	37	<0.01	0	0	0
LGV	31	<0.01	24	<0.01	7	0.01	2.6
HIV	333	0.03	333	0.03	0	0	0
All STIs	7983	0.70	6228	0.61	1755	1.52	2.51

NB. Hepatitis A is not included as there was only a single case identified for each group.

Table 4.2 presents the frequencies of STI cases per individual over the full data period. It indicates that overall, 38% of MSM acquired one or more STIs (4238/11415). When exploring the groups, we see that the non-PrEP cohort had a slightly lower STI acquisition rate, with 35% acquiring one or more STIs (3642/10262). The PrEP cohort shows a quite different picture, with 60% acquiring one or more STIs (686/1153), with the rate of acquisition being 1.7 times higher for the PrEP cohort. As the number of infections increases, the rate ratio between the PrEP and non-PrEP cohorts also increases, with the PrEP cohort for more than six infections being 5.7 times higher than the non-PrEP cohort.

Table 4.2 Overall STI frequency per individual (2012-2019)

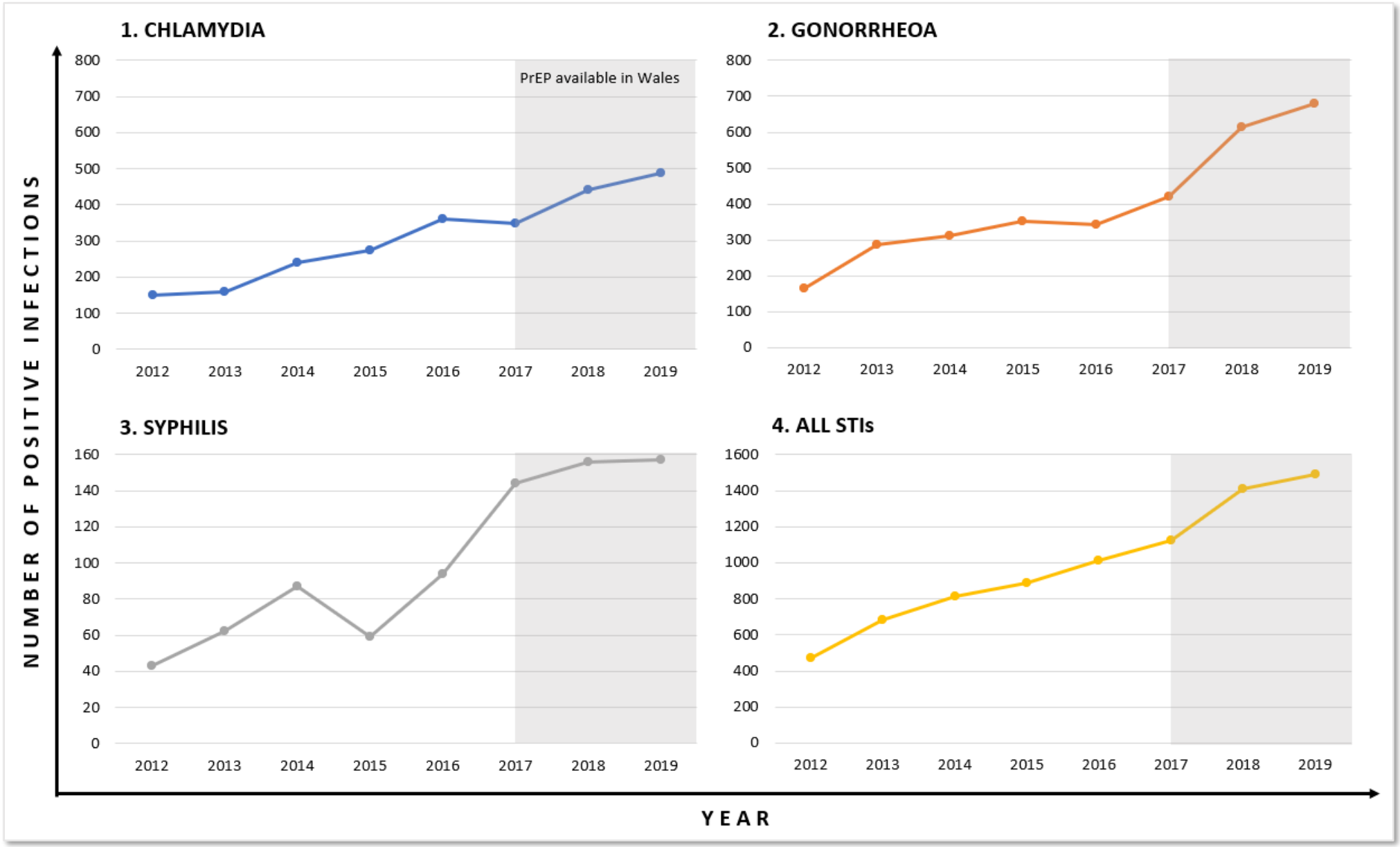
	All MSM [N=11415]		No PrEP cohort [N=10262]		PrEP cohort [N=1153]		Rate ratio (PrEP/No PrEP)
	Range 1-14		Range 1-14		Range 1-13		
	Freq	%	Freq	%	Freq	%	
No infections	7087	62.08	6620	64.51	467	40.50	0.63
One infection	2597	22.75	2315	22.56	282	24.46	1.08
Two	933	8.17	787	7.67	146	12.66	1.65
Three	369	3.23	263	2.56	106	9.19	3.59
Four	166	1.45	110	1.07	56	4.86	4.53
Five	104	0.91	67	0.65	37	3.21	4.92
Six	64	0.56	42	0.41	22	1.91	4.66
More than six	95	0.83	58	0.57	37	3.21	5.68
Total*	4328	37.92	3642	35.49	686	59.50	1.68

NB. *Total number of people with a positive STI result per group.

4.4.5 Trends in STIs

Since 2012, there has been a steady increase in the number of new infections identified across MSM in Wales (see Figure 4.7). Gonorrhoea has the highest number of cases, with cases doubling from 2012 to 2013, followed by a steady increase leading to a sharper increase in 2018, returning to a gentler increase in 2019. Chlamydia has had a steadier increase in cases over time, closely following the trend of gonorrhoea infections but with fewer peaks. However, in 2016, we can see that cases of gonorrhoea and chlamydia were at similar levels. The image of syphilis cases presents very differently, with a strong upward trend from 2012 before a drop in cases in 2015, followed by a stronger increase until cases plateau in 2018–2019. Chlamydia has had a stable increase in cases since 2012, while cases of gonorrhoea and syphilis have experienced greater jumps. Overall, this data highlights that STI cases have been increasing over time among MSM.

Figure 4.7 Trends in positive STI cases for all MSM.



NB. 1=positive chlamydia infections, 2=positive gonorrhoea infections 3=positive syphilis infections, 4=all positive STIs (includes previous three infections and HIV, LGV, genital warts, genital herpes, and Hepatitis A/B/C).

STIs and PrEP use

Figure 4.8 presents the STI cases each year, separated by PrEP use.

Chlamydia: Among the PrEP cohort, cases of chlamydia increased steadily from 2012 until 2017, increasing steeply between 2017 and 2018, with double the number of cases in 2018 (170) compared to 2017. Cases rose again in 2019, but only slightly in relation to the previous rise. For the non-PrEP cohort, there was a gradual increase in cases from 2013, peaking in 2016, with 292 new infections, dropping in 2017, and increasing again in 2018 and 2019.

Gonorrhoea: Cases doubled from 2012 to 2013 among the PrEP cohort, remaining stable at around 40 cases per year until 2016. Cases doubled in 2017, doubling again in 2018, and continued to rise in 2019, peaking at 268 cases. For the non-PrEP cohort, 2013 also experienced an increase of 100 cases compared to the previous year, with the yearly increase in cases slowing until slightly dipping in 2016. Similarly, in the PrEP cohort, a surge in cases in 2018 was identified but stabilised in 2019 at around 400 cases per year.

Syphilis: Cases have remained low, with the PrEP cohort having less than five cases each year until 2015. In 2016, there was a rise to 13 cases, doubling each following year until 2018, peaking at 55 before decreasing slightly in 2019. Among the non-PrEP cohort, cases rose from 2012, peaking in 2014 at 82, dipping in 2015 before continuing to increase, hitting a record high in 2017 of 118 cases and stabilising around 100 cases per year onward.

All STIs: Examining the trends for all STIs, since 2012 there has been a year-on-year increase in STI cases for all MSM. The PrEP cohort had a more gradual rise, increasing by 20 to 30 cases each year until 2017 when cases doubled in 2018 compared to the previous year. In 2019, there was another increase, hitting a record high of 541 cases. For the non-PrEP cohort, there was a gradual uptrend in all STIs, with 2013 having the largest increase by almost 200 cases. Every year after 2013, there was a stable upward trend, with a larger increase between 2017 and 2018, before plateauing between 2018 and 2019.

Positivity rates and PrEP use

A description of the number of infections is a good initial examination, but findings are heavily influenced by the amount of testing conducted. Positivity rates provide a more meaningful examination as they adjust for the testing to provide a less biased result. Figure 4.9 presents the positivity rates for the various infections from 2012 to 2019, separated by PrEP use.

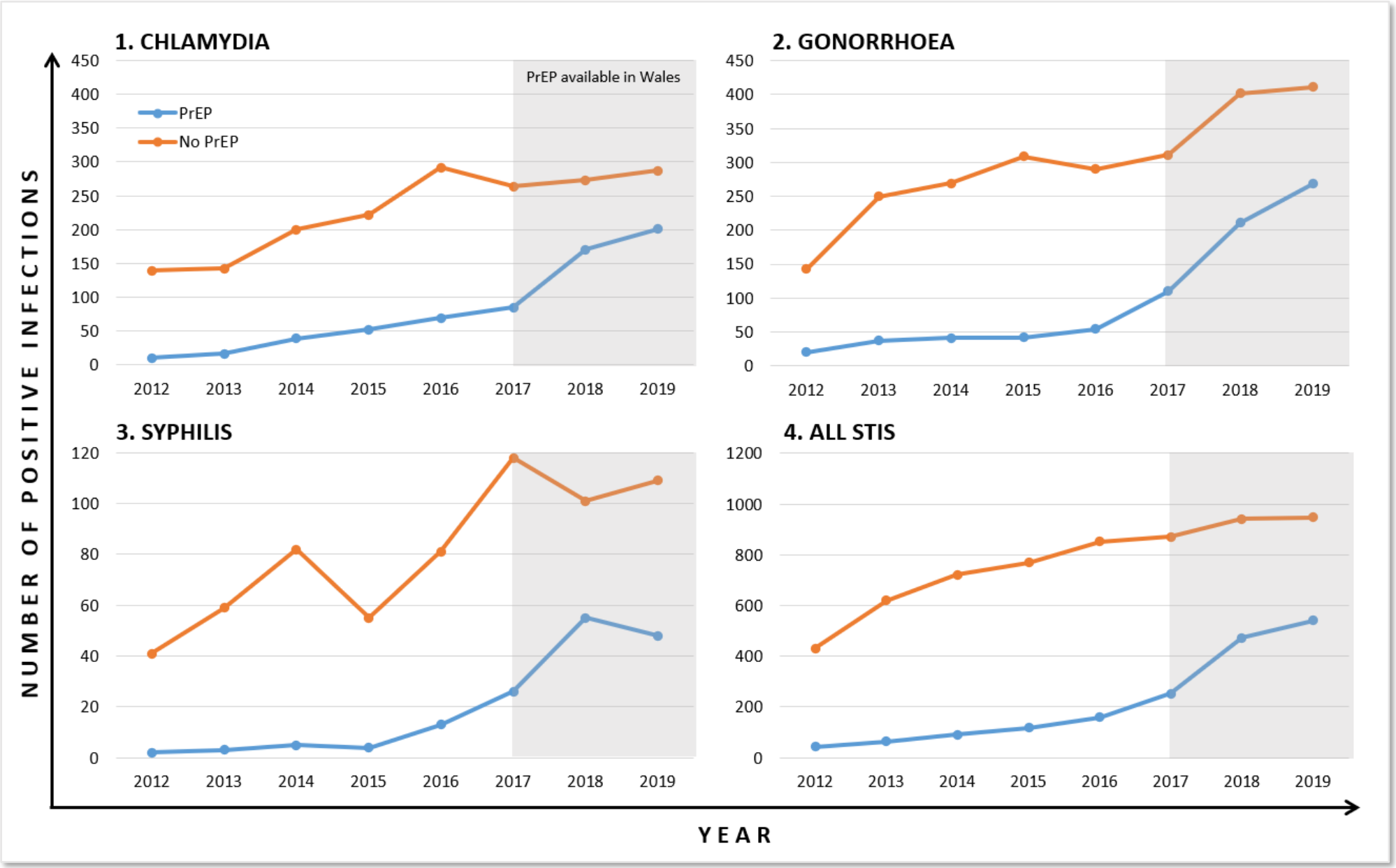
Chlamydia: From 2013, rates remained higher among the PrEP cohort; within this group, from 2012, there was an upward trend, with a sharp increase in 2013, hitting a high of 13.1% in 2015. In the following years, the positivity rate among the PrEP cohort decreased to 7.5% in 2017, stabilising between seven and eight percent in 2018 and 2019. In comparison, the non-PrEP cohort started with a drop from 2012 to 2013, dropping to 7.5%. From here, the rate stabilised, slightly rising in 2016 to 8.8% before beginning a continuous downward trend from 2017, hitting an all-time low of 4.5% in 2019.

Gonorrhoea: The rates among the PrEP cohort were higher overall than the non-PrEP cohort. For the PrEP cohort, the positivity rate for gonorrhoea infections had a steep increase in 2013, hitting a high peak positivity rate of 17.8%. From this point on, the positivity rate experienced a decline before stabilising at around nine percent from 2016 onwards. In the non-PrEP cohort, rates peaked in 2013, with the positivity rate at 13.1%, before also starting a downward trend that continued until 2019, with a rate of 6.5%, one of the lowest positivity rates recorded for gonorrhoea.

Syphilis: The positivity rates for syphilis are the lowest of the infections, remaining under 4%. Within the PrEP cohort, the positivity rates remained under 2% until 2015, with the trend changing to an upward trajectory, reaching a rate of 3.7% in 2018 before decreasing slightly in 2019. The non-PrEP cohort positivity rate remained higher for most years, although consistently between 2 and 4 percent. Between 2012 and 2014, the positivity rates remained between 3 and 4 percent, dropping in 2015 to its lowest rate of 2% before steadily increasing to a peak in 2017 at 3% and returning to a downward trajectory.

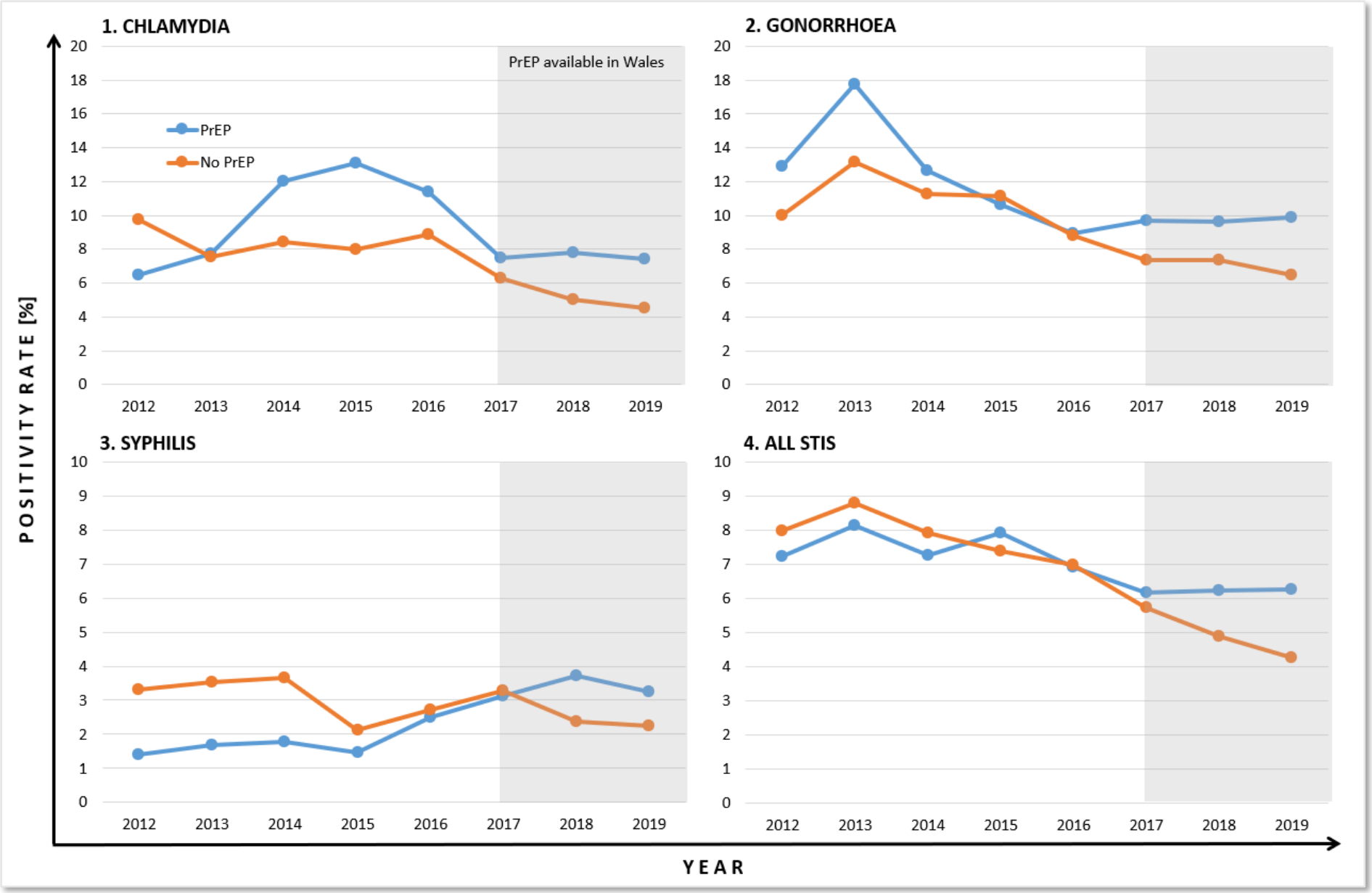
All STIs: For all STIs, the PrEP cohort positive rates mostly remained between six and eight percent. From 2012 until 2016, rates intermittently rose and dropped between seven and eight percent, dropping to six percent in 2017 and stabilising. For the non-PrEP cohort, rates peaked in 2013 at 8.8%; after this point, positivity rates began a downward trend, reducing to a greater level after 2016 and ending in 2019 at 4.5%. Overall, the positivity rates were similar up to 2017, but after this point, where levels stabilised among the PrEP cohort, rates continued to decrease among the non-PrEP cohort, hitting an all-time low in 2019.

Figure 4.8 Trends in positive STI cases among PrEP and non-PrEP using MSM.



NB. 1=positive chlamydia infections, 2=positive gonorrhoea infections 3=positive syphilis infections, 4=all positive STIs (includes previous three infections and HIV, LGV, genital warts, genital herpes, and Hepatitis A/B/C).

Figure 4.9 Trends in STI positivity rates among PrEP and non-PrEP using MSM.



NB. 1=positivity rates for chlamydia, 2=positivity rates for gonorrhoea, 3=positivity rates for syphilis, 4=positivity rates for all STIs (includes previous three infections and HIV, LGV, genital warts, genital herpes, and Hepatitis A/B/C).

4.4.6 Time Series Analysis

An interrupted time series analysis was conducted, results provided in Table 4.3, with the findings visually presented in Figure 4.10. For clarification:

- Prior to the introduction of PrEP: baseline, this accounts for the period from January 2012 to June 2017.
- After the introduction of PrEP: intervention point, July 2017 to December 2019.
- PrEP cohort: people who accessed PrEP via the NHS after its introduction in 2017. It is unknown if this population previously accessed PrEP online before 2017.
- Non-PrEP cohort: people who have never received PrEP from the NHS. It is unknown if any of this population currently or previously accessed PrEP via other means (e.g., ordered online, shared a friend's prescription).

Chlamydia: Prior to the introduction of PrEP, there was a small statistically significant increase in the trend for chlamydia among PrEP users. Positivity rates for the non-PrEP cohort were on a slight, though significant, decrease. Among both groups, a reduction in the level was present after the introduction of PrEP (intervention point), but for both, these were non-significant. For the PrEP cohort, there was a significant decreasing trend after the introduction of PrEP (trend change = -0.78, 95% CI = -0.99 to -0.56, p = 0.02). The non-PrEP cohort was found to have a non-significant, decreasing trend.

Gonorrhoea: Prior to the introduction of PrEP, rates of gonorrhoea were found to be reducing each quarter in the PrEP cohort; rates were also reducing each quarter in the non-PrEP cohort, but this reduction was not significant. After the introduction of PrEP, there was only a slight level change in the PrEP cohort (trend change = -0.30, 95% CI = -3.40 TO 8.53, p = 0.32), with a larger level drop among the non-PrEP cohort (trend change = -3.38, 95% CI = -7.08, 1.35, p = 0.12), although non-significant. The trend changes were found to flip, increasing each quarter among the PrEP (trend change = 0.54, 95% CI = -0.49, 1.22, p = 0.41) and non-PrEP cohorts (trend change = 0.17, 95% CI = -0.05, 0.72, p = 0.57), but again, these changes were non-significant.

Syphilis: From the start of the observation period in 2012, rates of syphilis were at a significant slight increase each quarter for the PrEP cohort. While non-significant, cases within the non-PrEP cohort were very slightly decreasing each quarter. After the introduction of PrEP, there was an increase in level (trend change = 1.16, 95% CI = -1.35, 3.62, p = 0.26) among the PrEP cohort with a slight decreasing trend (trend change = -0.08, 95% CI = -0.40, 0.32, p = 0.70), but both results were non-significant. The non-PrEP cohort had a non-significant, minor decreasing level and trend change (trend change = -0.02, 95% CI = -1.93, 1.58, p = 0.98; trend change = -0.03, 95% CI = -0.27, 0.23, p = 0.80), following the counterfactual line.

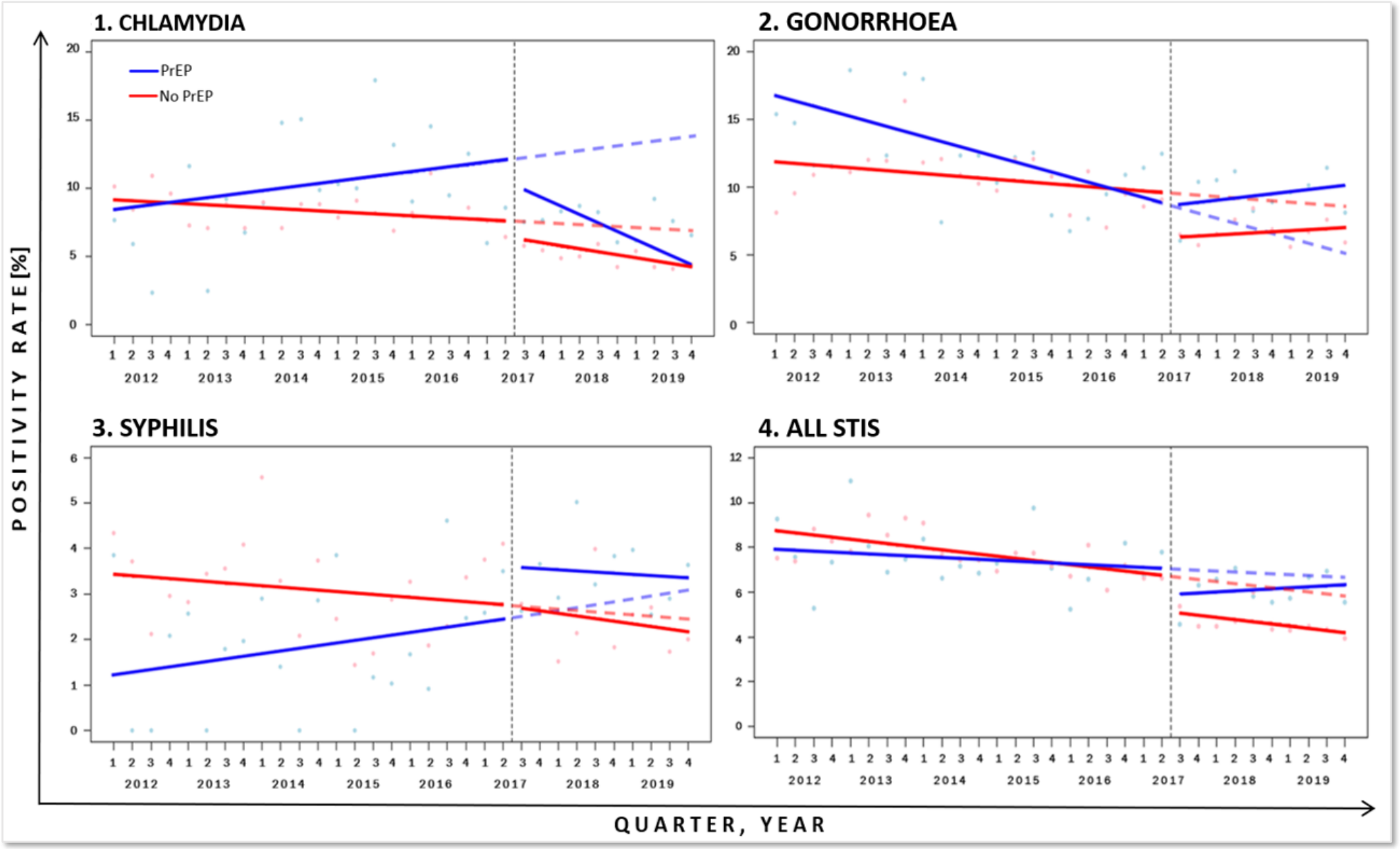
All STIs: For all infections, the PrEP cohort was found to have decreasing rates of infections before the introduction of PrEP, experiencing a decrease in level after PrEP was introduced, followed by a slightly increasing trend but remaining below the counterfactual (dashed line in the graph); all results were non-significant. As for the non-PrEP cohort, a slight decrease in trend prior to PrEP was identified, followed by a significant level decrease at the introduction of PrEP (trend change = -1.59, 95% CI = -3.16, -0.08, p = 0.01). The trend had a non-significant decrease (trend change = -0.002, 95% CI = -0.24, 0.21, p = 0.98).

Table 4.3 Interrupted time series analysis of STIs rates among PrEP and non-PrEP using MSM.

	Group	Intercept		Time		Intervention (Level change)		Post-intervention (Trend change)	
		Value	*p*	Value	*p*	Coefficient 95% CI (LCI-UCI)	*p*	Coefficient 95% CI (LCI-UCI)	*p*
Chlamydia	PrEP cohort	8.28	0.02	0.17	0.00	-1.55 (-7.49, 3.25)	0.86	-0.78 (-0.99, -0.56)	0.02
	Non-PrEP cohort	9.25	0.00	-0.08	0.01	-1.19 (-5.78, 1.81)	0.41	-0.13 (-0.64, 0.45)	0.49
Gonorrhoea	PrEP cohort	17.11	0.00	-0.38	0.02	-0.30 (-3.40, 8.53)	0.32	0.54 (-0.49, 1.22)	0.41
	Non-PrEP cohort	11.95	0.00	-0.10	0.21	-3.38 (-7.08, 1.35)	0.12	0.17 (-0.05, 0.72)	0.57
Syphilis	PrEP cohort	1.18	0.00	0.06	0.03	1.16 (-1.35, 3.62)	0.26	-0.08 (-0.40, 0.32)	0.70
	Non-PrEP cohort	3.45	0.00	-0.03	0.29	-0.02 (-1.93, 1.58)	0.98	-0.03 (-0.27, 0.23)	0.80
All STIs	PrEP cohort	7.95	0.04	-0.04	0.11	-1.19 (-1.87, 2.49)	0.65	0.09 (-0.19, 0.43)	0.47
	Non-PrEP cohort	8.82	0.00	-0.09	0.00	-1.59 (-3.16, -0.08)	0.01	-0.002 (-0.24, 0.21)	0.98

NB.CI: 95% confidence interval, LCI: lower confidence interval, UCI: upper confidence interval.

Figure 4.10 Interrupted time series analysis (visual) of STI rates among PrEP and non-PrEP using MSM.



NB. Pink dots=non-PrEP cohort, blue dots=PrEP cohort, solid blue/red lines=secular trends, blue/red dotted line=continued trend without intervention. Grey horizontal dotted line=PrEP introduced in Wales. 1=positivity rates for chlamydia, 2=positivity rates for gonorrhoea, 3=positivity rates for syphilis, 4=positivity rates for all STIs (includes previous three infection and HIV, LGV, genital warts, genital herpes, and Hepatitis A/B/C).

4.4.7 AMR Demographics

There were 2580 samples assessed for bacterial (gonorrhoea) resistance, equating to 2277 individual service user records between 2012 and 2019. Within the AMR dataset, only age and health board were included. Originally, the intention was to match the AMR data to the STI data using the clinic number. Unfortunately, the clinic number variable within the AMR dataset was not reliable, with a mixture of alternative numbers and surnames being included in this variable. This resulted in only 44% (1012/2277) of service user records being accurately matched to the STI dataset to provide demographic and PrEP use data. From the matching possible, 418 (41.3%) of records were identified as PrEP users. All the data described in the following subsections can be viewed in Table 4.4.

Age

For all MSM, the mean age was 30 years, ranging from 15 to 83 years, with 18–25 being the largest group (974/2277, 43%). Those in the age bracket 26–34 made up 30% of the cohort (691/2277), 13% were aged between 35 and 44 (304/2277), 7% were aged 45–54 (153/2277), and those aged under 18, 55–64, and over 65 each accounted for less than 5% of the sample. Of those who were provided PrEP, the mean age was 31 years, with ages ranging between 16 and 70, with the non-PrEP cohort having a mean age of 29 years. Age range percentages were comparable to the overall group except that the PrEP use group had more individuals aged 35 to 54.

Health board

Overall, a third of samples originated from Cardiff and Vale Health Board (33%, 770/2277), 22% from Aneurin Bevan Health Board (520/2277), 14% (329/2277) from Betsi Cadwaladr, and 13% (304/2277) from Abertawe Bro Morgannwg Health Board. Less than 10% of samples came from Cwm Taf and Hywel Dda health boards, with only a single sample originating from Powys. Within the PrEP cohort, there were a larger number of samples originating from Cardiff and the Vale and Aneurin Bevan health boards.

Table 4.4 Age and health board breakdown among MSM, separated by PrEP use.

	All MSM data		Matched records for PrEP use			
			No		Yes	
	[N=2277]	%	[N=594]	%	[N=418]	%
Mean age (years)	30	.	29	.	31	.
Age range	15-83	.	15-83	.	16-70	.
<18	44	1.9	13	2.1	5	1.2
18-25	974	42.8	264	44.5	146	34.9
26-34	691	30.3	179	30.2	129	30.9
35-44	304	13.4	73	12.2	77	18.4
45-54	153	6.7	35	5.9	43	10.3
55-64	71	3.1	19	3.2	12	2.9
>65	26	1.1	7	1.2	4	1.0
Missing	14	0.6	<5	0.6	<5	0.5
Abertawe Bro Morgannwg UHB*	304	13.4	83	13.9	45	10.8
Aneurin Bevan HB	520	22.8	132	22.2	107	25.6
Betsi Cadwaladr UHB	329	14.4	92	15.4	43	10.3
Cardiff & Vale UHB	770	33.8	182	30.6	201	48.1
Cwm Taf HB	189	8.3	56	9.5	13	3.1
Hywel Dda HB	164	7.2	49	8.3	9	2.2
Powys Teaching HB	<5	0	0	0	0	0

NB. *Now known as Swansea Bay UHB.

4.4.8 AMR and PrEP use

Figure 4.11 presents the rates of gonorrhoea resistance from 2014 to 2019, separated by PrEP use. Data from 2012 and 2013 could not be included as the PrEP cohort did not have data in these years. For each antimicrobial mentioned below the history of the antimicrobial's introduction and any subsequent discontinuation is represented in Figure 2.2. The references to the use of antimicrobials as a recommended treatment are in line with the guidelines set out by BASHH as reported in their website.[14, 23, 26]

Penicillin: this antimicrobial has not been used as a treatment for gonorrhoea since the 1980s. The figure shows that levels of resistance are more stable within the non-PrEP cohort; in 2014, the levels of resistance were at 30%, staying stable at this point until it dropped to 20% in

2017, rising in 2018 so that a quarter of samples were identified as resistant before dropping again to 20% in 2019. For the PrEP cohort, resistance levels were higher among this population in comparison to the non-PrEP cohort. Levels of resistance started at 44% in 2014 and dropped by almost 10% in 2015 before rising to an all-time high in 2016, with half of the samples being identified as resistant to penicillin. Levels of resistance then dropped by half in 2017 to 27%, slightly reducing again in 2018, before rising in 2019 to 33%.

Tetracycline: was removed as a treatment option in 2000 due to widespread resistance. Overall percentage levels of resistance for Tetracycline remained in the high teens until 2017, with rises being identified in 2018 and 2019. Among PrEP users, in 2014, resistance was identified in 23% of samples. Resistance began to drop, hitting a low in 2016 of 15% before starting an upward trend and reaching an all-time high of 39% of samples being resistant in 2019. The non-PrEP cohort had an overall slight upward trend from 2014 to 2019, starting at 17% and ending at 26%. There was a drop in resistance in 2017 to a low of 15%.

Doxycycline: is not recommended for use in the treatment of gonorrhoea but is used for the treatment of chlamydia, so may be provided to a person in cases of multiple infections. Doxycycline resistance follows an almost identical pattern to Tetracycline as it is the original base, with Doxycycline having a newer and better synthesis. Resistance levels for Doxycycline are slightly lower than those for Tetracycline but as they are generally the same medication, resistance will be similar across both.

Ciprofloxacin: is currently only recommended to be used as a treatment for gonorrhoea when antimicrobial susceptibility is known before treatment. It was introduced as a treatment option in 1980 before being removed in 2005. Ciprofloxacin resistance was consistently higher among the PrEP cohort; among this group in 2014, half of the sample was identified as being resistant, slightly dropping in 2015 before hitting a high of 60% in 2016. The following year saw resistance drop by half before starting an upward trend, leading to 40% in 2019. Within the non-PrEP cohort, resistance remains between 20% and 40%, increasing yearly, peaking at 40% in 2016, dropping to 25% in 2017, and slightly increasing each year until 2019, with 30% of samples being found resistant.

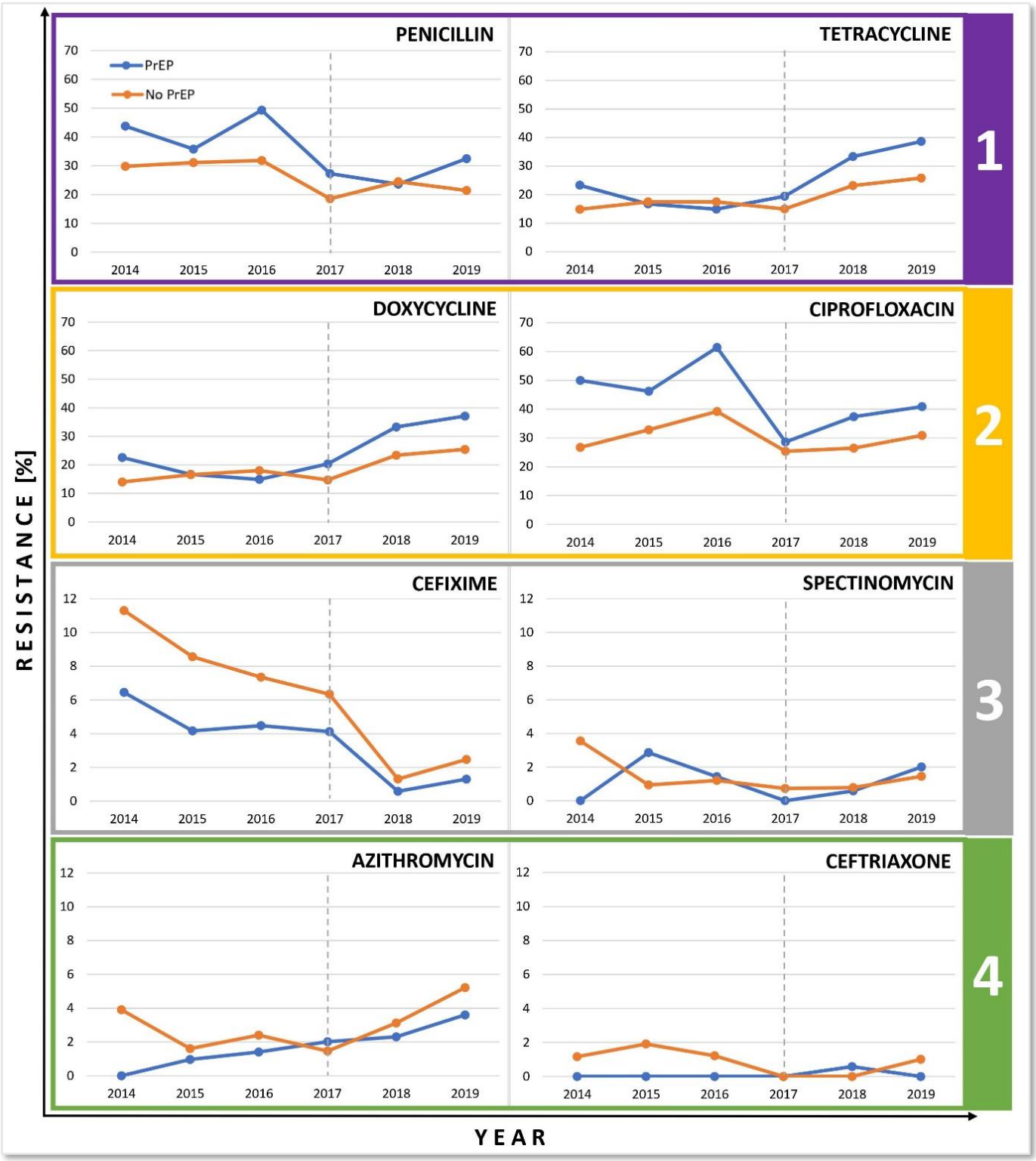
Cefixime: is an antibiotic that is used as an alternate treatment for gonorrhoea (other regimens may be used in cases where an allergy, a fear of needles, or other absolute or relative contraindications exist). Introduced in 1996, cefixime was no longer used as a first-line medication in 2012. According to the data, cefixime resistance has been steadily declining since 2014, with non-PrEP cohorts showing higher levels of resistance. The non-PrEP cohort showed the highest level of cefixime resistance in 2014, at 11%. Since then, resistance levels have been steadily declining, reaching a low of 1.3% in 2018 and then rising to 2.5% in 2019. Resistance among PrEP users, which was 6.5% in 2014, was almost half that of the non-PrEP group. Resistance decreased in 2015 to 4% and stabilised at this level until dropping to a low of 0.6% in 2018, doubling in 2019 to 1.3%.

Spectinomycin: is used as a substitute treatment plan. Although resistance varies significantly within the PrEP cohort, overall spectinomycin resistance for both groups stay below 2%. No resistance was found among the PrEP-cohort in 2014, but it increased to a high of 2.9% in 2015. Falling to zero once more in 2017, and then gradually increased by 1% each year after that. Resistance peaked in the non-PrEP cohort in 2014 at 3.6%, fell to 1% in 2015, stabilised at this level, and then increased to 1.4% in 2019.

Azithromycin: became a first-line treatment as a dual therapy in 2010 (Ceftriaxone and Azithromycin), but due to increasing Azithromycin resistance, it was removed as a first-line treatment in 2018. But it is still used in tandem with other alternative regimens as a dual therapy. Since 2014, resistance has been increasing in the PrEP cohort. Resistance was undetected in 2014, but it gradually increased and peaked in 2019, when it was found in 3.6% of the samples analysed. Resistance was discovered in the non-PrEP group at 3.9% in 2014, dropped to 1.6% in 2015, rose and dropped again in 2017, and then resumed to rise, reaching a peak of 5.2% in 2019.

Ceftriaxone: is the current recommended treatment for gonorrhoea. Cases of resistance are extremely low. Among the PrEP cohort, resistant cases were only identified in 2018, being identified in less than one percent of the samples. In the non-PrEP group, levels of resistance started at 1%, rising to 2% in 2015 before going on a downward trend with no cases of resistance being identified in 2017 or 2018. Resistance was identified among one percent of the sample in 2019.

Figure 4.11 Rates of gonorrhoea resistance across antimicrobials.



NB: Dotted vertical line = PrEP introduced in Wales

1. Neither penicillin nor tetracycline are currently used for the treatment of gonorrhoea under BASHH guidelines.

2. Doxycycline is not recommended for the treatment of gonorrhoea. Ciprofloxacin is only recommended when antimicrobial susceptibility is known prior to treatment.

3. Both cefixime and spectinomycin are alternative regimens, may be given due to allergy, or other contraindications.

4. Monotherapy Ceftriaxone is the current treatment for non-complicated gonorrhoea with Azithromycin provided alongside the alternative regimens mentioned above.

4.5 INTERPRETATION

4.5.1 PrEP and STIs

This is the first study analysing the association between HIV PrEP utilisation and STI rates in Wales and one of the few to study this at a country-wide level. Overall, PrEP users had a higher burden of STIs compared to non-PrEP users. The data revealed that the number of STI tests among MSM increased year-on-year, reaching new highs in 2019, with the frequency of tests per year also increasing. The evidence from this study found that PrEP cohorts have a higher burden of STIs in Wales, with this being the case before PrEP was introduced. This highlights this population's need for PrEP, as there is a higher risk of STIs among the population and, thus, a higher risk of acquiring HIV. Of course, the higher testing frequency and lack of behavioural data make it difficult to untangle the cause of this group's higher burden compared to their non-PrEP counterparts.

STI transmission has been increasing annually since 2012, with a greater rise in the number of new STI cases among the PrEP cohort since 2017, when PrEP was introduced. Interestingly, the rise is not witnessed in the non-PrEP cohort, despite both groups being part of the same community, where sexual networks will likely overlap. There is the potential that PrEP-related stigma may lead to a separation in the population, with individuals choosing sexual partners based on the use or non-use of PrEP. Examining the trends in positivity rates, a different picture emerges. The Figures (Figure 4.8, Figure 4.9) imply that STI positivity rates were similar among the non-PrEP and PrEP cohorts prior to PrEP's introduction (except for Chlamydia in the PrEP cohort, which did not reduce until after 2015), and then there seems to be a decrease in STIs in the non-PrEP cohort, which is not seen in the PrEP cohort following its introduction in 2017. The PrEP cohort positivity rates plateau, which may indicate a net increase in STIs among this group. As test frequency increases among this group to include asymptomatic screening as well as symptomatic testing, it would be expected that a reduction in positivity would occur. An increase in STI transmission would account for why the positivity rates have stabilised and are reducing in response to the increased testing frequency. Of course, not everyone in the PrEP cohort started taking PrEP in July 2017, so the stabilisation identified may represent a delayed response from initiation to increased identification of STIs before any potential reduction occurs.

From the ITS analysis, cases of chlamydia were identified to be on a significant upward trend in PrEP users in the period before PrEP's introduction. However, after its introduction, this changed to a significant downward trend, indicating that after the introduction of PrEP, positivity rates for chlamydia were reducing. For all STIs, the introduction of PrEP was seen to have an immediate effect on reducing STIs among the non-PrEP cohort. Apart from these, there were no significant changes, suggesting that the introduction of PrEP has had a limited impact on STI rates, with positivity rates for most infections decreasing yearly.

If we consider the STI cases in relation to the introduction of PrEP in Wales, among those who adopted PrEP, there was a definite rise across all infections in the year 2018, with a doubling of gonorrhoea cases in 2017 when PrEP was introduced. While a substantial increase is evident for gonorrhoea in 2018 among the non-PrEP cohort, cases of chlamydia and syphilis are relatively stable. Apart from gonorrhoea, the large increases in STIs identified among PrEP users are not also witnessed among the rest of MSM. Many previous studies have highlighted that when looking at the cases alone, analysis will highlight that STI incidence is higher among PrEP cohorts compared to non-PrEP cohorts. However, the higher incidence or significance of the finding disappears after the analysis or model adjusts for testing.[103,104] From looking at cases compared to positivity, there is a clear dramatic change from year-on-year increases in cases compared to a decrease in positivity for the non-PrEP cohort while stabilising among the PrEP cohort after the introduction of PrEP.

As for HIV, new infections have been consistently decreasing since 2013 (PrEP was introduced globally in 2012), leading to 2019 having a positivity rate of less than one percent. HIV testing among MSM has been continually rising since 2012, with a large jump in testing levels in 2018, potentially in response to the increased testing required for PrEP provision. Aper et al. 2020 provided a clinician perspective on the impact of PrEP on an STI clinic in Belgium and raised the point that the reduction in new HIV cases was occurring before the clinic adopted PrEP, stating the decrease among the MSM population started in 2012 and so could not be attributed to PrEP delivery.[156] However, this argument fails to acknowledge that PrEP has been available since 2012 via international online purchases. Therefore, PrEP's impact may have started before countries incorporated PrEP delivery in sexual health care in the 2015–2020 period. Of course, PrEP provision does not exist in a vacuum, and the reduced cases will be largely affected by the increasing testing, diagnosis, and maintained engagement with HIV

care, with individuals achieving undetectable status and thus preventing onward transmission even through condomless sexual intercourse. Now that levels of HIV transmission in high-income countries are low, PrEP provides additional support to maintain low levels of transmission.

4.5.2 PrEP and AMR

Minimal research has previously explored antimicrobial sensitivities among MSM, with this likely being the first study to explore a national dataset. The findings indicate that for Penicillin, Tetracycline, Doxycycline, and Ciprofloxacin (antimicrobials not currently used for treating gonorrhoea), resistance was higher among the PrEP cohort. For both groups, the rates of resistance were increasing, with around 40% of the samples tested having resistant isolates. Levels of Cefixime resistance have decreased since 2014, rising slightly in 2019, although levels remain below the five percent threshold for use as treatment. For Cefixime, the levels of resistance were consistently lower among the PrEP cohort, but both groups followed a similar trend over time. Azithromycin resistance continually rose among both groups; levels were higher among the non-PrEP cohort, and in 2019, they were at the threshold for stopping use. Ceftriaxone resistance remained low (below two percent), with the only cases of resistance identified in 2018 among the PrEP cohort. However, these cases were not flagged by the UKHSA, suggesting the treatment was successful despite being identified as meeting the resistance threshold.

No other studies have been identified that provide a breakdown in resistance between PrEP and non-PrEP cohorts, or even for all MSM at a national level, so comparison is difficult. From examining the data for Scotland in 2019 (which is formed of the full population with no stratification based on PrEP and non-PrEP users), it is evident that the resistance levels for Azithromycin and Ceftriaxone were at a similar level to those found in the Welsh data. However, Wales had higher rates of Cefixime resistance in comparison. In the PrEP cohort, rates of resistance for Ciprofloxacin and Tetracycline were higher than the Scottish data, but for these antibiotics, the non-PrEP cohort rates were lower.[157] The arguments and fears of a multidrug-resistant strain of gonorrhoea becoming endemic among the MSM population are understandable, but more work is needed to understand resistance rates within this population. As for the theory that PrEP will escalate AMR among MSM, for the current treatment options, resistance is lower among PrEP users. However, a different picture is seen

for previously used antimicrobials, so while it is lower now, ceftriaxone-resistant gonorrhoea strains may transmit through the population quicker to become dominant. There is a need for continued surveillance and further exploration of AMR among MSM, both in Wales and internationally.

One interesting point is that while BASHH sets out guidelines regarding best practices and appropriate treatment options for the use of antimicrobials, it is unknown how quickly new guidelines are adopted. For example, in 2018, Azithromycin was removed as a treatment option alongside Ceftriaxone as a dual therapy for monotherapy using Ceftriaxone. From Figure 4.11, we can see that resistance nearly doubled the following year in 2019, which may suggest that guidelines are not adopted as fast as required to curb resistance growth. It is important to remember that these antimicrobials are used to treat other infections, and thus resistance (and indeed, continued resistance even after removal as a treatment for gonorrhoea) may not be due to greater consumption by individuals for the treatment of an STI but for other infections or conditions.

4.5.3 Strengths and Limitations

The major strength of this study is the use of routinely collected data. The data were collected under real-world conditions and are therefore highly representative, including all MSM data from sexual health clinics across Wales. While it does not encapsulate all MSM in Wales, as those who have not received STI testing via sexual health clinics or have not identified themselves as MSM would not be covered by this dataset, this study presents the best estimation of the MSM population of Wales available. While STI testing may have occurred within other healthcare settings, such as A&E or GPs, discussions with a representative from PHW suggest this is likely to represent small numbers for MSM, although there are no reports or data regarding STI testing in other settings. Therefore, this study is likely to have incorporated the significant majority of STI data, which originates from sexual health clinics. Due to the limited work within this area on antibiotic resistance, it provides a starting point for other studies to follow and allows the research community to address the theoretical fears of PrEP increasing antibiotic resistance.

The benefit of using the SWS data is that it includes data from a sizable proportion of MSM from across Wales. However, the data are collected primarily for clinical and routine use

within specific clinics rather than for research or as part of a national outlook. This results in clinicians coding consultations using a variety of consultation codes that could refer to the symptom(s), tests offered or conducted, PrEP use, sexual health discussion, diagnosis, or treatment. Across the eight years of data, the codes differed over time and between clinics, with new codes being introduced, others being removed, and clear differences in the use of codes between clinics. While in the latter part of the data, there was improved consistency in the use of codes, clinic differences were still apparent, resulting in certain assumptions needing to be made around certain codes.

A limitation within the current case management system is that individuals do not receive a unique identifying number that spans across clinics. This means that if an individual moved locations and attended a new clinic, they would receive a new ID, and records would not be matched up with those from the previous clinic. This can result in individuals appearing multiple times within the dataset and being counted as separate individuals. For the example above of moving locations, this may not be so problematic as there would not be overlap in the same period. However, if an individual were to attend different clinics for testing within a year, they would then be counted multiple times and be overrepresented in the data. It is unknown if this occurs and how often, so until the new case management system is introduced, there is no way to address this issue of data quality. Within the current data, there is potential for interdependence of observations that cannot be accounted for, so there is a risk that the standard errors (and hence any confidence intervals and p-values) presented are artificially narrow and not a true presentation. Therefore, any conclusions drawn from these findings should be made with this in mind.

Records were extrapolated from the complete SWS dataset based on the identifying code of MSM; however, upon examination, sexuality only included gay and bisexual identities. MSM should encompass all sexualities, including those identifying as heterosexual but engaging in same-sex sexual relations. It is unknown if this group of heterosexual men who have sex with men is simply placed within the bisexual category in the system by the clinicians, in which case sexuality is not a variable truly identifying sexuality but represents who the individual engages in sexual contact with, or if the heterosexual men who have sex with other men are not included in this dataset.

Originally, one of the objectives was to develop a variable on sexual risk behaviour based on behavioural data known to be collected within clinic settings, but during analysis, it became apparent that this data was not uploaded into the service user record within the SWS. While this behavioural data is available, it exists as paper records stored within clinics. To acquire access, review all records, and input behavioural data into service user records would be a leviathan task, and so it was not deemed practical. Discussions were conducted amongst the PhD supervisory team around potentially exploring a subset of the sample, but the pandemic meant that attending clinics was not an option, and consequent delays to data being received from PHW resulted in this not being viable. Therefore, no risk variable could be derived. Without the behavioural data, conclusions drawn from this study became limited as the exploration of behaviour and risk concerning PrEP use and subsequent STIs could not be examined.

4.6 CHAPTER SUMMARY

Routinely collected data from sexual health clinics and laboratories in Wales were acquired and analysed to describe the trends in STIs and AMR between 2012 and 2019. PrEP users have a higher burden of STIs, but while STI cases have been increasing year on year since 2012, the non-PrEP cohort's positivity rates continued to decrease, but the PrEP cohort levelled off. The trend analysis indicates that the introduction of PrEP coincided with a reduction in the positivity of cases of chlamydia while having no significant impact on the other STIs. As for antimicrobial resistance, the rates were higher among PrEP users for Penicillin, Tetracycline, Doxycycline, and Ciprofloxacin (medications not used as treatment), while for Cefixime, Spectinomycin, Azithromycin, and Ceftriaxone, resistance rates were lower among PrEP users than non-PrEP users.

CHAPTER FIVE
THE IMPACT OF COVID-19 RESTRICTIONS ON SEXUAL BEHAVIOUR

This chapter explores the findings from a sub-study developed in response to the COVID-19 pandemic. Identifying how the lockdown and restrictions impacted sexual behaviours among MSM in Wales and if the pandemic resulted in any changes in attitudes towards infections. A brief background of the COVID-19 situation is explained for context, followed by a discussion of the methods used, including an online survey and interviews. Both methods are explained and justified, with findings summarised and triangulated.

5.1 BACKGROUND

The COVID-19 pandemic caused unprecedented lifestyle restrictions globally, with the UK government imposing a 'lockdown' on March 23rd, 2020. As health is a devolved power in the UK, each nation—England, Wales, Scotland, and Northern Ireland—made independent decisions regarding imposing and removing restrictions. However, the UK government, controlled powers relating to the furlough scheme, which heavily influenced the extent of devolved powers. From March 2020 until March 2021, there was a chaotic mix of easing and tightening of restrictions that controlled our capability to leave our homes, limited our physical interactions with people from other households, restricted the availability of hospitality venues, and even went so far as to inhibit the consumption of food and alcohol in hospitality settings. Figure 5.1 presents a COVID-19 timeline in Wales, developed from COVID-19 regulations provided by the Welsh government[158]. All these restrictions were in addition to the regulated use of hand sanitisers, face coverings, and social distancing measures. Wales maintained full lockdown measures until June 2020 and had a gradual, cautious opening of business. Restrictions started to be imposed again in September 2020 in response to rising cases of COVID-19, leading to a "firebreak" from October 23rd, 2020, to November 9th, 2020. November experienced a slight easing of restrictions before a tightening of restrictions in December 2020. This led to a lockdown in December 2020, which lasted until March 13th, 2021. From March, restrictions continued to ease until Wales entered "COVID level zero" on

August 7th, 2021, alleviating social distancing and controls on meeting people from other households. Social distancing continued to be advised but was no longer legally enforceable after this point.[158] This meant that for 18 months, individuals were legally prohibited from engaging in close contact with others outside of their household. In other terms, people were prohibited from engaging in any sexual contact with someone outside of their household or extended household (or 'bubble'). The British Association for Sexual Health and HIV provided guidelines to the public that discouraged sexual contact with anyone outside the household due to the potential for transmission of COVID-19, with these guidelines remaining in force until August 2021.[159] With these restrictions in force for such a long period, it raises the question of the level of adherence to these restrictions on sexual contact. If we consider that these restrictions were followed completely, they would have had significant impacts on the transmission of STIs.

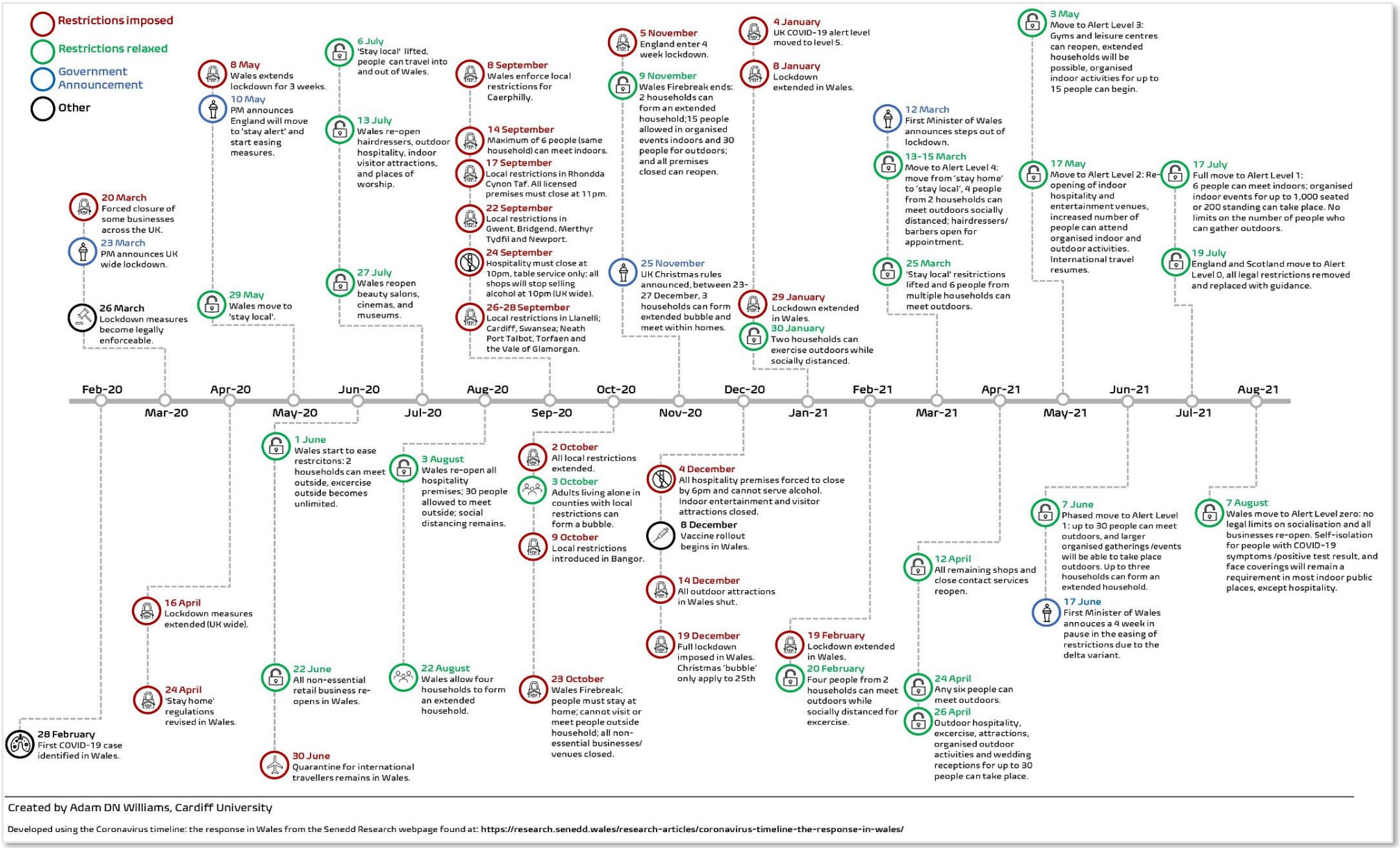
The few studies exploring adherence to COVID-19 restrictions among MSM have found varying levels of adherence. Findings from a sexual health clinic in London found that half of their cohort continued to be sexually active with people outside of their household while restrictions were imposed.[160] In contrast, studies in South Wales and Australia found a greater adherence to restrictions among MSM over a similar period.[161-162] Acknowledging that the COVID-19 restrictions would likely have significant impacts on sexual activity, with potential long-term impacts on behaviour, I decided an exploration of sexual activity, behaviours, and attitudes in response to the pandemic was required.

5.1.1 Aims and Objectives

The aim of this work is to gain an understanding of the potential impact of the COVID-19 pandemic on sexual activity and behaviour among MSM. The following objectives were set to achieve the aims:

- Identify whether, and to what extent, the COVID-19 pandemic and associated restrictions had an impact on sexual activity and behaviour among MSM.
- Explore if attitudes towards infections changed among MSM in response to experiencing the pandemic.

Figure 5.1 Timeline of COVID-19 restrictions imposed in Wales.



5.2 METHODS

Continuing the theme of the overall thesis, this sub-study adopted a mixed-methods design, using a survey to collect quantitative data with qualitative data collected within the interview study mentioned in Chapter Three. Both methodologies will be explained individually. For context, this study was developed in response to the COVID-19 pandemic. The introduction of the initial lockdown in March 2020 resulted in a delay in the qualitative study due to the university prohibiting new studies from starting data collection, and, with uncertainty about how long the pandemic would last at the time, it was not initially clear whether the interviews would move to a virtual setting or whether they could be done in person at a later date. Additionally, the quantitative study became delayed through the processes of requiring NHS ethics (as COVID studies were given priority through the IRAS system) and, secondly, due to PHW staff being re-deployed to the COVID-19 study and therefore not available to extract sexual health data. Therefore, the survey data reported in this chapter became the first dataset to be collected, with questions and probes added to the interview schedule relating to the impacts of the pandemic to later combine the data.

5.2.1 Survey Design

A cross-sectional online survey was proposed for this project to meet the aims of the study. The limited options available due to the circumstances of the COVID-19 pandemic played a significant role in determining the design. However, a survey was deemed most appropriate, as it could be conducted online with ease. The anonymity provided by an online survey allowed people to provide honest responses without fear of repercussions for admitting to breaching COVID-19 restrictions and regulations. Another advantage of surveys is that they can be set up quickly [163], which was important as the intention was to gather data about behaviours while under full lockdown restrictions. At the time, it was not clear when the restrictions might be lifted and to what degree, so speed was paramount to ensure people were responding while under severe restrictions. The low response rate, common in survey studies, was acknowledged with an acceptance that it was unknown how the restrictions may additionally affect response levels.[164] Another limitation of using surveys is that they can limit participants' ability to clarify their choices or opinions.[163] However, as the survey was planned to be combined with the interview data, it was viewed that this could provide some clarification that the surveys may miss. Open-text options would also be included within the

survey to allow for the elaboration of responses. For clarity, sexual activity refers to an individual engaging in sexual contact with another person and focuses on the frequency of the activity. Sexual behaviour refers to the types of sex conducted during sexual activity, such as oral or anal sex, condom use, and solo activities such as masturbation and the use of toys.

Survey development

The survey questions were developed on an ad hoc basis and reviewed by the research team and members of the stakeholder group. The final set of questions was agreed upon and grouped into five sections:

- About You (nine questions): Respondents were prompted to provide information about their demographic characteristics.
- Risk behaviours and sexual health testing (10 questions): these questions explored sexual risk behaviours and the frequency of sexual health testing, previous positive STIs, and the impact of the COVID-19 pandemic on testing.
- Sexual partners and activity (five questions): participants were asked about the average number of partners per month (pre-COVID), sexual positioning, condom use frequency, HIV status of partners, and how partners met.
- Sexual behaviour during lockdown (eight questions): respondents were asked about potential sexual activity during lockdown, who they engaged with, when, and frequency of new partners. A list of sexual behaviours was provided, and respondents were asked to identify changes in response to the COVID-19 restrictions.
- Concerns about COVID-19 (11 questions): these questions explored attitudes and anxieties towards COVID-19, the pandemic, and protective measures adopted.

The survey was developed on Qualtrics (an online survey software developed to conduct academic research; licence held by Cardiff University). This software was chosen due to its accessibility and familiarity. The survey contained multiple question styles, including open and closed formats. Most questions were closed, as the purposes of the research did not require multiple open-ended questions. The limitations of closed questions were acceptable, as they would be balanced with the qualitative element, providing a detailed expression of views. Of the closed-ended questions, formats included dichotomous (e.g., *Have you had sex during lockdown? Yes/No*), multiple choice, and a rating scale. Likert scales were employed for some

questions, each with a defined set of responses relating to the specific question. For certain responses, participants were provided with an open text box to elaborate or provide an answer not included. The survey was pilot-tested among the stakeholder group, which included MSM and third-sector members, to ensure the validity and understandability of the questions. All questions within the survey related to the initial UK lockdown ranged from March 23rd, 2020, to June 27th, 2020.

[See Appendix 5 for the survey, including information sheet and consent]

Ethical approval and considerations

Full ethical approval was received from Cardiff's School of Medicine Research Ethics Committee for the online survey (Ref: SMREC 20.56). Confidentiality and the anonymity of the respondents were maintained, with no identifiable information collected. After the closure of the survey, data was removed from the Qualtrics servers and stored on Cardiff University's secure drive, following the university's policy on data management and storage.

[See Appendix 1.2 for the ethical approval letter]

Inclusion criteria

Individuals were eligible to take part if they met the inclusion criteria:

- aged 18 years or older.
- living in Wales (funding requirement that research be focused within Wales).
- identified as a male or non-binary person who had sexual encounters with men.
- had engaged in sexual contact with a male in the previous 12 months.

Specifying that sexual encounters had occurred in the previous 12 months was necessary due to the survey exploring a change in sexual behaviour pre- and post-COVID-19 restrictions. Individuals were excluded if they did not have access to a device to complete the survey.

Sampling and recruitment

The sampling method used was a targeted sample, with participants recruited via advertisements. These were posted on the social media websites Facebook and Twitter, with LGBTQ+ focused Facebook groups being targeted. The advertisement posts consisted of a brief version of the PIS and functioned as a general invitation with a link to the online site hosting the survey. Adverts were also shared by various groups connected to the research

team, including clinicians, academics, Public Health Wales, Fast Track Cities Cardiff & Vale, and associated groups via social media. The survey was live from June 2020 to July 2020. This brief time frame was due to wanting the survey to be live while lockdown measures were still in force and the Welsh Government was starting to ease restrictions in July 2020.

Survey procedure

From the advertisements posted, individuals interested in participating would follow the links or scan the QR code provided. Upon entering the survey page, the full information sheet was presented for individuals to read, and then potential participants were asked to consent to participate. Participants only proceeded to survey questions if they agreed they fit the inclusion criteria and agreed to consent. All questions included 'forced response' within the survey, meaning all questions had to be answered before being able to move on. At the conclusion of the study, the participant was thanked for their participation. Participants did not receive reimbursement for their participation in this survey.

5.2.2 Interview design

The interviews conducted were part of the original design of the overall study. In response to the pandemic, an additional topic was added to the interview schedule to Inquire about the impacts of COVID-19 and its ongoing influence. Ethical approval was received to conduct the interviews (Ref: SMREC 20.21). The full methodology relating to the interviews is outlined in Chapter Three (3.3 Methods).

5.2.3 Data analysis

The procedures for converting raw data into meaningful information are similar to quantitative and qualitative methods. Processes involve preparing, exploring, and analysing data, followed by representing and interpreting the analysis along with validation and interpretation.[112] While the steps may be similar, the process differs between the two methods, with the quantitative process being linear while in qualitative research it is more iterative, and steps can occur simultaneously. Within mixed-methods studies, there are multiple options for analysing both quantitative and qualitative data, depending on whether the data is collected concurrently or sequentially. In sequential multi-stage studies, it is common to analyse data separately using suitable techniques for each phase. These can then

be triangulated at a later point, as was the case here. This section will explore the analysis plan for both the interview and survey, as well as the triangulation plan.

For the analysis, a triangulation protocol method was adopted. There are three main approaches used for triangulation, with the protocol method deemed most appropriate. It allows for datasets to be analysed separately, with the triangulation occurring after analysis, combining the findings from both datasets to form an interpretation of the findings.[165] Due to data collection occurring at different times with uncertainty around when the interview data may be collected due to COVID-19, the triangulation protocol approach fitted the circumstances best. Findings from both the survey and interviews will be presented separately and triangulated within the interpretation of the discussion.

5.2.4 Survey analysis

Screening

At the conclusion of the survey, the data were downloaded from Qualtrics before being screened and edited. This process ensures that the data are clean and set to be used for further analysis of both open-ended and closed-ended questions. There were 105 responses recorded, with two respondents not providing consent and so having no data attached. Examination of the 103 consenting responses revealed that 14 respondents had not completed any questions after consenting, with 19 not completing past Section 1. The data from the 33 respondents with such incomplete data was not considered in the main analysis, leaving 70 responses to be analysed.

Analysis of closed questions

Closed-question data were analysed using SPSS (Statistical Package for Social Sciences) software version 27.0. Descriptive statistics were calculated to clearly describe and present the features of the data collected, focusing on measures of frequency. Only descriptive analysis was completed on the data; this was due to the nature of the study, which aimed to identify levels of behaviour change rather than explore the reasons behind the changes. Additionally, the small sample size and limited sub-populations would not allow for statistically relevant inferences to be derived.

Analysis of open questions

For open questions, inductive content analysis was conducted on responses to identify the range of reasons and responses provided. The process involved familiarisation with the data, followed by initial coding of the answers, with the list of preliminary codes generated being collated and labelled.[166]

5.2.5 Interview analysis

Semi-structured interviews were conducted virtually over Zoom, digitally audio-recorded, transcribed, and imported into NVivo 12 (QSR International) before being analysed using Braun and Clarke's reflective thematic analysis method.[116] A full description of the analysis method is described previously in Chapter 3.5.

5.3 RESULTS

The results will be discussed separately with findings from the survey presented, followed by the findings from the interviews.

***NOTE**: Findings from this chapter have been published in BMC Public Health. This article is available from; https://doi.org/10.1186/s12889-022-12821-w*

5.3.1 Survey Findings

COVID context

The survey was live from June 2020 until July 2020; during this time, the Welsh Government was first starting to ease the restrictions from the initial lockdown since March 2020. During the time of data collection, there were restrictions related to allowing people to meet outdoors, but social distancing had to be maintained and mixing indoors was still prohibited (see Figure 5.1).

Sample characteristics

The sample included 70 participants; the median age of participants was 33 years, ranging from 18 to 66 years. Participants consisted mainly of white (66/70, 94%), gay (51/70, 73%), cisgender men (63/70, 90%), educated with a university degree or higher (45/70, 64%), and single (43/70, 61%). The study was open to all regions of Wales, most living in South Wales (60/70, 86%); Cardiff had the highest number of participants (21/70, 30%). One quarter were

using PrEP (17/70, 24%), and 36% reported having had sex with multiple people in one encounter. Over half reported having sex while under the influence of alcohol (45/70, 64%), with 10% reporting using recreational drugs during sex. Eleven respondents (16%) had been diagnosed with an STI, with almost half (5/11, 46%) reporting two or more infections.

Sexual behaviour baseline

All participants engaged in sex with men; 13% (9/70) also reported sexual contact with women, and 16% with trans and non-binary individuals (11/70). We asked participants about their average number of partners, regular and casual, per month pre-pandemic. For regular partners, numbers ranged from none to five new partners; half reported having one regular sexual partner (36/70, 51%), 11% (8/70) had two or more regular partners, and the rest had no regular partners (26/70, 37%). The number of new casual partners ranged from 0 to 20 per month, with a mean of two partners. One quarter reported having no casual partners (17/70, 24%), 29% reported one new partner (20/70), 16% had two new partners (11/70), and 17% (12/70) reported three or more new casual partners per month, ranging from 3 to 20. Participants indicated that they met sexual partners on dating apps targeted at gay and bisexual men (51/70, 73%), through friends (25/70, 36%), in bars and clubs (22/70, 31%), on-premises for sexual contact (gay saunas, sex clubs) (16/70, 23%), and outdoor cruising areas (10/70, 14%).

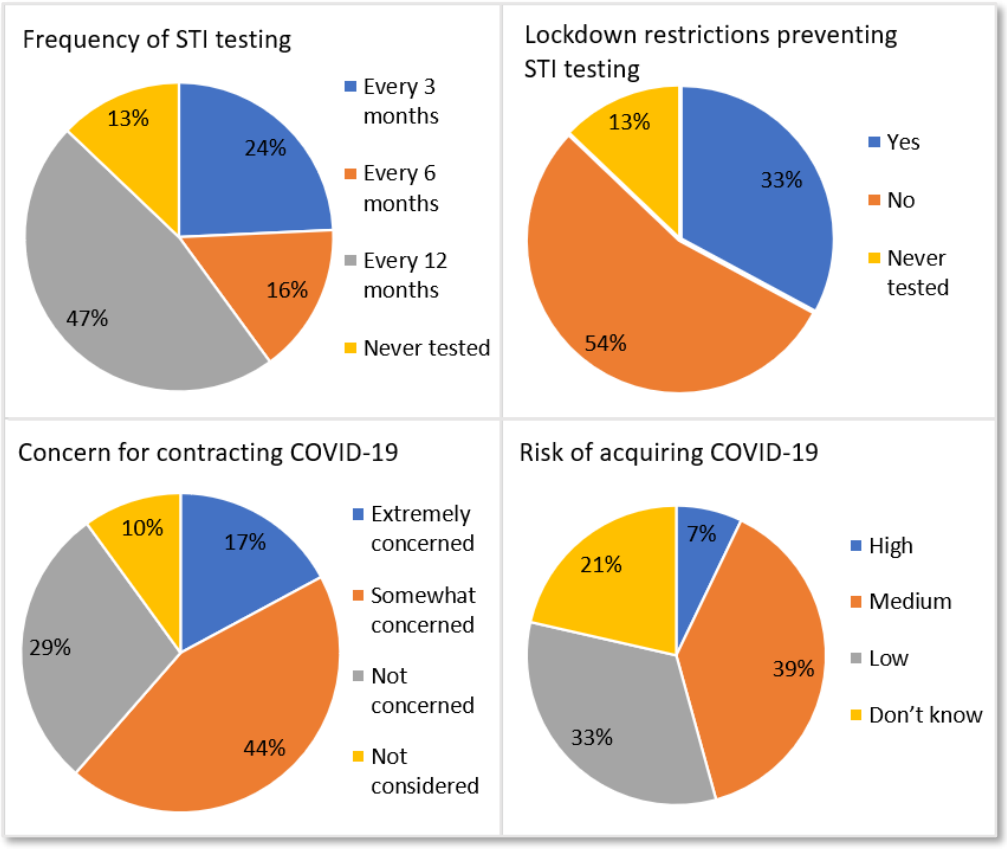
STI testing

Participants were asked their frequency of STI testing, see Figure 5.2. A quarter of participants (17/70) reported receiving an STI test every 3 months, 16% (11/70) every six months, and half tested every 12 months (33/70, 47%). Nine participants (13%) had never received an STI test. When asked if the lockdown had prevented the individual from getting an STI test, 23/70 (33%) reported that it had. In the analysis of the open-ended response asking participants to explain why they could not get tested, over half reported that it was due to the closure of the walk-in clinics in response to the pandemic. Other reasons included not being sexually active and therefore not needing a test, not wanting to be a burden on the NHS, fear of contracting COVID-19, and because they were self-isolating. During the first lockdown, Wales introduced postal testing for STIs (May 2020), but among our sample, only half were aware of the service (33/70, 47%).

Concern for COVID-19

From the questions exploring concern around COVID-19, it was indicated that most did have concern around contracting COVID-19 (somewhat concerned: 31/70, 44%; extremely concerned: 12/70, 17%), see Figure 5.2. Interestingly, 29% (20/70) were not concerned about COVID-19, with 10% (7/70) not considering it. This finding is reflected in the data on perceived risk, as 39% (27/70) perceived their risk of COVID-19 to be medium, with 33% (23/70) low, with these mapping onto those in the somewhat concerned and not concerned categories mentioned previously. Despite most participants not having prominent levels of concern or a perceived risk of COVID-19, most participants agreed with the lockdown measures (62/70, 89%). Two-thirds of people reported protective behaviours (such as reducing contact and avoiding public spaces) before the lockdown measures were mandated (44/70, 63%). One-third of participants reported using face coverings in public spaces (25/70, 36%; note, at the time of data collection, face coverings were not mandatory).

Figure 5.2 Frequency of STI testing and concern for COVID-19.



NB. Risk relates to perceived risk.

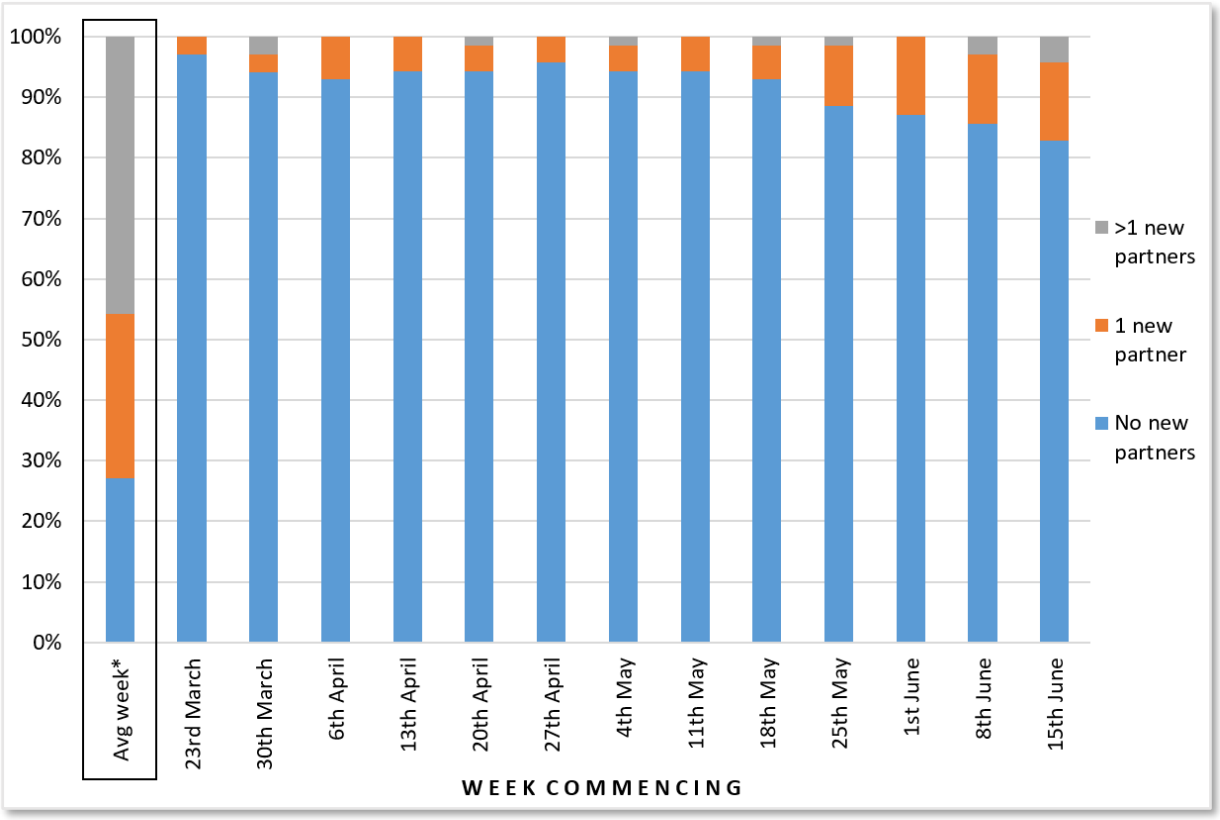
Impact of COVID-19 on sexual behaviours

Participants were asked if they had engaged in sexual behaviour since the introduction of the COVID-19 restrictions, which were initiated on March 23rd, 2020. Forty percent indicated that they had engaged in sexual activity since the introduction of restrictions (28/70). Of those having sex during the restrictions, half reported that their sexual partners were people outside of their household (14/28, 50%). Most participants reported that their sexual partners were known to them before the pandemic (23/28, 82%); many were regular partners (19/23, 83%); and a third engaged in sexual contact with partners they had met after the COVID-19 lockdown measures were introduced (9/28, 32%).

Figure 5.3 presents how the lockdown measures reduced the sexual behaviour of participants, with almost half (32/70, 46%) reporting that in an average week (pre-COVID), they would engage in sexual activity with two or more new partners. In comparison, during the 12 weeks of lockdown (March 23rd, 2020, to June 15th, 2020), over 80% (56/70) reported no new sexual partners each week. The survey data also indicated that the number of participants engaging in sex with new partners increased as each week passed since March 23rd, 2020.

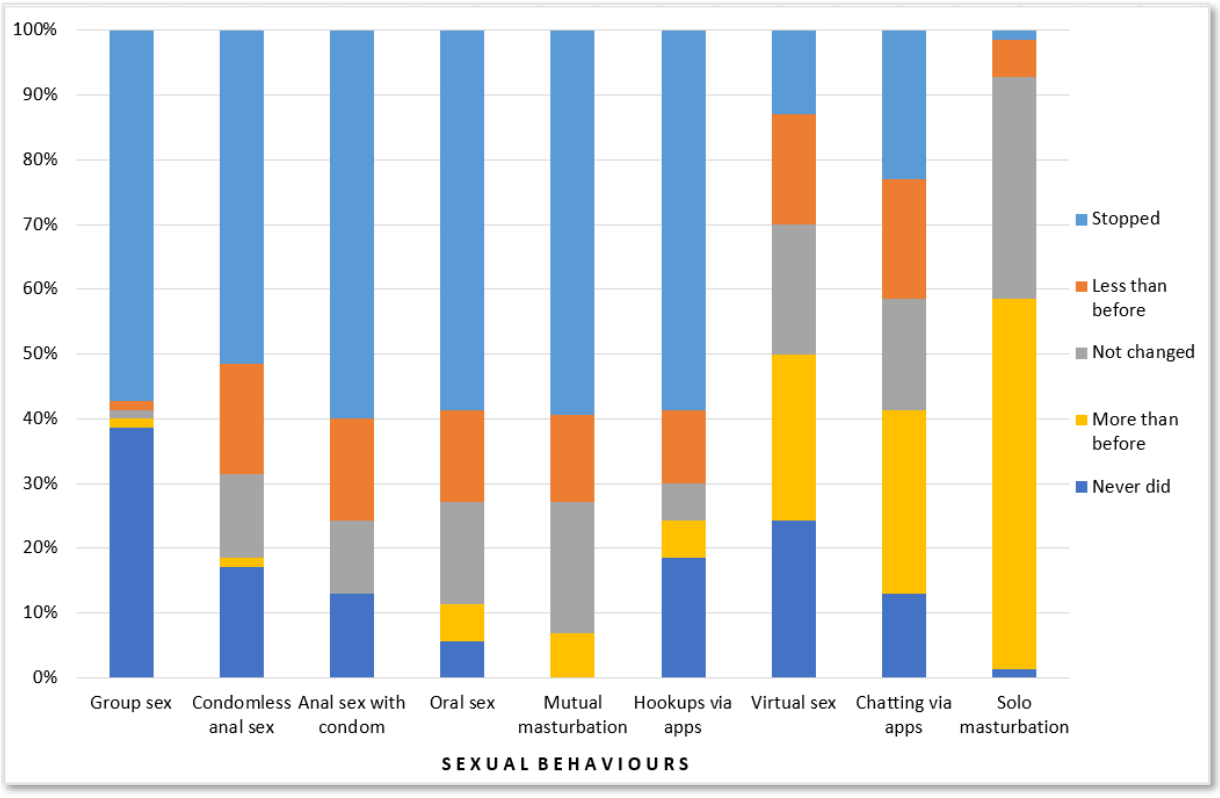
The results in Figure 5.4 indicate that multiple sexual behaviours were reduced or stopped due to the lockdown measures. Many participants reported to stop or reduce engaging in 'hook-ups' via apps (49/70; 70%), meeting people for oral sex (51/70, 73%), meeting for anal sex with a condom (53/70, 76%), anal sex without a condom (48/70, 69%), and group sex (40/70, 57%). Masturbation was reported to increase among half of participants (39/70, 56%). Virtual sex showed a mixture of responses across all options. Some indicated that the pandemic led to increased concern relating to other infections besides COVID-19 (yes: 14/70, 20%; somewhat: 22/70, 31.4%), the highest concern being for HIV/STIs (21/36, 58.3%), followed by the flu/common cold (14/36, 38.9%) and pneumonia (9/36, 25%).

Figure 5.3 Frequency of new sexual partners during the COVID-19 lockdown.



NB. *average week.

Figure 5.4 Reported sexual behaviours in response to the COVID-19 pandemic.



5.3.2 Interview Findings

COVID context

Twenty interviews were conducted, occurring between September 2020 and February 2021. Figure 5.1 shows that during this time, Wales started to enforce local lockdowns, with limitations imposed on leaving the local area. As winter approached, more restrictions were imposed, with a two-week "firebreak" occurring and a winter lockdown enforced from December 25th, 2020, until March 2021. Social distancing from those outside the household continued to be legally enforceable, with limits placed on the number of people allowed to mix throughout the time of data collection.

Sample characteristics

All participants were MSM, with ages ranging from 19 to 53 years. Most participants reported being white British, gay (both 17/20, 85%), and single (14/20, 70%). Of the six men in a relationship, two-thirds had an open arrangement. The sample was well educated, with 75% (15/20) having achieved an undergraduate degree or higher. Participants mostly lived in Southeast Wales (16/20, 80%), mainly in Cardiff. Sample characteristics of those interviewed can be found in Chapter Three, Table 3.1.

Sex during the pandemic

Interview data indicated that the pandemic and associated restrictions resulted in major changes to participants' own sexual behaviours, with a perception of change in others' behaviour. For many, adherence to COVID-19 regulations was reported to be absolute, with the avoidance of sexual contact occurring since the pandemic's introduction.

> *"I, during COVID, have physically touched no one, and I intend to continue that way. But that's a personal choice." P04*

Many expressed their awareness or beliefs of other people breaching the rules, either occasionally or consistently throughout the period, with some admitting their lapses in adherence to the restrictions. This indicates that there will likely always be a portion of people who will not follow restrictions on their sexual behaviours and continue their desired behaviours, regardless of the consequences.

"I went through a period between the initial lockdown and July where I did not have sex at all. The sod it button came out, and I thought, oh fuck it, I'll just go and… [engage in sexual activity]." P13

"There has been definitely a shift in people's opinions on going out and getting sex in a number of people that I speak to and that I know personally. However, I also know that throughout the lockdown, some people were still engaging in like sex parties or very, very risky, unhealthy behaviours." P01

On reflection, from the initial lockdown to their current situation of tightening restrictions (September 2020 onwards), it was perceived that social distancing measures would not be strictly adhered to, with the level of overall measures in place determining the extent of sexual behaviour. During times of extensive restrictions, sexual contact and mixing would diminish, with a surge in activity once restrictions started to ease. This reported surge in sexual behaviour was reported to be in part due to adherence to restrictions imposed, creating an increased desire. This suggests that levels of adherence could map onto levels of restrictions, with sexual behaviour adjusting accordingly.

"Well, I think last year it [the first restrictions] definitely did [reduce sexual activity], but I don't think it's going to be long-lasting. My perspective of it, is, the sooner lockdown's… well, the moment lockdowns start to ease, people are going to be, in some ways, a bit worse than they were before, because they're going to have missed that social contact. After the main lockdown of March and May last year, my friends were definitely a lot more wanting to do stuff because they thought, oh well, we can now. I don't think we're going to find people have less sex or do less things. But I think they're just more restrained while we have lockdowns in place. The moment they get lifted, most of my friends are straight back onto Grindr." P19

"I went through a period between the initial lockdown and July where I did not have sex at all. The sod it button came out… so that's when I started being able to take PrEP. And was a little more active between about July and November. It tended to be people I already knew, people I'd maybe met with a dozen times or so before, regular partners but on a casual basis. I've not done anything since December, as things [COVID-19 cases] have got worse, progressively." P13

However, for some it was perceived that there was an element of lockdown fatigue occurring. While adherence was high at the beginning of the pandemic, as time continued attitudes towards the restrictions changed which led to a reduction in adherence. This resulted in less compliance to the heightened lockdown measures introduced from December 2020.

> *"At the start of lockdown, the first one in March, I feel like it was just like the general consensus that most people weren't meeting. But we're in a full lockdown now [winter lockdown], and I don't think people have the same attitude." P16*

Shame

Among those who reported engaging in sexual activity during the pandemic, some described a sense of shame towards themselves for their behaviour. However, engagement in sexual activity was described as a coping mechanism, distracting them from the difficulties experienced by the pandemic and its severe impact on daily life. These respondents presented sex as an activity to ease mental distress and 'escape' reality.

> *"I would be telling a lie if I said that I hadn't hooked up with somebody during this... during this pandemic. Does that make me proud? Does that make me happy? No. But is it what I've needed in that moment to... you know, to not feel completely shut off from everything? And also, just to kind of... also sex is escapism, to forget this massive, horrible situation that is happening right now, right? And again, I'm not here to moralise anybody." P05*

This sense of shame was also predicted to occur externally, with a perception that people would avoid situations that require disclosure of sexual behaviour due to concerns about being judged for their behaviours. There was concern that this would result in less integration with services, having negative consequences for sexual health.

> *"They aren't going to a sexual health clinic because they're not supposed to be out and about. When the whole Covid… when the whole lockdown, there was people from the group that were still going out, having unprotected sex, and having sex with people. And it was only afterwards when we got to the end that we found out that some… that some people were… [continuing to have sex]. So, it's kind of… I think what it's done is kind of driven it a bit more underground." P02*

Restricting STI transmission

Despite the pandemic and associated restrictions having a severe negative impact on people's lives, some participants were able to identify some positive aspects. For sexual health, at least, it was perceived that there would be a reduction in the transmission of infections, reducing the overall number. Even with some continuing to engage in sexual activity despite the regulations, their pool of potential participants would be smaller, and this was seen as a positive for reducing STIs.

> *"COVID-19 has forced people to limit the amount of people they see and limit the amount of like random encounters that people have. So, in terms of spreading STIs, and STDs, it's limited in that sense, because people are meeting less." P10*

However, concern was raised over the potential for reduced testing during the pandemic. Clinic closures resulted in walk-in appointments not being available, and while PHW did introduce postal testing for STIs, there was limited outreach for promoting the service. This opens the potential for problems if people continue to engage in sexual activity and transmit infections while experiencing an unmet need for STI testing.

> *"But general sleeping around has got to have reduced over that time. If there was proper, you know, testing like these postal tests, like I did around that time, I would imagine it's had a positive effect in reducing the amount of STIs spreading around. But on the other hand, if people don't know about those tests… the postal tests, like you said, they might have, you know, not… they might have missed two or three opportunities to go to a clinic when they had something." P03*

Life after COVID-19

While the lockdown and restrictions are seen to have a positive impact on the transmission of STIs, many of those interviewed suggested that once all restrictions are lifted, there would be a large rise in STI rates due to a surge in sexual activity among MSM.

> *"I say a bit of a spike, a huge orgy of activity once lockdown is finally lifted. And… yeah. I think everyone's going to go wild, quite frankly. So that'll be interesting to see how that happens." P13*

Many participants agreed with this sentiment and believed that the pandemic would have little influence over behaviour long-term, with people returning to their previous pattern of behaviour as soon as possible. However, this view was not universal, with some indicating that the pandemic had altered their perspective with the need for enhanced conversations prior to sexual activity with partners.

> *"But I think, you know, any [sexual activity] would have to... involve probably an even deeper conversation than would have been the case previously." P04*

5.4 INTERPRETATION

5.4.1 Pandemic Response

The findings indicate that the COVID-19 pandemic and associated restrictions had a substantial impact on sexual activity and behaviours for many MSM. Both the survey and interview suggest that during the initial lockdown (March 2020), there was a prominent level of adherence to the restrictions, with many MSM avoiding having sex with others outside of the household. The survey identified how some individuals reduced meeting others before restrictions were legally enforced, indicating that people were regulating their behaviours as COVID-19 cases began to rise in Wales. From exploring behaviours, the results show a change in participants from engaging in sex with others to an increase in solo masturbation, virtual sex, and chatting via apps. As social activities moved online, sex followed. The strong adherence to regulations at the onset of restrictions identified from the data is similarly presented in findings from a cohort study of PrEP users in Wales[161], along with a survey conducted across Australia[162]. However, this was not a universal finding; similar survey studies exploring sexual activity and behaviour among MSM in London, Israel, Brazil, and Portugal presented evidence that half of participants continued to engage in sexual activity, breaching COVID-19 regulations.[160, 167, 168] These studies included measures that explored attitudes towards COVID-19, and the data in this study makes clear that those continuing to engage in casual sex during times of restrictions had low concerns about being infected and did not adopt many protective measures. This studies sample of MSM had a high concern for COVID-19 and supported the lockdown measures. It is reasonable to assume that a person's attitude towards COVID-19 would impact whether they follow the regulations and engage in sexual activity. The hypothesis would be that those individuals who have concerns

about acquiring or passing on the COVID-19 infection are more likely to follow regulations and not engage in sexual activity. Interestingly, from the interviews, there was mention of how others known to them were not following regulations and were continuing to engage in sexual contact with others, even having "sex parties." This may indicate that the survey sample consisted of more adherent individuals, missing those who were breaching the COVID rules, whereas the less-adherent individuals were absorbed in the London, Brazil, and Peru surveys. With varying findings from countries, a question could be asked as to what informed the attitude towards COVID-19. Wales and Australia had a more cautious approach to COVID-19 and reducing regulations than England and especially the Latin American nations. There remains a question of whether government regulatory stances impact people's adherence and potentially explain the varying degrees of adherence to social distancing regulations. An exploration of how government response affected adherence to measures is important to understand how to respond to future pandemics.

5.4.2 Lockdown Fatigue

From both datasets, it was clear that adherence waned over the pandemic, particularly once the restrictions started to be lifted for people having sex with partners outside of the household. While sexual activity and behaviours did not return to pre-pandemic levels, people's adherence to regulations did waver. Some explained how the lifting restrictions were interpreted as a signal to freely engage in sexual activity again. Understandably, more people breached social distancing regulations once households were allowed to mix. It would have been easy to slip into previous behaviours, and after a long time of isolation, the desire for contact with another individual would likely have been high. Sexual desire is a key motivation for behaviour, with evidence showing how sexual desire can lead people to engage in risky sexual behaviours such as condomless sex as well as "morally questionable" behaviour.[169] For those who did engage in sexual activity and breach the regulations, likely, their building desire, reducing concern, and regulation fatigue all led to their sexual activity, outstripping concern for infection with COVID-19 or consequences from breaching regulations. From the interview responses relating to shame, while sexual desire may have led them to engage in sex with others, a negative backlash was felt by some. However, this was weighed against the benefits provided by engaging in sexual activity; it was viewed as beneficial to their mental well-being by providing an escape from the difficulties of the new reality experienced. Some

participants indicated that they had to weigh their own needs for sexual interaction with the potential for infection and the safety of the community. The use of sex as a coping mechanism to deal with the pandemic situation and the guilt expressed afterwards are similar to findings from the London survey.[160]

5.4.3 Impact on Sexual Health

Initially, the pandemic resulted in an intensified concern for other infections, particularly HIV/STIs. However, as time progressed, that focus diminished. As the population being studied was MSM, there may have been a pre-existing focus on STIs due to the many campaigns on STIs targeted at MSM and the higher health literacy in sexual health for MSM.[170] The inability to test for STIs at the onset of the pandemic due to clinic closures may have also influenced this attention. From the interviews, it was evident that participants did not expect a long-term change in behaviours or increased concern for other infections, such as STIs. Many believed that once restrictions eased, behaviours would return quickly to pre-pandemic behaviours. The main impact of the pandemic on STIs was viewed by many as reducing the transmission of STIs in the community. From the reported reduction in sexual behaviour, a break in STI transmission will likely have occurred, hopefully reducing levels of infection in the community. The pandemic's positive impact on reducing the transmission of HIV/STIs will be more profound if the individuals previously sexually active continue to be tested and treated during the period of restrictions. The interview sample had a greater awareness of the STI postal testing service in Wales compared to the survey sample (only half were aware of the service). However, it had only recently been launched when the survey was conducted, which could explain the low awareness, and the interview sample was better informed about sexual health generally.[171-172]

The pandemic provided a unique opportunity to reduce the accelerating STI rates identified in Wales and across the globe. To capitalise on the benefits provided by the pandemic, funding and policy focus should have been placed on sexual health to prevent STI rates from returning to pre-pandemic levels. Unfortunately, this was not the case and since the COVID-19 restrictions were lifted there has been an MPOX outbreak and currently there are unprecedented surges in STI rates in Wales and across the UK.[173-175]

5.4.4 Strengths and Limitations

A key strength of this study is the use of two approaches to data collection. It allowed us to explore the complexities and changes around sexual behaviour in a more detailed manner. The survey allowed behavioural data to be collected during the ongoing situation rather than relying on memories of previous behaviour, although some recall bias may still have affected the responses. Additionally, having the two datasets collected at different time points provides a glimpse at how behaviours and attitudes changed throughout the course of the first year of the pandemic. Moving the interviews online was beneficial in improving the efficiency and quality of the interview data.

The survey was limited by its small sample size, despite its wide reach and repeated promotion. A major difficulty was getting organisations, such as Pride Cymru and Welsh LGBTQ+ businesses and groups, to promote the survey. We received no response from most groups contacted, likely due to difficulties experienced during the pandemic. The small sample size may have resulted in self-selection biases, with the potential impact on the results being unknown. Another limitation of the sample was that neither the survey nor the interviews were ethnically diverse, limiting the representativeness of the findings. The lack of engagement from ethnic minorities within sexual health research is common[141-142], but it is clear that tailored recruitment strategies are required to achieve an ethnically diverse sample.

Despite the limitations of the survey element of this study, the circumstances surrounding its design and implementation were not ideal. It was developed in response to the pandemic and delays impacting the other elements of this thesis. Due to the uncertainty of how restrictions would be lifted at the time, speed was essential to ensure the survey's delivery while individuals were still under lockdown-level restrictions. This resulted in the design and recruitment strategies not being as well considered as they may have been under normal circumstances.

Additionally, the strengths and weaknesses of the interviews conducted are detailed in Chapter 3.6.3.

5.5 CHAPTER SUMMARY

This chapter presents the findings from a survey conducted to examine sexual behaviour during the lockdown and combining this data with the findings related to COVID-19 and the pandemic from the interviews conducted in Chapter 3. The findings suggest the pandemic had significant impacts on sexual activity and behaviour amongst MSM, with high adherence to the restrictions imposed in Wales. Adherence to COVID-19 restrictions was waived over time once the first set of restrictions were eased. This suggests that advice around social restrictions may need to be better considered or communicated if similar measures need to be introduced for future pandemics. The chapter also highlights how continuous increasing and decreasing of restrictions tends to reduce people's concern, with fatigue leading to increased breaching of rules. The desire and intention to return to pre-pandemic behaviours allowed people to endure the restrictions but resulted in the pandemic having little long-term impact on the sexual behaviours of most MSM.

CHAPTER SIX
A CONCEPTUAL FRAMEWORK OF RISK COMPENSATION IN RELATION TO PREP, STIS AND AMR

This chapter is dedicated to presenting the conceptual framework for risk compensation (RC) concerning PrEP use, STIs, and AMR. The framework combines the concepts, theories, and findings from the previous chapters and presents them visually. The method of framework development is explained before a discussion of the various variables, data sources, and analysis.

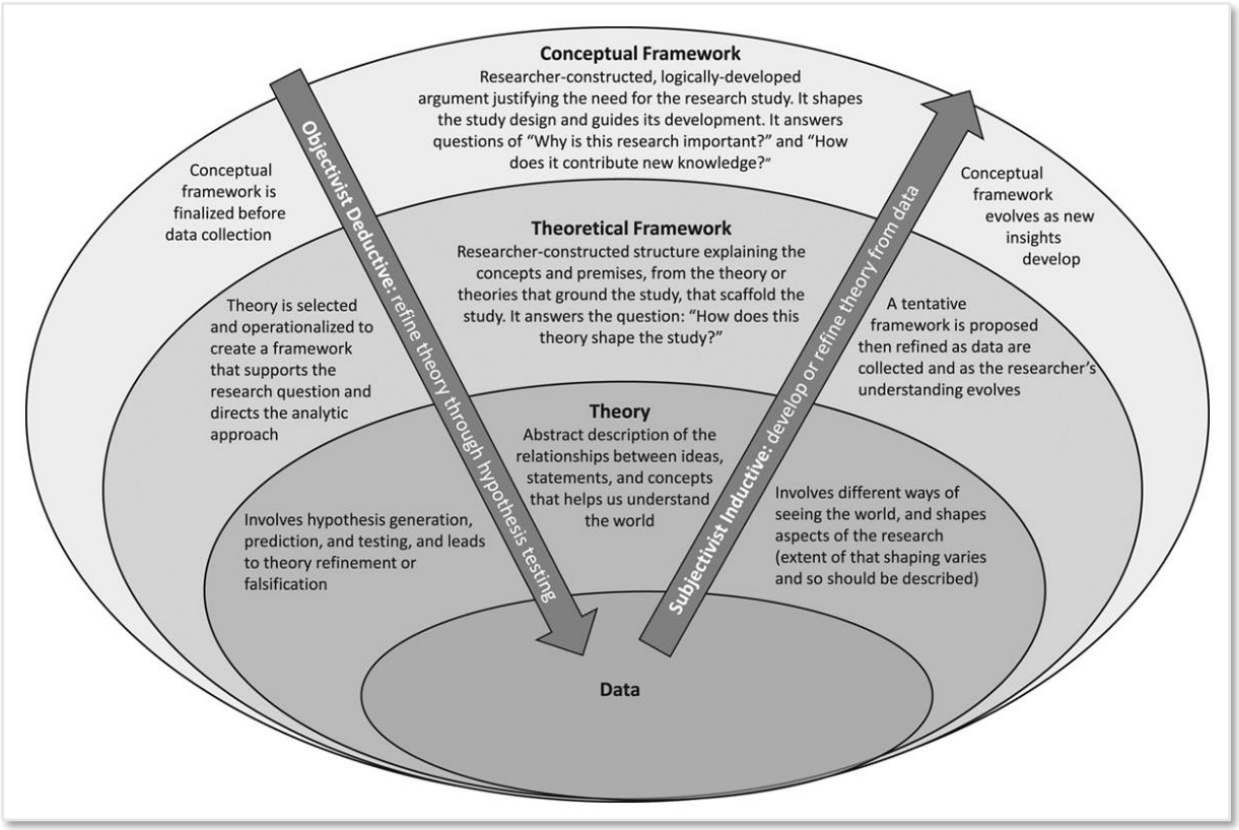
6.1 CONCEPTUAL FRAMEWORKS

Conceptual frameworks are visual representations of the expected relationships between variables being studied.[176] However, this basic terminology can also be used to explain theories and theoretical frameworks. This has led to the three terms “theory,” “theoretical frameworks,” and “conceptual frameworks,” often being confused and used interchangeably within academic writing without acknowledgement of the differences. Additionally, the meaning of these terms can change based on the research design or the research discipline. In 2020, Varpio et al. proposed a clarification of the differences between the three terms and the methodological approaches to their creation. The authors indicate theory to be an “abstract description of the relationships between concepts,” not yet evaluated in data, with a range of formats. A theoretical framework is suggested to be a “scaffold” to a study, developed from the researcher’s logic to connect the variables within the study, while a conceptual framework is a justification for the research to be conducted. It has three elements:

- describes the current knowledge of the relationship,
- highlights the current gaps in understanding,
- summarises the required methodological foundations.

The authors promote two approaches to conducting a conceptual framework: the objectivist deductive approach, or the subjectivist inductive approach. Figure 6.1 (below), presented in the paper by Varpio et al., visually demonstrates how theory, theoretical framework, and conceptual framework work in relation to the objectivist deductive and the subjectivist inductive approaches.[177] When adopting the objectivist deductive approach, the framework is designed and finalised at the formulation of the research idea, informing the research questions and hypotheses, and refined through the testing. Within the subjectivist inductive approach, the framework develops and refines throughout the study, having the data inform the framework. This approach evolves with the data, leading to a finalised framework at the completion of the research.

Figure 6.1 Visual depiction of the similarities and differences between theory, theoretical framework, and conceptual framework.



Source: Image from Varpio, et al. [177]

6.2 DEVELOPMENT OF THE FRAMEWORK

In this PhD, a subjectivist inductive approach was adopted, allowing the framework to be informed by the findings from each study to produce a framework. The development of the framework went through various stages. At the onset of the studentship, an initial theory of the relationship between the variables was developed from the literature review and formed using the method of Evidence Synthesis for Constructing Directed Acyclic Graphs (ESC-DAGs).[178] The initial framework informed each study, with the findings going on to further advance the framework until the finalised conceptual framework was formed. At each stage of development, discussion among the research team was a crucial factor in formalising the framework by providing an opportunity for reflexive discussion that included multiple perspectives and disciplines from the social and clinical sciences.

6.2.1 Early Ideas - ESC DAG

Directed acyclic graphs (DAGs) allow researchers to identify and present causal relationships between variables, along with the required adjustments. [179-180] DAGs are presented as nodes with arrows; the presence of an arrow between nodes indicates a causal effect, and nodes can be measured or unmeasured. While the publication of DAGs is rare, they have had greater adoption by researchers in the development phases of studies and can be used to contribute to understanding the problem at hand.[181] One benefit of DAG creation is that it supports the identification of potential biases within observational research. [182]

A review by Tennant et al. (2017) on the limitations of DAGs highlighted the need for DAG guidelines.[179] This call was answered through the novel method of Evidence Synthesis for Constructing Directed Acyclic Graphs (ESC-DAGs).[178] This is a theory-driven approach where the models are built from the topical literature and act as a representative summary of the literature, which can be used to direct data analysis. The ESC-DAG method proposes following the core processes of ‘mapping,’ ‘translation,’ and ‘integration.’ Mapping refers to the process of drawing conclusions from related literature and developing initial ‘implied graphs’ of the variables involved, which function as a template to build from. Next is translation, which is where causal theory is applied to the implied graphs and assessed using a counterfactual thought experiment. The last process of integration has two stages: synthesis, merging the translated DAGs into a single model, and recombination, combining

certain nodes, either to reduce complexity or establish consistency. The development of the ESC-DAG should include all variables, regardless of data availability, to ensure a true picture is being presented. Researchers are criticised for omitting variables due to a lack of data, as this is considered too simplistic and does not highlight areas where further data collection is required to successfully identify causal inference.

For the purposes of this study an initial DAG was developed using the ESC-DAG approach. Following a review of the existing literature, including quantitative and qualitative studies exploring the relationship between PrEP, STIs and AMR, as well as theory-based discussion around risk compensation, the initial DAG was developed identifying the main variables. The DAG informed the planning and analysis of other chapters.

6.2.2 Confirming the Framework

As the studies were conducted and findings analysed, the model evolved and moved away from being a DAG and instead formed into a conceptual model. After the completion of each study within this thesis, the findings were used to inform and develop the relationships within the DAG, expanding and being formed into a conceptual framework. All new developments were discussed within the research team, and with their expertise, the framework evolved. The initial DAG ideas were developed by hand before being transferred into DAGitty,[183] a browser-based environment developed for the creation of causal diagrams. The finalised framework was produced in Microsoft Excel for greater visualisation control.

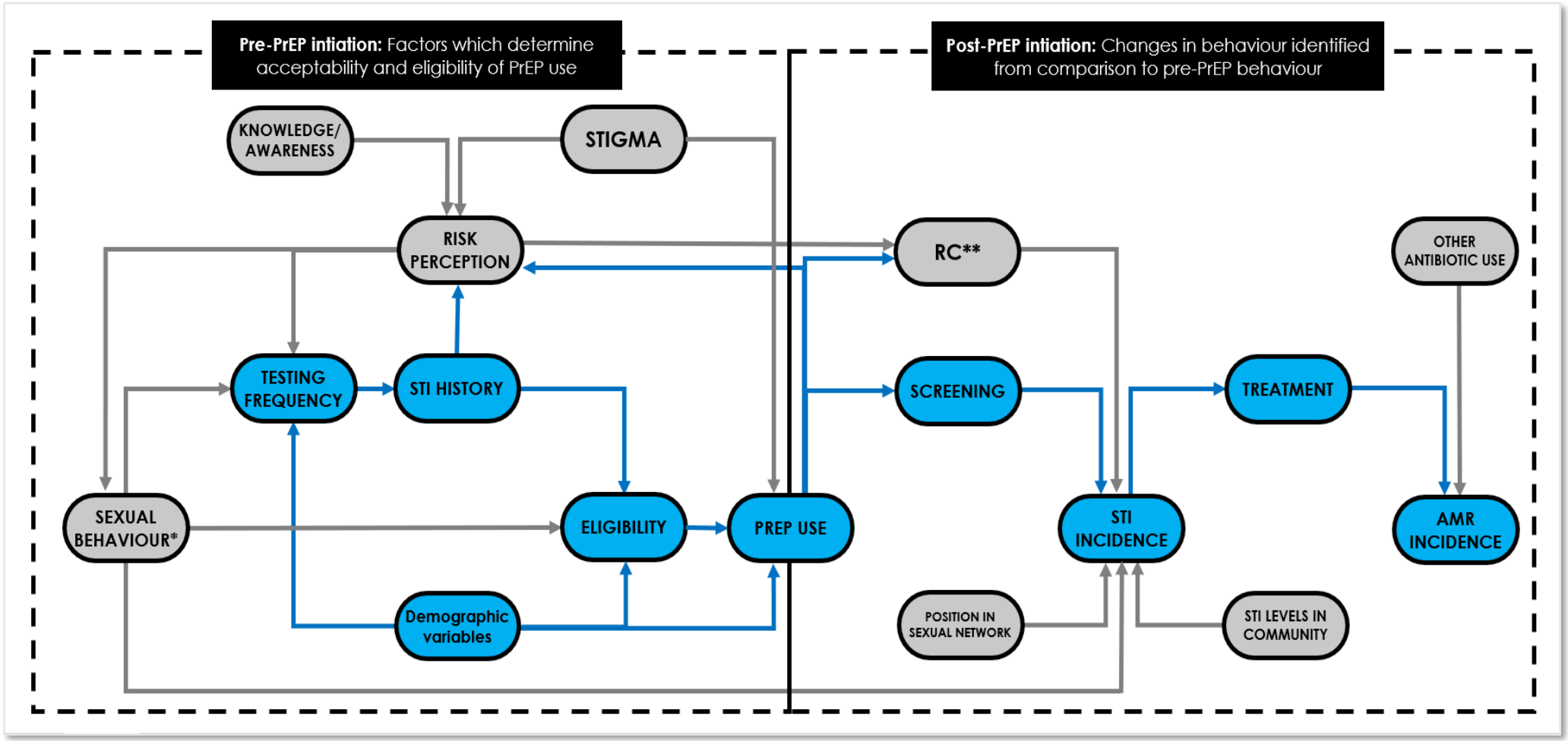
6.3 A CONCEPTUAL FRAMEWORK OF RISK COMPENSATION

Figure 6.2 visually presents the conceptual framework of RC relating to PrEP use, STIs, and AMR. The various variables, relationships, and pathways are presented, regardless of whether there is current data available or not. The various elements of the framework will each be discussed to present current knowledge along with the methodological challenges associated with the various variables and concepts. The discussion will incorporate evidence from the literature and relate to findings from previous chapters.

6.3.1 Behavioural Exploration of Risk Compensation

RC is a complex theory, starting life as an economic theory and later being applied to health behaviours and risk.[90-91]. It is centred around behaviour change theories and so requires detailed understandings of behaviour before and after the introduction of whichever variable of interest is resulting in the proposed RC. As an unobservable variable, researchers must consider and aim to identify all relevant variables that would influence and be influenced by RC. Appropriate data collection for the variables identified would need to be conducted to allow for the examination of potential changes. The literature suggests that in the case of PrEP use, RC would present as a reduction in the frequency of condom use, increasing the frequency of sexual partners and engagement in riskier sexual scenarios such as group sex parties or chem sex, with these behaviours resulting in increased transmission of other STIs.[5,93-95] Therefore, it was decided that these behaviours were the ones to focus on. Despite the identification of multiple variables related to RC in response to PrEP use, previous research evidence has focused on condom use and STI incidence.[5, 93-95,184] However, a true depiction of RC needs to account for the multiple variables that are involved and their interconnectedness. Figure 6.2 presents the current understanding of RC in relation to PrEP use, STIs, and AMR, and I will argue that two important variables are missing from the previous explorations of RC in this setting: sexual positioning and risk perception. Below, each of these variables affected by potential RC will be discussed, highlighting the current collection within the literature, challenges, and suggestions for optimised exploration within research. Findings from previous chapters will be applied where appropriate.

Figure 6.2 Conceptual framework of the pathway of risk compensation and related variables required in its analysis.



NB. Blue: data is currently available in Wales. Grey: Data not available.

* Sexual behaviour encompasses sexual positioning, condom use frequency, partner type/frequency and engagement in higher STI risk scenarios.

**RC = risk compensation, this can present as reduced condom use, change in sexual position, increase in frequency of new partners, new or increased engagement in higher STI risk scenarios.

Condom use

A decrease in condom use is the central argument of RC pertaining to PrEP use. However, its monitoring of pre- and post-PrEP initiation in previous studies has been limited, with its analysis being challenged by biases. The limited examination of condom usage to identify risk compensation may be due to the difficulty of collecting data on this variable accurately, as it relies on self-reporting and memory recall, which can be affected by multiple biases.[185-187]

While self-report is the only way to collect data on this variable, the findings from Chapter Three suggest there may be a perception bias occurring. Multiple participants highlighted a reduction in their condom usage when first asked, but after further exploration of their behaviours and the scenarios under which condoms were adopted, for many, the scenarios of condom use had not changed since before PrEP. Some participants reported that they used condoms with new partners but not with regular partners, while others stated they provided their partner with the choice regarding condom use and would engage in either scenario (sex with a condom or condomless sex). The perception of using PrEP, potentially influenced by the stigma within the community, may have influenced individuals to believe their condom use was far less when, in fact, condom use had not significantly changed. This highlights that there may be inaccuracies in condom use data, particularly when using a cross-sectional methodology to measure change, as if misjudged perceptions are occurring, it may result in biased reports of reduced condom use at a single data collection point.

Additionally, due to condom use being a health-protective measure and non-use being commonly categorised as a "high-risk behaviour," the impact of social desirability bias is likely significant. An examination of social desirability bias associated with HIV risk behaviours found that social desirability bias was associated with increased reporting of condom use.[188] If we consider condom use reported by PrEP and non-PrEP users within the context of social desirability bias, it could be argued that people using PrEP report their condom use levels more accurately as they are less affected by social desirability as they have already demonstrated actions of 'responsible' behaviour, and also due to the need to disclose low condom use as evidence of eligibility for PrEP. Whereas non-PrEP users may be more heavily influenced by the need to present socially desirable actions, resulting in the reported rates of condom use potentially being inflated and the actual rates of condom use being closer to

those using PrEP. However, this argument is predicated on the assumption that condom use is deemed socially desirable, and while this may be the case within a healthcare setting, the population in a community setting may have a different view since reported condom use continues to decline.[131-134]

Multiple data collection points using a prospective longitudinal study design provide the best chance of accurately collecting condom use data. One successful attempt has been made in a study examining PrEP adherence. The DO-PrEP study collected data using an ecological momentary assessment study of PrEP use and sexual behaviour, which was repeated weekly over nine months.[189] This method provides multiple data entry points to allow for improved accuracy over time, and additionally, repetitive self-reporting may reduce the potential impact of biases over time. The DO-PrEP study adopted weekly data collection, but this could be extended to biweekly or monthly if the overall data collection period was extended. Alternatively, data collection could start weekly, and throughout the study, the data collection periods could extend.

Sample bias may also occur in cohort studies that compare PrEP and non-PrEP due to the eligibility requirements of PrEP, which have been promoted by the WHO and adopted globally.[3,4] In Wales, one eligibility requirement is for a MSM who "report[s] condomless intercourse in the past 3 months and affirm[s] likelihood of condomless intercourse in the next 3 months"[86] with the other nations of the UK adopting a similar requirement. [77-80] Therefore, it is expected that PrEP users are identified as having low condom use compared to non-PrEP cohorts. An open-label study measuring medication adherence, condom use, and STIs among PrEP users in Australia identified that at baseline, over 75% of people reported condomless anal sex with casual partners and 35% reported condomless anal sex with a man living with HIV,[102] with similar findings reported by various PrEP studies.[190-192] The requirement of low condom usage to receive PrEP brings into question the findings of any studies that compare PrEP and non-PrEP cohorts on the variable of condom use, as there is a clear difference between the two samples. In addition, there are problems in making comparisons before and after PrEP use without extensive examination of condom usage, as this provides little tangible evidence of increases occurring due to the provision of PrEP. Low condom usage among the PrEP cohort, compared to non-PrEP, will have existed before the initiation of PrEP; to be eligible for PrEP, frequent CAS must be reported.

Increased partner frequency

Partner frequency is often collected in PrEP studies as an indicator of increased risk of STI acquisition.[1,2,7-9] However, not all studies consider partner frequency an indicator of risk and collect this data. A more detailed understanding of the impact of changes to sexual partner frequency is required to identify the potential influence of PrEP more accurately. The impact of PrEP on partner frequency would need to be the focus of separate research, as many factors could influence this variable. Interview data reported in Chapter Three identified that when a person is feeling low or experiencing emotional discomfort, they are more likely to engage in more sexual activity with more partners as a coping mechanism (see Chapter 3.6.3, Influence of Mental Health).

Additionally, there may be a seasonality pattern to sexual activity within MSM during the summer months due to holidays and Pride events that occur across cities in the UK (although this was not found in the analysis conducted on the SWS data). It is reasonable to assume that the influx of new MSM to cities, coupled with an event associated with alcohol consumption and freedom of expression, may increase the frequency of sexual partners.[193-196] To identify the potential effects of seasonality, a detailed examination of partner frequency over 12 months would be required to consider this in relation to when a person started PrEP and control for the effects of seasonality. Similarly, for condom usage, a longitudinal examination before and after PrEP initiation is required to provide a more accurate reflection of the impact of PrEP on partner frequency. Furthermore, a population-based study exploring sexual network structures and their association with STI risk identified that those at the centre of a sexual network had six-fold increased odds of infection compared to those in a confirmed dyad (each being the other's only sexual partner). Individuals on the periphery of a sexual network have been nearly five times more likely to acquire an STI than individuals in confirmed dyads, despite having only one partner.[197] This suggests a deeper exploration is required to determine the risk of STI acquisition, where partner frequency is measured and an individual's place within a sexual network is determined. For example, an individual may have three partners, but if, for each partner, they are exclusively each other's sole partners, then the risk will be lower than an individual having one partner, but that partner is the centre of a multi-person sexual network.

Engagement in higher-risk activities

Higher-risk activities may relate to the situation and circumstances under which people are having sexual intercourse. This can include chem sex, group sex, sex within saunas or sex clubs, or cruising in outdoor areas. These high-risk activities are a proxy or surrogate for high-risk sexual behaviour as they are heavily associated with higher partner frequency, condomless sexual activity, and high STI incidence.[198-200] However, engagement in them does not determine a person's risk of STI acquisition. Someone could attend and have a sexual encounter using a condom with a single person, as much as they are likely to have condomless sex with multiple people. Engagement in condomless sexual intercourse in these settings suggests a need for PrEP, as the individual will be identified as engaging in high-risk sexual activity. However, if a person is simply using these locations as a place to have sex (either due to not being able to do so at home or perhaps enjoying the voyeuristic aspects of sex in public) and the sex is with condoms, then the risk of STI acquisition is low, and therefore the need for PrEP is diminished. These examples highlight the importance of context when interpreting data. While some studies examining PrEP and RC do collect information on engagement in high-risk activities, it is often simplistic, with little detail of the activities and no in-depth exploration of the relationships between engagement in these scenarios and other variables such as condom use.[191] Engagement in these activities alone is not deterministic of a higher risk of an STI but is dependent on the sexual activity occurring in these situations. For these reasons, assumptions should not be made about changes to risk simply based on engagement in these activities in relation to PrEP use, as the sexual act itself is what determines the risk.

Sexual positioning

Different sexual activities have varying levels of STI transmission and acquisition. Penetrative sexual acts have higher transmission and acquisition risks than oral activities, but in penetrative sex, the risk is higher among the receptive than the penetrative partner.[201] Among MSM, the sexual roles are determined by choice and self-identification as "top" (penetrative partner), "bottom" (receptive partner), or "versatile" (will perform either role, usually determined by partners' preferences). Some identifying as versatile will also indicate a preference for a versatile top or versatile bottom, while others will indicate conditions for sexual position. For example, a versatile top may indicate to new casual partners, they take the position of top but will adopt a bottom position if with a regular partner.[202-203] Sexual

positioning is important due to the differences in risk of STI acquisition, with changes to positioning needing to be explored. If an individual adopts the receptive role for CAS after initiating PrEP, then the risk of infection is far higher than before PrEP if their position was insertive before PrEP. To determine changes in behaviour and risk, a detailed examination of sexual positioning is required. Few studies collect this data, and it is rarely applied to risk matrices or explored in depth. Variables determining risk usually include the number of partners, condom frequency, and previous infections, with sexual positioning being overlooked.[1,2,7-9] Within the literature, it is documented that MSM will alter their sexual positioning in an act of behavioural HIV prevention known as strategic positioning or sero-positioning. This refers to situations of CAS between an HIV-negative individual and a PLWH where partners acknowledge that HIV transmission is less likely to occur when the PLWH is in the receptive position and thus the HIV-negative person adopts the penetrative position.[204] As there is an array of literature relating to the alteration of sexual positioning for HIV prevention, it seems likely that the initiation of PrEP will have an impact. While the risk of HIV is mitigated, the risk of other infections is heightened if a receptive role is adopted after initiating PrEP. The risk of STI acquisition is further impacted by changes in partner frequency and sexual scenarios, which can influence an individual's sexual positioning.

***RESEARCHER PERSPECTIVE**: being a gay male exploring MSM, it is interesting to review literature where there are elements of male-on-male sexual encounters that I believe are often overlooked. Likely deriving from a lack of awareness by heterosexual researchers and ignorance of imposing heterosexual norms onto the subject, important variables such as sexual positioning are ignored or avoided. Within heterosexual encounters, sexual positioning is fixed by genitalia, while male-on-male sexual encounters have a dynamic of sexual positioning preference and self-labelling, which does not exist in heterosexual dynamics, as partners have the options in relation to penetrative sex. Additionally, personality and behavioural traits are attributed to sexual position, resulting in a complex sociological system within the community. MSM often refers to sexual position (their own or others) in initial conversations (socially or sexually), with sexual positioning being a key factor highlighted on apps such as Grindr to identify potential partners. As a member of the community, I am aware of these complexities, yet rarely are they reflected in research or public health messaging.*

6.3.2 Role of Risk Perception

Risk perception is an individual's subjective assessment of the characteristics and severity of a risk. It is a key tenant of RC, with alterations in perception being a driving factor in behaviour change.[90] It will permeate through all variables mentioned and can aid in identifying reasons relating to behaviour change. Since PrEP's introduction, there has been a greater focus on HIV risk perception to encourage acceptance and greater adoption of PrEP. Literature highlights that HIV risk perception is associated with PrEP interest and adoption.[205-206] Factors associated with HIV risk perception include previous HIV testing, inconsistent condom use, drug use, uncertainty in STI history, having multiple partners or group sex, and previous STI acquisition.[207-208] However, the literature indicates that perception does not consistently reflect actual risk. Some individuals who engage in sexually high-risk behaviours may not acknowledge their risk, while others who engage in low-risk behaviours may perceive themselves to be at elevated risk and adopt PrEP. Certain individuals will also acknowledge risk but not engage in protective behaviours.[207-209]. While studies have explored how risk perception affects PrEP interest and adoption, its impact within the RC argument is mostly absent. Within the theory of risk compensation, it is explained that increased risk behaviour occurs due to a change in risk perception. Despite this, its measurement is limited and often measured using a self-report scale.[205-209]

The varying ways risk perception can affect behaviour were identified from the interview data and are presented in Figure 3.1**.** The Health Belief Model demonstrates how individuals perceived severity, susceptibility (risk), and benefits of certain behaviours affect their actions. Whether it is the severity of an infection, risk or susceptibility, or benefits, understanding individuals' perceptions is important to comprehend behaviour change. RC would be triggered by a change in one's perception of risk, and so any attempt to measure RC requires the identification of a change in perception.

6.3.3 STIs and Implications to Risk Compensation

Due to the difficulties of examining the behavioural variables to assess potential risk compensation, many researchers opt to measure STI cases or incidence and infer risk compensation if an increase in STIs is identified. This provides an assessment of the potential impact of RC but does not indicate the mechanisms through which RC may be working and thus limits the development and adoption of targeted interventions.

STI incidence

STI cases or incidence (referred to as incidence going forward) is one of the variables suggested as evidence for RC within the literature. Among many PrEP trials, participants received a full STI screening at baseline and were also tested regularly throughout the study period.[1,2,7] Analysis is completed on the STI incidence over the study period, with discussions often suggesting RC as an argument for any increase in STI incidence identified over the study period. However, this is not a compelling argument, as there is no evidence of STI incidence before the initiation of PrEP. If the longitudinal trend of STI incidence is increasing within the wider population, then the study findings may simply have identified part of the existing trend of increasing STI incidence over time. Some studies have attempted to address this by examining STI incidence 12 months pre- and post-PrEP initiation,[8,9] but this has the same problem if STI incidence is on an increasing trend. The trend analysis findings from Chapter 4, Figure 4.7, show that since 2012, there has been a clear positive upward trend in all infections up to 2019. If we assume that a comparable situation has occurred among MSM globally, then findings of increased STI incidences in previous literature are more likely to identify the existing increasing trend, which started before PrEP was provided, than evidence of RC. An extended review of an individual's STI history would present a more comprehensive understanding of the RC argument. However, any analysis would need to carefully address changes in STI testing, and this would be difficult for those who did not previously engage with sexual health services.

Additionally, the previous PrEP trials did not have power for an STI outcome, so any analysis is likely to be underpowered (i.e., need a larger sample size to detect effects of a reasonable size). Furthermore, these trials would need to collect data over a longer period to examine long-term impacts on STIs and examine community transmission in addition to individual risk (as the individual risk may be elevated, but if this risk is increased in people belonging to dense sexual networks engaging in high-risk sexual behaviour and they are also being treated and tested more regularly, then at the community level this may lead to a net decrease in STIs). The trials conducted have been too small and too short to examine the impact on STI incidence effectively. Furthermore, now that PrEP has been demonstrated to be highly efficacious and provided through healthcare systems, it is no longer ethical to do randomised experiments.

STI testing and screening

STI testing and screening bring challenges to the review of STI cases and incidence due to testing bias. Screening refers to the individuals taking PrEP who are required to have a full STI screening every 3 months to receive PrEP (regardless of symptoms). STI testing relates to when individuals choose to test for STIs; this could be testing for a specific infection or all STIs but is at the individual's discretion and may be in response to experiencing symptoms. A recent example of this was witnessed during the COVID-19 pandemic. Each day, testing would increase dramatically, but the data presented simply included data on diagnosed cases and did not adjust for increases or decreases in testing. This approach therefore showed large increases in the number of cases, which were driven by increased rollout and uptake of testing, rather than presenting a true reflection of the infection prevalence at the time. A similar problem occurs in many of the studies presenting data on STIs among MSM. A requirement of PrEP provision is quarterly (every 3 months) HIV/STI screening, which leads to surveillance bias affecting comparisons with non-PrEP users as well as within-individual comparisons pre-PrEP (when screening for STIs was not occurring as standard). Therefore, it is important to identify the frequency of STI testing in the pre-PrEP period, as any increase in STIs is likely to also reflect enhanced testing rather than being solely attributable to RC. Authors who have measured STI incidence as an indicator of RC have highlighted that their findings are limited by surveillance bias.[7,9,102-103,190] Despite this acknowledgement, findings are still being used as evidence for RC, which could be a reason for policymakers to avoid or stop the provision of PrEP. Uncertain evidence and conclusions drawn by authors in papers can easily be used as evidence for policymakers to act in response; this was most commonly seen during the COVID-19 pandemic, where uncertain evidence was promoted as justification to suspend policy decisions.[210-211] Studies that conduct appropriate adjustments for STI testing frequency often report a reduced or no effect of PrEP on STI incidence,[1,9,104] but these studies are few compared to the many that fail to adjust for STI testing and make inferences with little supporting evidence. The findings identified within Chapter 4, highlight the difference in potential conclusions drawn when examining STI cases versus positivity rates, which adjust for testing. Any future explorations of RC with measurements of STI rates should ensure that the analysis accounts for the surveillance bias and adjusts for testing rates to accurately describe changes in STI rates.

6.3.4 Risk Compensation and Antimicrobial Resistance

The suggestion that RC leads to increased AMR seems simple enough: reduced condom usage leads to higher and more repetitive transmission of STIs, leading to an increased consumption of antimicrobials, enhancing the chance of AMR.[5] However, identifying the causal relationship is complicated.

Within the literature, the exploration of resistance among bacterial STIs and PrEP provision is very minimal. PrEP studies have focused on the potential development of HIV resistance from PrEP failure, but levels have remained low. A review in 2021 identified that globally there have been 10 cases of 'true' PrEP failure (acquisition of HIV while having sufficient medication levels for prevention), and of these, 6 individuals had drug-resistant strains of HIV.[212] For antimicrobial consumption and AMR in bacterial STIs among PrEP cohorts, I have only identified two papers. The first is a sub-study from the ANRS IPERGAY PrEP trial, which examined the prevalence of mycoplasma genitalium, and related antibiotic resistance. In this trial, the authors identified a high prevalence of AMR among MSM using PrEP, with high rates of Azithromycin and Fluoroquinolone (Ciprofloxacin) resistance present. [213] This study simply explored prevalence among the cohort and did not examine PrEP use and AMR. The second paper explored antimicrobial consumption in a Belgian PrEP cohort and compared the results to the national community levels of antimicrobial consumption in 30 European countries. The study found that the use of macrolides among the PrEP cohort was higher than in the community sample in all 30 countries—between 2 and 52 times higher, depending on the country. Fluoroquinolone (Ciprofloxacin) use was higher among PrEP users in all countries except Cyprus. The use of third generation cephalosporins (Ceftriaxone) was higher among PrEP users in 25 countries, and for Tetracycline, it was higher among PrEP users in 19 countries. The PrEP cohort exceeded the community-level consumption for Belgium for every antimicrobial examined. The paper indicates that the elevated level of consumption was driven by mandated screening for PrEP users and the identification of high amounts of asymptomatic STIs.[214] The high level of antimicrobial consumption among the PrEP cohort is concerning, as it is documented that increased use of antibiotics drives resistance.[49,50]

These articles provide evidence to support the points raised in the paper by Holt et al.,[5] identifying a high rate of resistance for Azithromycin and Fluoroquinolones along with high consumption across antimicrobial classes. However, as no pre-PrEP comparison was available,

it is unknown if the findings already existed or were exacerbated by PrEP use. The Belgian paper identified that within the PrEP cohort, there was a dramatic rise in the number of asymptomatic infections identified, which, without the mandatory STI screening for PrEP use, may not have been identified. For asymptomatic infections, individuals may have 'self-cured' (spontaneous remission) and thus not require the provision of antimicrobial therapy. However, these individuals could continue the onward transmission while not showing symptoms. The scientific understanding of spontaneous remission for STIs is still in its infancy, so there are many unknowns.[215-216] This indicates the extent of the understanding regarding the relationship between PrEP and antimicrobial resistance, with a question needing to be answered regarding the optimal care for individuals with an asymptomatic STI diagnosis.

The findings from Chapter 4 (see 4.4.8) provide the only data for longitudinal trends of AMR rates between PrEP and non-PrEP using MSM. Figure 4.11 presents the findings to highlight that rates of AMR for Penicillin, Tetracycline, Doxycycline, and Ciprofloxacin are higher among the PrEP cohorts than those not using PrEP, with positive trends visible in both groups, except for Penicillin. Cefixime and Azithromycin resistance is higher among the non-PrEP cohort, with Spectinomycin resistance rates being similar between groups. The most important consideration is Ceftriaxone resistance, as it is the current first-line treatment option for gonorrhoea. Data indicates a low rate of Ceftriaxone resistance among the PrEP cohort, with no resistance identified for multiple years. This analysis is, however, merely descriptive and cannot determine if PrEP use and potential RC influence changes.

6.4.5 Variables for Consideration

The framework I have presented includes a variable for demographics; this can include numerous factors, but for this work, I will focus on age, ethnicity, and sexuality. It is important to consider who is represented within the data and if stratification is required.

Age

As indicated in Chapter Four (4.4.1), of those MSM engaging in STI testing, 40% were aged 18–25, with 25% being 26–35, with the percentage dropping for each increasing age bracket. As this data is pan-Wales, it highlights that the majority of MSM receiving STI testing are under 26 years old. When examining STI testing, it may be important to consider the variances in

levels of testing among age groups. Of those initiating PrEP in Wales, while the age range is vast, the majority are within the age group of 18–25, and individuals of different ages may engage with condoms and risk differently.

Ethnicity

Ethnicity is an important variable concerning engagement with health services. It is well documented that PrEP and sexual health services are underutilised by ethnic minority groups.[217] When examining data, it is important to consider what groups are reflected within the data and to whom the findings may relate. From my experience reviewing the PrEP literature, white gay cisgender men are dominant, and so theories and findings may not apply to groups outside of this demographic.

Sexuality

Among MSM, there are various sexualities incorporated: gay, bisexual, heterosexual, queer, pansexual, etc., but among most MSM samples, there is an overabundance of gay males, which is likely to skew results to reflect their behaviours and attitudes as dominant within the sample.[218-219] PrEP has largely been adopted by gay men, and the levels of RC may be different between groups. While the various sexualities are grouped to form MSM, there are likely to be differing behavioural constructs that need to be considered.

6.3.6 Community-level Risk Compensation

As mentioned in Chapter 2.5, RC may also exist at the community level. Briefly, it suggests that individuals not using PrEP may reduce their condom use due to a perception that there is less risk of HIV acquisition, as others within their sexual network will be using PrEP or receiving treatment.[96-97] Alongside reduced HIV transmission within the community, due to the requirement for regular STI screening by those taking PrEP, some could assume that this would lead to reduced transmission of all other STIs over time due to earlier and increased identification and treatment. This assumption would not be farfetched, as a study modelling the long-term impact of PrEP identified that this scenario would occur in the instance of regular STI testing as an element of PrEP provision.[220]

The framework presented is centred on individual-level RC, but if you remove the variables eligibility, PrEP use, and screening (instead of these informing knowledge/awareness and risk perception), then the framework applies to non-PrEP using MSM. The focus changes as the

understanding of RC at a community level requires a detailed understanding of knowledge, attitudes, and perceptions of the impact of PrEP within their community or sexual network. Others within the community taking PrEP would be so far removed from an individual that traditional measures of attempting to measure RC via condom use or STI incidence could not be argued to be compelling evidence of RC as there are a host of factors within sexual behaviour that would have a more direct impact. A measure could be developed that attempts to quantify community-level RC, but this would first require detailed qualitative work to identify the various elements and constructs that may form this variable. Community-level RC research is in its infancy and requires far more detailed work to understand its impact. Interestingly, I conducted a brief scoping literature search exploring community RC and identified that most community RC research is associated to PrEP. This is despite RC having a range of applications to public health, such as the COVID-19 pandemic.

6.4 IMPLICATIONS / THE FUTURE OF RC

The conceptual framework developed (Figure 6.2) presents the complexity of RC when additional challenges are added when applied to sexual behaviour. We can see that numerous variables and factors need to be identified and addressed before any conclusion regarding RC can be presumed. This is important for any future development and application of public health interventions to consider. The framework provides an outline of the extensive behavioural data required to measure any behaviour change related to an intervention. The process explained is useful to anyone developing an intervention to ensure they consider all potentially related variables and not simply focus on those which include data as they responses to the behaviour may be influenced by variables not measured and this is important to understand.

The framework brings doubt to previous explorations around the phenomenon, as most fail to account for many of the variables, and, in most cases, there is a lack of synthesis of a pre-PrEP behaviour pattern or risk profile. As discussed, this approach would eliminate any potential for exploring behaviour change, as a baseline measurement at study onset or STI history reaching back 12 months does not provide an accurate account of this. Additionally, the multiple factors influencing a person's choice to initiate PrEP and the requirements for eligibility criteria predetermine a population with a history of STI acquisition and infrequent condom use behaviours. Therefore, any change would be minimal by nature and difficult to

identify. The existing literature also fails to acknowledge that regular STI testing is a health-protective measure, and, while their behaviour may be high-risk, consistent regular testing does protect as it breaks the chain of transmission more quickly than if an individual's testing is infrequent.

The argument that the use of PrEP increases antimicrobial resistance follows under the assumption that RC is a major factor driving a rise in STI transmission, identification, and treatment. However, without that certainty, the potential for PrEP to drive AMR is slim. To conclude a causal relationship between PrEP use and AMR, there would need to be an understanding of the mechanisms of the relationship, requiring an extensive research project.

The argument of RC is quickly provided as an unintended outcome of new interventions and can be adopted as a reason to avoid providing a necessary medical prevention. However, evidence for RC is limited and is provided as an explanation of findings without any causal inference being proven. The framework presents the complexity of the RC argument for PrEP, indicating the many variables and biases that can easily influence findings. Any future explorations of RC need to ensure it is examined thoroughly, addresses all variables, and accounts for biases that will exist in the data. This applies to PrEP and any other areas where RC is promoted as a potential consequence of an intervention. Theorising without evidence to support an argument can be damaging to the introduction of new interventions, and while RC is often simplified, there will always be a host of associated behavioural variables that require detailed examination before assuming it is a cause of behaviour change.

6.5 CHAPTER SUMMARY

This chapter has detailed the risk compensation argument with PrEP, presenting the variables involved that link RC to STIs and AMR. The framework presents a detailed understanding of the relationship between the variables, followed by a discussion of the requirements to accurately measure, and identify the causal relationship of RC.

CHAPTER SEVEN
AN OVERALL DISCUSSION

This chapter reports the main themes and synthesises the findings from the studies forming this thesis. The thesis design and methodology are appraised before the implications for practice and future research are considered.

7.1 SUMMARY OF THE MAIN FINDINGS

The summary of findings will be centred on the objectives set within the introduction chapter to meet the aim of understanding the impact PrEP provision has had on sexually transmitted infections and antimicrobial resistance among men who have sex with men in Wales.

- There is a lower concern for gonorrhoea and chlamydia, despite the commonality of transmission, and while there is a higher concern for syphilis, HIV is 'exceptionalised' within the minds of MSM. HIV is perceived as more serious than other STIs and a greater threat to health, leading to greater potential for behaviour change, such as adopting PrEP. [Chapter 3]
- Some participants perceptions conformed to the risk compensation argument that there would be decreased condom use after initiating PrEP. However, on the exploration of condom use behaviours, it became clear condom use was either non-existent or irregular for many participants before PrEP use was initiated. Others reported using PrEP to allow for circumstantial condomless sex (with regular sexual partners). [Chapter 3]
- Beliefs and behaviours that are in line with risk compensation amongst MSM are likely being perpetuated by PrEP stigma, which needs to be better addressed. [Chapter 3]
- Better public awareness of the causes and consequences of resistance is required for MSM and others to better understand antimicrobial resistance. [Chapter 3]
- The evidence highlights that PrEP users have a higher burden of STIs, which was present before PrEP was introduced. Positivity rates for all MSM have been slowly decreasing since 2012, and, following the introduction of PrEP in 2017, there was a

stabilisation of positivity rates for PrEP users and decreases in the non-PrEP cohort. [Chapter 4]

- STI cases and positivity rates suggest quite different conclusions about the situation of STI transmission in MSM. Reviewing cases alone would raise concerns due to the high number of cases, but this becomes explained when viewed in context with the high testing levels and positivity rates dropping. [Chapter 4]
- Positivity rates alone do not provide the whole picture, and adjustments for sexual behaviour also need to be made to understand STI transmission in MSM. Researchers should exercise caution when drawing conclusions from analyses that do not include the appropriate adjustments. [Chapter 4]
- Rates of antimicrobial resistance for gonorrhoea differed among PrEP and non-PrEP users. The PrEP cohort presented with lower rates of resistance for those antimicrobials currently used therapeutically to treat gonorrhoea infections (Cefixime, Spectinomycin, Azithromycin, and Ceftriaxone), with higher rates of resistance for the antimicrobials not currently used as treatments (Penicillin, Tetracycline, Doxycycline, and Ciprofloxacin). [Chapter 4]
- Findings suggest that PrEP has a minimally significant impact on STI rates or antimicrobial resistance. [Chapters 3, 4, and 6]
- The pandemic had a significant impact on people's sexual behaviours and practices. Due to social restrictions, it is likely there was a decrease in the transmission of STIs. [Chapter 5]
- Existing attempts to identify and assess risk compensation are reductive and do not acknowledge or adjust for important variables to provide an estimate of the causal effect of PrEP on risk compensation behaviours. [Chapter 6]

7.2 A SYNTHESIS OF FINDINGS

The numerous studies have separately identified and explored aspects of the relationship between PrEP, STIs, and AMR among MSM. This section presents a combination of findings related to MSM sexual health, the impact of PrEP, and a definitive risk compensation study.

7.2.1 Impact of PrEP

Before discussing PrEP impact, it is important to address an important finding, which was that there was a definitive need for PrEP to be introduced. Findings highlight that from 2012 to 2017, there was a consistent increase in STI transmission, year on year, among MSM in Wales, with a particular concentration among those who would go on to adopt PrEP. While there is no data on condom use, the elevated levels of transmission are an indicator of condomless sex among the population. The engagement in CAS and high levels of STI rates provided the necessary context for PrEP provision.[3,4] Without its introduction in 2017, the current situation of new HIV infections in Wales could be very different, and Wales may not be on track to end HIV transmission by 2030.[85,221] However, considering Figure 4.5, there was a downward trajectory in HIV diagnoses prior to PrEP's introduction, and that trajectory has remained fairly consistent since, suggesting that PrEP's introduction has had a limited impact on the trajectory of HIV diagnoses.

Despite the theory that STIs might have increased since the introduction of PrEP in 2017, this thesis has shown that there has been a reduction in STI rates since the introduction of PrEP, among all MSM but more concentrated in the PrEP cohort. While a causal argument for PrEP reducing STI rates is difficult to determine, the identified reduction supports the mathematical model produced by Jenness et al. 2017,[222] which proposed that enhanced STI screening as a condition of PrEP provision would increase early identification and treatment, cutting the transmission roots early. The increased access to testing provided by the introduction of the postal testing service during the pandemic will likely have a similar effect on reducing STI transmission via early detection.

There was no singular behavioural change identified from the adoption of PrEP by MSM interviewed. The interpretation in Chapter 3.7 presents a typology of PrEP user behaviours, but overall, there was a consistency to behaviour, with an overall continuation of behaviour from before initiating PrEP to after its adoption. Therefore, PrEP was not found to result in a

significant behaviour change, with little direct evidence of risk compensation being identified. While some individuals did likely engage with PrEP to then experience CAS, this was not the majority of those interviewed. Behaviour change is complex and difficult to maintain, which is not appreciated within the RC argument. Previous literature provides similar findings regarding the consistency of behaviour.[223-224] Longitudinal studies identifying change found healthier behaviours to be short-lived before individuals reverted to their former behaviours, including condom use.[224-226] The results from this thesis challenge the accuracy of cross-sectional self-reported data regarding behaviour change and PrEP use, as there was a strong perception of change with little evidence of change upon qualitative exploration. The reports of PrEP stigma may have been internalised, therefore influencing perceptions, and reported actions. Previous research has aimed to examine the reduction in condom use associated with PrEP through cross-sectional surveys.[102,209] These studies reported lower use of condoms among PrEP users but with no context. If we take the findings from the current study and assume a similarity within previous studies, then reduction may be context-specific and not across all encounters. This thesis presents a more accurate picture of behaviour where there is a slight change to the new stimulus. Long-term behaviour is rarely so dramatic in its change, and the findings presented in previous chapters show a more nuanced change occurring under certain conditions. For example, in the case of sexual positioning, people could switch from top to bottom for CAS once PrEP was initiated, increasing the risk of acquiring bacterial STIs despite reducing the risk of HIV.

The AMR situation for STIs continues to be a concern,[47,55] but the link between AMR and PrEP is limited. With only gonorrhoea being examined for resistance and the limited resistance identified in Wales, there is difficulty in determining casual or mediating factors. The potential for resistance to occur due to seroconversion is a possibility, but globally, cases remain low, and to date, there have been no such cases reported in Wales. There are varying levels of resistance across medications for gonorrhoea, with the PrEP cohort presenting higher levels of resistance for older medications not currently used as treatment options (Ciprofloxacin, Doxycycline, Penicillin, and Tetracycline), with levels lower than the non-PrEP cohort for currently used antimicrobials. An examination of the levels among the rest of the population would provide an interesting comparison to identify where levels currently lie for MSM. The PrEP-RC argument and connection to AMR is difficult to determine with accuracy.

It could be argued that the higher levels of AMR among the PrEP cohort mentioned are evidence of RC; however, there are other explanations. One example is that individuals' sexual networks overlap as MSM is a limited population, which may be reduced further by the segregation of sexual networks based on PrEP use. This overlapping of networks in a small population can lead to resistant strains proliferating and becoming the dominant strain.

The sharp increases in Doxycycline resistance since 2017 is concerning, as there are calls to adopt this medication as pre-exposure prophylaxis to reduce the transmission of bacterial STIs, with trials being conducted to test efficacy.[227-229] However, with roughly a third of gonorrhoea samples presenting resistance in Wales, its use may be short-lived and drive resistance further without providing the desired benefit. There could be a trade-off between doxycycline being a PrEP for chlamydia and syphilis at the expense of gonorrhoea. For this to occur, the rates of resistance would need to be carefully monitored, and the current data management system is not dynamic enough to provide a timely view of the situation.

7.2.2 MSM and Sexual Health

The findings suggest that in Wales, the MSM who engage with sexual health are frequent testers, knowledgeable about STIs and risk, and will actively engage in prevention. MSM have been identified as having high health literacy related to sexual health in previous studies.[170]. Previous literature has also identified higher levels of STI testing among MSM and a greater uptake of PEP/PrEP and vaccination within MSM communities.[16-20, 87,230] The recent MPOX (previously known as monkeypox) outbreak, which resulted in many MSM actively seeking out vaccinations, indicates the community's positive engagement with sexual health protection and prevention.[231-232] This greater engagement with sexual health services by MSM questions their continued labelling as "high risk" within health communities. Condomless sex is common among heterosexuals, increasing with the growing number of options relating to contraception.[233-234] Heterosexuals are less engaged with sexual health services and STI prevention than LGBTQ+ individuals.[16-20,235-236] Yet MSM continues to be automatically considered high-risk, presuming a homogeneity among the population that does not exist and ignoring engagement with health protection. This labelling is often compounded by the elevated level of STI rates identified among MSM. However, as the study and literature presented in this thesis suggest, the pitfalls of surveillance bias may also exist here. MSM engage in testing more frequently than heterosexuals and are a much

smaller population, presenting a false view of the true rates of STIs between sexualities. The positive engagement with sexual health services and adoption of health-protective measures by MSM is often ignored in favour of a blanket reference to the “high-risk population,” but this needs to be reassessed among the medical and research communities.

An individual's health literacy for sexual health likely informs the differing attitudes highlighted towards STIs. The findings suggested a high degree of concern for HIV relative to other STIs, which had an impact on altering behaviour. Reasons for this can be due to a range of factors, including historical or secondary trauma, the longevity of infection, or even stigma. Currently, the concern expressed about being infected with HIV is not comparable to its current severity. HIV is now a chronic condition, managed with daily medication that prevents viral replication and stops the potential for transmission.[28] The rate of transmission of HIV is one of the lowest amongst all STIs (at under 2%), whereas a single unprotected sexual encounter with a partner who has gonorrhoea has a 25% odds of transmission, 40% for chlamydia, and up to 60% for syphilis.[237] While a level of concern for HIV is rational, it overshadows the current risk. Gonorrhoea currently has the highest burden among MSM communities; it has a high rate of transmission, and the growing identification of antibiotic-resistant strains increases the severity of this infection. With the threat of AMR for gonorrhoea and rising cases of syphilis in Wales, it is paramount that work begins to realign public sentiment with the current trepidations within sexual health.

7.2.3 A Definitive Risk Compensation Study

This thesis has presented that risk compensation is a complex concept, making both measurement and interpretation challenging. The existing attempts to explore it have been reductive and fail to acknowledge the intricacies of MSM sexual behaviour. The findings have been collated to determine a set of principles that should be used to inform any future risk compensation study within sexual health:

Approach: The various complexities and requirements result in the requirement for a future study on risk compensation to adopt a mixed-methods design, incorporating quantitative and qualitative data sources. The benefits of a mixed-methods design have been detailed previously in this thesis, which highlights the many benefits. Chapter 6 provides a fully formed conceptual framework and provides a starting point for any future study exploring this area.

Future research teams should develop a conceptual framework tailored to their study and use it to identify the relevant variables and pathways as possible to inform their decisions regarding data collection and analysis.

Population: When considering population in a future study, it is important to ensure a spectrum of identities is included in sufficient quantities, even within a sample such as MSM. As indicated, MSM is not a homogenous group, and they include various identities, which all need representation to draw appropriate conclusions regarding behaviour and impact. To achieve this, the sampling methods will need to be varied and informed in partnership with PPI and stakeholder groups to ensure diversity in variables such as age, ethnicity, sexual identity, educational background, and any others identified within the conceptual framework. If PrEP becomes more widely adopted outside of MSM populations, it will be important to consider the various identities and factors affecting behaviour among the additional groups, alongside the factors mentioned above.

Tools and data collection: As consistently mentioned, risk compensation is a behaviour change; therefore, its examination requires extensive behavioural data collection to determine a detailed baseline to compare change. The determination of baseline behaviour cannot be achieved via a cross-sectional design, with a longitudinal design being vital. Baseline data collection should be conducted via repeated measures to determine an average baseline of behaviour. This could take the form of a biweekly or monthly survey collecting data on various elements of sexual activity and behaviours highlighted within the conceptual framework. Any time points after the intervention would also require repeated measures to ensure a sustained change in behaviour and not a single anomaly impacted by factors such as mental health. A tool should be developed to determine a risk profile from the various behavioural data to allow a more accurate comparison of PrEP and non-PrEP users to address the sample bias. Alongside behaviour, a measure of risk perception must be included to identify risk compensation, as perceptions will alter and then lead to behaviour change. Data collected should be paired with any historical patient records available to develop a testing and STI history. Additionally, it will be important to collect qualitative data to inform findings. This can take the form of interviews or focus groups but should explore mitigation and health protective measures alongside risk behaviours. For the behavioural items suggested, important considerations need to be made around participant burden, measurement

reactivity, and social desirability biases. The tools and data collection will require detailed discussion around cost and benefit to determine the measures adopted.

Analysis: The analysis should be determined by the research questions and data collection and ensure that the appropriate biases are addressed. Learning from the limitations of previous research addressed in this thesis, surveillance and testing bias must be accurately addressed along with sample bias (this could be addressed by the creation of the risk profile scores suggested above). Appropriate measures should be taken to explore and address as many confounding variables as possible. Any model needs to take account of the absolute risk exposure. Someone who goes from engaging in CAS in half of encounters to CAS occurring with every partner, this has a vastly different risk associated with this reduction depending on the number of sexual partners over the period. It is also important to identify if their volume of sexual partners and/or types of sexual behaviour increases during this period.

7.3 STRENGTHS AND LIMITATIONS OF THE THESIS

Strengths and limitations were discussed within each study chapter. The following section addresses the macroconditions of the methodologies and the scientific rigour adopted.

7.3.1 Research Team

This research team supporting my PhD studentship was a major strength and demonstrates the value of interdisciplinary teams for PhD supervision and in healthcare research. The collaborative effort provided a wider group of people to support and challenge my ideas and draw upon many skills to boost the impact of this work. My background is in health psychology, with experience in both quantitative and qualitative data collection and analysis, with previous research focusing on health inequalities among LGBTQ+ individuals. My own experience as a young gay man living in Wales also supported the understanding of the dynamics of sexual behaviour within the population examined through my own lived experience. The study was designed, conducted, and analysed by me with input from the wider team, including two statisticians, a medical sociologist, a GP, and a public health professional, with their expertise ranging across quantitative and qualitative methodologies, medical sociology, health sciences, medicine, and sexual health, providing multiple perspectives. The perspectives of the research team facilitated a broader analysis and understanding of impact, increasing the trustworthiness of the analysis as expertise was

available across multiple disciplines.[238] The team approach to qualitative research supported a more structured analysis to improve validity and reliability among the multiple team members.[239] The support throughout this PhD was bi-directional, with myself supporting my supervisor's post-doctoral fellowship (focused on PrEP adherence) and Public Health Wales' projects in sexual health, providing my own lived experience and psychological understanding. Additionally, I supported four medical student research projects and three MSc dissertations, extending my practice of supporting others while being supported.

At the outset of the PhD, I came in with views and assumptions that leaned towards believing the RC theory. Looking back, I may have been influenced by the same PrEP stigma that some of the participants referenced in the interviews. I always have my doubts regarding the evidence due to the many biases within the samples and around testing which were not often addressed. However, as I was exposed to more material and attitudes, I began to view this as less likely, while some will have taken the opportunity of PrEP to safely engage in condomless sex, many behaviours will have remained the same. It is important to support people however they are choosing to behave and not attempt to fit people into deemed "good behaviour" as it will perpetuate stigma and reduce service engagement.

7.3.2 Patient and Public Involvement

Patient and Public Involvement (PPI) is important to research, and the HIV field has had a strong history of PPI since its emergence.[240] While not as common, there is a growing push to have doctoral research include PPI.[241] As with many aspects of academic life, funding for PPI is limited, and successful PPI input requires those involved to be reimbursed for their time and expertise. However, doctoral studentships are rarely provided with the required funds to support such work, resulting in reliance on unpaid PPI. In the initial months of the studentship, I worked towards setting up a PPI group that included a member of the public (MSM who used PrEP) and a sexual health consultant. They supported the development of the information sheets, consent forms, and interview schedules for the qualitative work. This all occurred within the first six months of the PhD; however, as the COVID-19 pandemic struck, the public members moved away and ceased their involvement. I attempted to replace the lost lay member but was unsuccessful. However, I became more engaged with the community group Fast Track Cardiff and Vale, leading to members of this group and the sexual health consultant becoming a form of stakeholder group. Together, their involvement included

identifying priorities, co-developing information and consent forms and other research materials for the survey and contributing to dissemination. Any application of PPI within research is beneficial to improving the quality of the research and closing the gap between research and the public. Its use was beneficial to this thesis in the consideration of the design of materials and dissemination of work through the Fast Track Cardiff and Vale website and newsletters. The lack of layperson PPI representation throughout the PhD was a limitation, as the quality and impact of the findings have been reduced. This experience has provided lessons to learn when attempting to plan and conduct successful PPI in the future.

7.3.3 Study Design

This study's mixed-methods design provided both breadth and depth in the approach to comprehending PrEP's impact, gaining detailed perspectives from the MSM community, understanding the influence of PrEP on people's sexual encounters and behaviour, and greater knowledge of risk compensation and how to measure it than either a quantitative or qualitative approach alone could provide.[112,242] Furthermore, a mixed-methods approach is pragmatic; it allows the study design to adapt to the research questions rather than be specified by paradigms, offering the most robust methods to be adopted at each stage of the study.[242] An underpinning principle of mixed-methods research is its advantage of allowing the comparison, contrast, and integration of various forms of data, also known as triangulation. Triangulation remains new in the realms of methodology, but academics suggest it increases the scientific credibility of study findings by improving both internal consistency and generalisability, minimising biases, and allowing the researcher to better consider multiple perspectives and realities,[243-244] providing strength to its use within this thesis. With the development of the conceptual framework being an iterative process, the thesis was designed and conducted to continually cross-check and evaluate findings. A multiple triangulation approach is being taken (several methods of data collection with some input from multiple investigators of varied expertise) across the four triangulation types: data, methodological, theoretical, and investigator.[245-246] Achieving these various forms of triangulation has increased the credibility of the research findings and enabled a justified approach to forming the conceptual model via the research findings. Additionally, the number of conference presentations and journal publications at each step of the process provided an even wider peer review of the work.

While the benefits are numerous, there are also limitations to the triangulation methodology. Its use adds layers of complexity to research, which makes it more time-consuming, which is challenging considering the limited time resources available for a PhD studentship. Additionally, the application of triangulation is complex as it requires tailoring to studies. This results in a lack of uniformity and consistency in its application, raising limitations for the replicability of research.[247-248] The use of triangulation and the processes involved require a skilled analyst.[247] This was my first attempt at conducting a triangulation study, and while I engaged in various trainings, my analysis may not be as comprehensive as that conducted by a more senior analyst. This limitation was mitigated by the research team, which is made up of experienced researchers from various backgrounds, but the application of the triangulation within this study may still lack the desirable robustness.

The methods of recruitment require specific mention. The sample biases have been previously indicated in Chapter 3 and Chapter 5 but the recruitment methods may have led to the bias identified. The use of social media and snowball sampling likely led to a specific population being targeted. The lack of ethnic, sexuality, and educational diversity likely reflects the recruitment strategy with a need for greater effort to engage these individuals. Challenges were added due to the pandemic influence with a lack of ability to use traditional recruitment strategies such as posters in community hubs. However, it is important for any future work to put greater effort into engaging populations who are continually missing from research populations but often those who are in greatest need of support and access to services.

7.4 RECOMMENDATIONS

From this thesis, there are multiple recommendations which are split between direct recommendations from the findings and recommendations for future research in this area.

7.4.1 Recommendations from Findings

This project has identified the complexity associated with RC and its data collection. Until RC is adequately explored with confounders and bias appropriately addressed, its use as an explanation should be done with caution. The term has power within people's consciousness, and it can easily become a dominant argument despite the lack of evidence.[5-9]

The perception of the low importance of bacterial STIs compared to HIV is a principal factor that needs to be addressed. Many participants perceived chlamydia and gonorrhoea as being of low seriousness due to the ease of treatment options available, despite being aware of the high rates within the community. Syphilis was of greater concern to those who were aware of it, but this was not common among all participants. HIV continues to dominate people's consciousness due to the permanence of the infection, while transmission and new infections are exceptionally low. The growing identification of multi-drug-resistant gonorrhoea and current explosions in the rates of gonorrhoea and syphilis require a focus to be placed on these infections. Highlighting the complications associated with bacterial STIs may adjust people's perceptions and concerns towards these infections, providing an opportunity for behaviour change or at least better acknowledgement of risk.

Any health messaging should be done with sensitivity to avoid the rhetoric and stigma that linger from the 1980s HIV campaigns. The focus being continually placed on MSM is still present, perpetuating stigma and stereotypes and diverting attention away from others at risk of HIV. In 2020 and 2021, the number of new HIV diagnoses among heterosexuals was higher than for gay and bisexual men.[249-250] While this is an absolute number and not a rate, it still highlights the need for work to be dedicated to addressing HIV transmission in heterosexuals and not just MSM. Evidence-based messaging techniques need to be adopted to ensure impact before any interventions are attempted, as the low concern for bacterial STIs identified in this thesis needs to be addressed. As the uptake of PrEP and recent response to the MPox (formerly monkeypox) outbreak have proven, MSM are health-literate and able to assess their risks and respond appropriately. The provision of clear, understandable information and access to services will have a substantial impact on the community.

The qualitative findings indicate that some will not use condoms out of personal preference, and it is important to avoid pushing condoms onto people, instead addressing their risk with alternative methods such as PrEP, vaccines, and STI testing. Support should also be provided for the safe use of substances during chemsex sessions.

7.4.2 Recommendations for Future Research

Developing a case-management system

The current data management system for sexual health data in Wales is not fit for understanding the picture across Wales. This is because the data used comes from a system that was designed only to assist in managing patients in clinics. The merging of various databases into a single system within Public Health Wales does not provide clear and up-to-date information about HIV and STIs figures in Wales. The recent HIV Action Plan for Wales explicitly indicates the need for a case management system in Wales.[221] The challenges identified within the analysis of this thesis should be considered in the development of a future case management system. Alongside this, an essential element is unifying the input process to remove coding inconsistencies between healthcare professionals, clinics, and health boards. While Public Health Wales has provided a guide to coding, the input process allows for variability, which needs to be addressed. An audit and feedback intervention around coding would be one way to improve the consistency of coding between clinics and clinicians. Achieving this will massively improve the data quality and ease of future analyses. With the need for closer scrutiny of STIs, the case management system will need to feed into a live surveillance system for tracking and monitoring clusters and outbreaks. Demographic details will be required to ensure fast, responsive, and targeted work can be completed whenever new clusters are identified to ramp up the 'test and treat' provision, reducing transmission. Evidence-based lessons from the COVID-19 pandemic response should be considered when developing the future of sexual health in Wales.

Impact of the COVID-19 pandemic

This research was conducted during the onset of the COVID-19 pandemic and, through the sub-study survey and interviews, explored a brief glimpse of the impact of COVID-19 on people and their sexual behaviours. The ITS analysis was limited to pre-COVID data, but since enough time has passed for us to return to an unrestricted life, it would be interesting to continue the ITS throughout the pandemic period up to today. In the interviews, participants expressed that they expected an "explosion" in sexual activity once restrictions were lifted, leading to a surge in STI transmission after the pandemics forced a reduction. This increase in STI cases has been identified across the UK, with currently higher rates than experienced in decades.[174,251] The ITS would allow for an understanding of the reduction and identify

when cases started to rise again, which could be mapped against the COVID-19 restriction timeline. It is important to understand how quickly STI transmission bounces back after forced reduction through governmental restrictions to better prepare services in the future if similar COVID-19 restrictions are required. When planning and preparing for future pandemics, plans must be put in place for the process of easing restrictions as well as their introduction. The pandemic health measures to prevent the spread of COVID-19 had a similar effect on the transmission of STIs and other infections. For those in the field of infectious disease, we should aim to learn as much as possible about the impact of pandemics on infectious diseases, so that when there is a future pandemic, we are better prepared to capitalise on the introduction of restrictions that could assist in the elimination or major reduction of multiple infections, not all rushing to focus on the pandemic-causing infection.

Expanding access to HIV PrEP

The current thesis examined only MSM as, up to the point of the data collection, this group was the dominant population who had taken up PrEP in Wales. However, all individuals who are at risk of acquiring HIV must have access to and be encouraged to take PrEP where appropriate. Heterosexual men and women, transgender individuals, and ethnic minorities all need to be enabled to adopt PrEP where it is required. The association of PrEP with MSM extends the stigma of the past, linking gay men to HIV, resulting in other populations not considering it a risk. Work is required to better engage other populations with PrEP services where their use would be beneficial. As more groups of individuals engage with PrEP, work must be conducted to evaluate its adoption.

7.5 CONCLUSION

Despite the onset of a global pandemic, I have provided the most detailed epidemiological and behavioural account of the impact of PrEP in Wales that currently exists. The use of secondary data posed unexpected challenges as initial assumptions regarding data availability and quality were proven incorrect. Regardless, I was able to use the available data to draw out some interesting findings on the trends of STI testing and transmission and their relation to PrEP's introduction. I was also able to provide one of the few examinations of longitudinal trends of antimicrobial resistance among MSM. During the data collection and analysis, the COVID-19 pandemic was ongoing, and there was a lack of certainty of how and when it would

end. This resulted in the exploration being mostly limited to pre-pandemic times. The extent of the pandemic's impact and how the current situation compares is still unknown.

This thesis has presented multiple studies to enhance our understanding of PrEP's impact on the MSM community. I found PrEP has had little to no statistical effect on STI rates, with rates reducing among many STIs since PrEP's introduction. It was demonstrated that people's perceptions of their behaviour may not provide an accurate reflection of actual behaviour, and external influences such as stereotypes and stigma can affect self-perceptions. This thesis has provided a detailed account of RC and presents how its previous examination has been incomplete, and thus it should be used with caution. The qualitative findings indicate typologies of behaviour, with RC not prominent in the typology. Behaviour change is a complicated metric, but it is typically stable and difficult to change.

This thesis addressed the importance of adjusting for bias within data and the need for caution when simple metrics of cases are reported without acknowledging the impact of testing frequency or behaviour, which influences results. It is important to be cautious of simple case data, which is not an accurate reflection of the STI situation. Comprehensive data are required to identify populations in need of attention and potential outbreaks.

If we hope to introduce new interventions to tackle the high levels of STIs and better understand the sexual health situation in Wales, a new and comprehensive data management system must be developed that is informed by all healthcare settings in Wales, with uniformity at input being a core principle.

REFERENCES

1. McCormack, S., Dunn, D. T., Desai, M., … Gill, O. N. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): Effectiveness results from the pilot phase of a pragmatic open-label randomised trial. The Lancet, 2016;387(10013):53–60. https://doi.org/10.1016/S0140-6736(15)00056-2
2. Molina, J.-M., Capitant, C., Spire, B., … Delfraissy, J.-F. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. New England Journal of Medicine, 2015;373(23):2237–2246. https://doi.org/10.1056/nejmoa1506273
3. World Health Organization. Policy Brief. Pre-exposure prophylaxis (PrEP). WHO expands recommendation on oral pre-exposure prophylaxis of HIV infection (PrEP). Nov 2016. Available from: http://www.who.int/hiv/pub/prep/policy-brief-prep-2015/en/
4. Kennedy C, Fonner V. Pre-exposure prophylaxis for men who have sex with men: A systematic review. In: Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations – 2016 Update. Geneva: World Health Organization; 2016. Annex 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK379693/
5. Holt, M., Newman, C.E., Lancaster, K., Smith, A.K., Hughes, S. and Truong, H.H.M. HIV pre-exposure prophylaxis and the 'problems' of reduced condom use and sexually transmitted infections in Australia: a critical analysis from an evidence-making intervention perspective. Sociology of Health & Illness. 2019; 41(8):1535-1548. https://doi.org/10.1111/1467-9566.12967
6. Rojas Castro, D., Delabre, R. M., & Molina, J. M. Give PrEP a chance: moving on from the "risk compensation" concept. Journal of the International AIDS Society, 2019;22(S6):50–56. https://doi.org/10.1002/jia2.25351
7. Montanõ, M. A., Dombrowski, J. C., Dasgupta, S., et al. Differences in sexually transmitted infection risk comparing preexposure prophylaxis users and propensity score matched historical controls in a clinic setting. Aids, 2019;33(11):1773–1780. https://doi.org/10.1097/QAD.0000000000002281
8. Nguyen, V. K., Greenwald, Z. R., Trottier, H., … Thomas, R. Incidence of sexually transmitted infections before and after preexposure prophylaxis for HIV. Aids, 2018;32(4):523–530. https://doi.org/10.1097/QAD.0000000000001718
9. Beymer, M. R., DeVost, M. A., Weiss, R. E., Dierst-Davies, R., … Bolan, R. K. Does HIV pre-exposure prophylaxis use lead to a higher incidence of sexually transmitted infections? A case-crossover study of

men who have sex with men in Los Angeles, California. Sexually Transmitted Infections, 2018; 94(6):457–462. https://doi.org/10.1136/sextrans-2017-053377

10. Shorten A, Smith J. Mixed methods research: expanding the evidence base. Evidence-Based Nursing 2017; 20:74-75. http://dx.doi.org/10.1136/eb-2017-102699
11. Morse J M. Principle of mixed methods and multimethod research design. In: Tashakkori, A and Teddlie, C eds. Handbook of Mixed Methods in Social & Behavioural Research. SAGE. 2003:189-208.
12. UKHSA. Health Matters: Preventing STIs [blog]. 2019 [accessed 14 Feb 2022]. Available from: https://ukhsa.blog.gov.uk/2019/08/21/health-matters-preventing-stis/]
13. NHS. Overview: Gonorrhoea. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/gonorrhoea
14. British Association for Sexual Health and HIV (BASHH). UK national guideline for the management of infection with Neisseria gonorrhoeae. 2018 (accessed 14 Feb 2022). Available from: https://www.bashhguidelines.org/current-guidelines/urethritis-and-cervicitis/gonorrhoea-2018/
15. Public Health Wales. Sexual Health Wales: Postal testing pilot. 2022. Available from: https://www.friskywales.org/chlamydia-and-gonorrhoea-home-testing-pilot.html
16. Public Health Wales. Sexual Health in Wales Surveillance Scheme (SWS) Quarterly Report. July 2019 (accessed 14 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/sexual-health-reports/sexual-health-in-wales-surveillance-scheme-quarterly-report-july-2019/
17. Public Health Wales. SWS Quarterly Report: Data to end March 2018. August 2018 (accessed 14 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/sexual-health-reports/aug2018
18. Public Health Wales. SWS Quarterly Report: Data to end June 2018. October 2018 (accessed 14 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/sexual-health-reports/oct2018/
19. Public Health Wales. SWS Quarterly Report: Data to end September 2018. January 2019 (accessed 14 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/sexual-health-reports/jan2019
20. Public Health Wales. SWS Quarterly Report: Data to end December 2018. April 2019 (accessed 14 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/sexual-health-reports/april-2019/
21. UKHSA. Antimicrobial resistance in Neisseria gonorrhoeae in England and Wales. 2021 (accessed 14 Feb 2022). Available from: https://assets.publishing.service.gov.uk/GRASP_2020_Report.pdf
22. NHS. Overview: Chlamydia. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/chlamydia/
23. BASHH. BASHH Guidelines for Chlamydia. 2015 (accessed 14 Feb 2022). Available from: https://www.bashhguidelines.org/current-guidelines/urethritis-and-cervicitis/chlamydia-2015/
24. Public Health Wales. About Chlamydia. (Accessed 14 Feb 2022). Available from: https://www.friskywales.org/about-chlamydia.html

25. NHS. Overview: Syphilis. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/syphilis/
26. BASHH. BASHH Guidelines Syphilis. 2015 (accessed 14 Feb 2022). Available from: https://www.bashhguidelines.org/current-guidelines/genital-ulceration/syphilis-2015/
27. Public Health Wales. About Syphilis. (Accessed 14 Feb 2022). Available from: https://www.friskywales.org/about-syphilis.html
28. NHS. Overview: HIV and AIDS. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/hiv-and-aids/
29. Public Health Wales. About HIV. (Accessed 14 Feb 2022). Available from: https://www.friskywales.org/about-hiv.html
30. Welsh Government. Programme for Government – update. 2021 (accessed 15 Feb 2022). Available from: https://gov.wales/files/publications/2022-01/programme-for-government-update-december-2021.pdf
31. Fast Track Cardiff and Vale. HIV action plan for Wales. 2022 (accessed 15 Feb 2022). Available from: https://fasttrackcardiff.wales/hiv-action-plan-for-wales/
32. Public Health Wales. About Genital Warts. (Accessed 14 Feb 2022). Available from: https://www.friskywales.org/about-genital-warts.html
33. NHS. Overview: Genital warts. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/genital-warts/
34. Public Health Wales. About Herpes. (Accessed 14 Feb 2022). Available from: https://www.friskywales.org/about-herpes.html
35. NHS. Overview: Genital Herpes. 2021 (accessed 14 Feb 2022). Available from: https://www.nhs.uk/conditions/genital-herpes/
36. Public Health Wales. About Hepatitis B. (Accessed 14 Apr 2022). Available from: https://www.friskywales.org/about-hepatitis-b.html
37. NHS. Overview: Hepatitis B. 2021 (accessed 14 Apr 2022). Accessed from: https://www.nhs.uk/conditions/hepatitis-b/
38. Public Health Wales. About Hepatitis C. (Accessed 14 Apr 2022). Available from: https://www.friskywales.org/about-hepatitis-c.html
39. NHS. Overview: Hepatitis C. 2021 (accessed 14 Apr 2022). Accessed from: https://www.nhs.uk/conditions/hepatitis-c/
40. Terrence Higgins Trust. LGV (lymphogranuloma venereum). 2022 (accessed 14 Feb 2022). Available from: https://www.tht.org.uk/hiv-and-sexual-health/sexual-health/stis/lgv-lymphogranuloma
41. NHS. Lymphogranuloma Venereum (LGV). 2022 (accessed 14 Feb 2022). Available from: https://www.nhsinform.scot/illnesses-and-conditions/sexual-and-reproductive/lgv

42. IUSTI. Mycoplasma - Patient information leaflet. 2017 [accessed 14 Feb 2022]. Available from: https://bcuhb.nhs.wales/links/external-links/mycoplasma-iusti/
43. Spiller OB, Rees CL, Morris DJ, Davies RL, Jones LC. Mycoplasma genitalium prevalence in Welsh sexual health patients: Low antimicrobial resistance markers and no association of symptoms to bacterial load. Microb Pathog. 2020. DOI:10.1016/j.micpath.2019.103872
44. CAVUHB. Sexually transmitted infection (STI). [Accessed: 14 Feb 2022]. Available from: https://cavuhb.nhs.wales/our-services/sexual-health/services-provided/sti/
45. UKHSA. Rise in extremely drug resistant Shigella in gay and bisexual men [press release]. 2022 [accessed 14 Feb 2022]. Available from: https://www.gov.uk/government/news/rise-in-shigella
46. BCUHB. STI. [Accessed 14 Feb 2022]. Available from: https://cavuhb.nhs.wales/our-services/sexual-health/services-provided/sexually-transmitted-infection-sti/
47. World Health Organisation (WHO). Antimicrobial Resistance. 2021 (accessed 17 Feb 2022). Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
48. REACT Group. The discovery of antibiotics. (Accessed 17 Feb 2022). Available from: https://www.reactgroup.org/antibiotic-resistance/
49. Medina E., & Pieper, DH. The antibiotic resistance crisis: part 1: causes and threats. Current Topics in Microbiology and Immunology, 2016, 398: 3–33 DOI:10.1007/82_2016_492
50. Strasfeld L, Chou S. Antiviral drug resistance: mechanisms and clinical implications. Infect Dis Clin North Am. 2010;24(2):413-437. DOI: 10.1016/j.idc.2010.01.001
51. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book. Elsevier Health Sciences; 2019. Available from: https://www.sciencedirect.com/book/9781455748013/mandell-douglas-and-bennetts-principles-and-practice-of-infectious-diseases
52. Michael CA, Dominey-Howes D, Labbate M. The antibiotic resistance crisis: causes, consequences, and management. Front Public Health 2014;2:145 DOI: 10.3389/fpubh.2014.00145
53. Public Health England. Research reveals levels of inappropriate prescriptions in England [press release]. 2018 (accessed 1 Mar 2022). Available from: https://www.gov.uk/government/news/research-reveals-levels-of-inappropriate-prescriptions-in-england
54. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014;5(6):229-241. doi:10.1177/2042098614554919
55. WHO. Antibiotic resistance. 2022 (accessed 14 Feb 2022). Available from: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance
56. Bartlett JG, Gilbert DN, Spellberg B. Seven ways to preserve the miracle of antibiotics. Clin Infect Dis, 2013;56(10):1445-50. DOI: 10.1093/cid/cit070

57. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. 2016. London: Review on Antimicrobial Resistance. Available from: https://amr-review.org/sites/default/files/.pdf
58. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, Han C, Bisignano C, Rao P, Wool E, Johnson SC. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022; 399, 629-655. DOI: https://doi.org/10.1016/S0140-6736(21)02724-0
59. Suay-García B, Pérez-Gracia MT. Drug-resistant Neisseria gonorrhoeae: latest developments. Eur J Clin Microbiol Infect Dis. 2017 Jul;36(7):1065-1071. https://doi.org/10.1007/s10096-017-2931-x
60. CDC. Latest data on antibiotic resistant gonorrhoea. 2016 [accessed 14 Apr]. Available from: https://www.cdc.gov/nchhstp/newsroom/2016/data-on-antibiotic-resistant-gonorrhea.html
61. UKHSA. More cases of antibiotic resistant gonorrhoea identified in England [press release]. 2022 [accessed 14 Feb 2022]. Available from: https://www.gov.uk/government/news/amr
62. Tien V, Punjabi C, Holubar MK. Antimicrobial resistance in sexually transmitted infections. J Travel Med. 2020 Feb 3;27(1):taz101. DOI: 10.1093/jtm/taz101
63. Sandoz KM, Rockey DD. Antibiotic resistance in Chlamydiae. Future Microbiol. 2010 Sep;5(9):1427-42. https://doi.org/10.2217/fmb.10.96
64. Abraham S, Juel HB, Bang Pet al. Safety and immunogenicity of the chlamydia vaccine candidate CTH522 adjuvanted with CAF01liposomes or aluminium hydroxide: a first-in-human, randomised, double-blind, placebo-controlled, phase 1 trial. Lancet Infect Dis2019;19:1091–1100. DOI: 10.1016/S1473-3099(19)30279-8
65. WHO. HIV drug resistance. 2021 [accessed 14 Apr 2022]. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-drug-resistance.
66. National Institute of Health. Experimental mRNA HIV vaccine safe, shows promise in animals (press release). 2021 [accessed 14 Apr 2022]. Available from: https://www.nih.gov/news-events/news-releases/experimental-mrna-hiv-vaccine-safe-shows-promise-animals
67. UKHSA. Antiviral Unit. 2020 [accessed 14 Apr 2022]. Available from: https://www.gov.uk/guidance/antiviral-unit-avu-reference-services
68. Bacon TH, Levin MJ, Leary JJ, Sarisky RT, Sutton D. Herpes simplex virus resistance to acyclovir and penciclovir after two decades of antiviral therapy. Clin Microbiol Rev. 2003 Jan;16(1):114-28. DOI: 10.1128/CMR.16.1.114-128.2003
69. Zoulim F, Locarnini S: Hepatitis B virus resistance to nucleos(t)ide analogues. Gastroenterology, 2009; 137:1593–1608. DOI: 10.1053/j.gastro.2009.08.063
70. Wyles DL, Luetkemeyer AF. Understanding Hepatitis C Virus Drug Resistance: Clinical Implications for Current and Future Regimens. Top Antivir Med. 2017 Jul/Aug;25(3):103-109. PMCID: PMC5935211

71. Russell CD, Fairfield CJ, Drake TM, Turtle L, Seaton RA, Wootton DG, Sigfrid L, Harrison EM, Docherty AB, de Silva TI, Egan C. Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study. The Lancet Microbe. 2021 Aug 1;2(8):e354-65. DOI: 10.1016/S2666-5247(21)00090-2
72. Langford BJ, So M, Raybardhan S, Leung V, Soucy JP, Westwood D, Daneman N, MacFadden DR. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clinical microbiology and infection. 2021 Apr 1;27(4):520-31. DOI: 10.1016/j.cmi.2020.12.018
73. Rawson TM, Moore LSP, Castro-Sanchez E, Charani E, Davies F, Satta G, et al. COVID-19 and the potential long-term impact on antimicrobial resistance. J Antimicrob Chemother 2020;75:1681e4. https://doi.org/10.1016/j.cmi.2020.04.024.
74. Huttner B, Catho G, Pano-Pardo JR, Pulcini C, Schouten J. COVID-19: don't neglect antimicrobial stewardship principles! Clin Microbiol Infect 2020;26:808e10. DOI: 10.1016/j.cmi.2020.04.024
75. Gilead Sciences, Inc. U.S. Food and Drug Administration Approves Gilead's Truvada® for Reducing the Risk of Acquiring HIV. (Press Release) 2012 (accessed 22 Jul 2021). Available from: https://www.gilead.com/news-and-press/press-room/press-releases/2012/PREP
76. Centre for Disease Control and Prevention (CDC). HIV PrEP (Pre-exposure Prophylaxis). 2021 (accessed 22 July 2021). Available from: https://www.cdc.gov/hiv/basics/prep.html
77. Welsh Government. Funding for a study into the availability of pre-exposure prophylaxis (Truvada®) to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. (Written statement). 2017 (accessed 11 Feb 2022). Available from: http://gov.wales/about/cabinet/2017/truvada/?lang=en
78. Waverly Care. PrEP in Scotland - Two Years on the NHS. Available from: https://www.waverleycare.org/news/prep-scotland-two-years-nhs
79. NHS. PrEP trial updates. 2020 (accessed 11 Feb 2022) Available from: https://www.england.nhs.uk/commissioning/npc-crg/blood-and-infection-group-f/
80. Transgender NI. Accessing PrEP in Northern Ireland. 2022 (accessed 11 Feb 2022) Available from: https://transgenderni.org.uk/prep-service-ni/
81. Terrence Higgins Trust. IWantPrEPNow – What is PrEP? 2022 (accessed 11 Feb 2022). Available from: https://www.iwantprepnow.co.uk/
82. Egan, J. E., Ho, K., Stall, R., Drucker, M. T., … & Mayer, K. H. (2020). Feasibility of Short-Term PrEP Uptake for Men Who Have Sex with Men with Episodic Periods of Increased HIV Risk. Journal of Acquired Immune Deficiency Syndromes, 84(5), 508–513. https://doi.org/10.1097/QAI.0000000000002382
83. CDC. PrEP effectiveness. 2021 (accessed 14 Apr 2022). Available from: https://www.cdc.gov/hiv/basics/prep/prep-effectiveness.html

84. HIV Expert Group. Pre-Exposure Prophylaxis for HIV-Operational Guide. Public Health Wales. 2017.
85. Welsh Government. Availability of Pre-Exposure Prophylaxis (PrEP) to prevent HIV (written statement). 2020 (accessed 11 Feb 2022). Available from: https://gov.wales/statement-availability-PREP
86. Public Health Wales. PrEPARED in Wales. 2021 (accessed 11 Feb 2022). Available from: https://www.friskywales.org/wales-prep-project.html
87. Public Health Wales. Pre-exposure prophylaxis for HIV provision in Wales. 2019 (accessed from 11 Feb 2022). Available from: https://phw.nhs.wales/topics/sexual-health/prep-in-wales-2017-2019/
88. Gillespie, D, Wood, F, Williams, A, et al. Experiences of men who have sex with men when initiating, implementing, and persisting with HIV pre-exposure prophylaxis. Health Expect, 2022; 1-10 DOI: 10.1111/hex.13446
89. Sullivan A, for the IMPACT study group. HIV and STI incidence among MSM users and non-users of HIV PrEP in England: results from the IMPACT trial. 18th European AIDS Conference, London, poster discussion, abstract number BPD2/7, 2021. Available from: https://eacs2021.abstractserver.com/program/details/presentations/381
90. Inouye, J. Risk Perception: Theories, Strategies, And Next Steps. 2014. Campbell Institute.
91. Hogben M, Liddon N. Disinhibition, and risk compensation: scope, definitions, and perspective. Sex Transm Dis. 2008;35(12):1009–10. DOI: 10.1097/OLQ.0b013e31818eb752
92. Luckman A, Zeitoun H, Isoni A, Loomes G, Vlaev I, Powdthavee N, Read D. Risk compensation during COVID-19: The impact of face mask usage on social distancing. J Exp Psychol Appl. 2021 Dec;27(4):722-738. DOI: 10.1037/xap0000382
93. Powell, V. E., Gibas, K. M., DuBow, J., & Krakower, D. S. Update on HIV Preexposure Prophylaxis: Effectiveness, Drug Resistance, and Risk Compensation. Current Infectious Disease Reports, 2019;21(8). https://doi.org/10.1007/s11908-019-0685-6
94. Calabrese SK, Magnus M, Mayer KH, Krakower DS, Eldahan AI, Hawkins LAG, et al. "Support Your Client at the Space That They're in": HIV pre-exposure prophylaxis (PrEP) prescribers' perspectives on PrEP-related risk compensation. AIDS. 2017;31(4):196–204. https://doi.org/10.1089/apc.2017.0002
95. Traeger, M. W., Schroeder, S. E., Wright, E. J., Hellard, M. E., Cornelisse, V. J., Doyle, J. S., & Stoové, M. A. Effects of Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection on Sexual Risk Behavior in Men Who Have Sex with Men: A Systematic Review and Meta-analysis. Clinical Infectious Diseases, 2018; 67(5): 676–686. https://doi.org/10.1093/cid/ciy182
96. Chen YH, Snowden JM, McFarland W, Raymond HF. Pre-exposure Prophylaxis (PrEP) Use, Seroadaptation, and Sexual Behavior Among Men Who Have Sex with Men, San Francisco, 2004-2014. AIDS Behav. 2016 Dec;20(12):2791-2797. DOI: 10.1007/s10461-016-1357-2

97. Holt M, Murphy DA. Individual Versus Community-Level Risk Compensation Following Preexposure Prophylaxis of HIV. Am J Public Health. 2017;107(10):1568-1571. DOI: 10.2105/AJPH.2017.303930
98. Thomas R, Galanakis C, Vezina S, et al. PrEP in Montreal :Good adherence, no seroconversion, and no evidence of risk compensation. J Sex Med 2016. DOI: https://doi.org/10.1016/j.jsxm.2016.03.217
99. Doblecki-Lewis, S., Cohen, S., & Liu, A. Clinical Treatment Options Infectious Diseases: Update on PrEP Implementation, Adherence, and Advances in Delivery. Current Treatment Options in Infectious Diseases, 2015; 7(2):101–112. https://doi.org/10.1007/s40506-015-0046-4
100. Cembalo, L., Cicia, G. and Verneau, F. How to improve risk perception evaluation in food safety: A psychometric approach. International European Forum on System Dynamics and Innovation in Food Networks. 2009; 423-433. https://api.semanticscholar.org/CorpusID:53967603
101. Adams J. Risk, 1996, UCL Press Limited, UK: London.
102. Lal, L., Audsley, J., Murphy, D. A., Fairley, C. K., … Willcox, J. Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. Aids, 2017;31(12), 1709–1714. https://doi.org/10.1097/QAD.0000000000001519
103. Serpa, J. A., Huynh, G. N., Nickell, J. B., & Miao, H. Human Immunodeficiency Virus Pre-exposure Prophylaxis and Increased Incidence of Sexually Transmitted Infections in the United States. Clinical Infectious Diseases, 2020, 70(9), 1884–1890. https://doi.org/10.1093/cid/ciz552
104. Traeger, M. W., Cornelisse, V. J., Asselin, J., Price, B., … Wright, E. J. Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection. JAMA, 2019; 321(14), 1380–1390. https://doi.org/10.1001/jama.2019.2947
105. Green, J., and Thorogood, N. 2018. *Qualitative methods for health research*. 4th ed. LA, CA: SAGE.
106. Mason, J. Qualitative researching, 2002 2nd ed. London: SAGE.
107. Jones, M., Verity, F., Warin, M., Ratcliffe, J., Cobiac, L., Swinburn, B., & Cargo, M. OPALesence: Epistemological pluralism in the evaluation of a systems-wide childhood obesity prevention program. *Evaluation*, 2016, 22(1), pp. 29-48. https://doi.org/10.1177/1356389015623142
108. Lewin, S., Glenton, C. Are we entering a new era for qualitative research? Using qualitative evidence to support guidance and guideline development by the World Health Organization. *Int J Equity Health,* 2018, 17(126). https://doi.org/10.1186/s12939-018-0841-x
109. Wood, F. 2021. Doing qualitative health services research remotely: A rejoinder to 'Collecting qualitative data during a pandemic' by David Silverman. Communication and Medicine. DOI: https://doi.org/10.1558/cam.19749
110. King, N., Horrocks, C., and Brooks J. 2019. *Interviews in qualitative research*. 2nd ed. London, Sage

111. Miller, R.J. and Gibson, A.M. Supervision by videoconference with rural probationary psychologists. *IJISME* 2004, 11, pp.22-28. Available at: https://openjournals.library.sydney.edu.au/index.php/CAL/article/view/6065

112. Creswell, J. 2014. *Research design (international student edition).* Los Angeles: Sage

113. Baltar, F and Brunet, I. Social research 2.0: virtual snowball sampling method using Facebook. *Internet Research,* 2012; 22, pp: 57-74. https://www.emerald.com/insight/content/doi/10.1108/10662241211199960/full/html

114. Braun, V and Clarke, V. Using thematic analysis in psychology, *Qualitative Research in Psychology*, 2006; 3(2), pp: 77-101, https://doi.org/10.1191/1478088706qp063oa

115. Braun V., Clarke V., Hayfield N., Terry G. 2019. Thematic Analysis. In: Liamputtong P. (eds) *Handbook of Research Methods in Health Social Sciences.* Springer, Singapore. https://doi.org/10.1007/978-981

116. Braun, V and Clarke, V. 2021 One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qualitative Research in Psychology, 18:3, 328-352, https://doi.org/10.1080/14780887.2020.1769238

117. O'Connor C, Joffe H. Intercoder Reliability in Qualitative Research: Debates and Practical Guidelines. International Journal of Qualitative Methods. 2020. https://doi.org/10.1177/1609406919899220

118. Clarke, V. and Braun, V. Successful qualitative research: A practical guide for beginners. 2013. London: Sage.

119. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. *Qualitative Health Research.* 2016; 26(13):1753-1760. DOI: 10.1177/1049732315617444

120. Llewelyn M J, Fitzpatrick J M, Darwin E, et al. The antibiotic course has had its day BMJ 2017; 358 :j3418 DOI: 10.1136/bmj.j3418

121. Hunt, A. ''Risk and moralization in everyday life'', in Ericson, R.V. and Doyle, A. (Eds), Risk and Morality, University of Toronto Press, Toronto, 2003; 165-92. Available from: http://dx.doi.org/10.3138/9781442679382-010

122. Zhao, J., Song, F., Ren, S., … Sun, Y. Predictors of condom use behaviours based on the Health Belief Model among female sex workers: a cross-sectional study in Hubei Province, China. *PloS one,* 2012; 7(11). DOI: 10.1371/journal.pone.0049542

123. Champion VL, & Skinner CS. The health belief model. Health behaviour and health education: Theory, research, and practice 4. 2008. Available from: https://psycnet.apa.org/record/2008-17146-003

124. Stoutenborough JW, Vedlitz A, Liu X. The Influence of Specific Risk Perceptions on Public Policy Support: An Examination of Energy Policy. *The ANNALS of the American Academy of Political and Social Science*. 2015;658(1):102-120. https://doi.org/10.1177/0002716214556472

125. Elkington KS, Hackler D, Walsh TA, et al. Perceived Mental Illness Stigma, Intimate Relationships, and Sexual Risk Behavior in Youth with Mental Illness. Journal of Adolescent Research. 2013;28(3):378-404. DOI: 10.1177/0743558412467686

126. Rendina, H.J., Gamarel, K.E., Pachankis, J.E. et al. Extending the Minority Stress Model to Incorporate HIV-Positive Gay and Bisexual Men's Experiences: A Longitudinal Examination of Mental Health and Sexual Risk Behavior. Ann behav med. 2017;51,147–158. https://doi-org.abc.cardiff.ac.uk/10.1007/s12160-016-9822-8

127. Pachankis JE, Rendina HJ, Restar A, Ventuneac A, Grov C, Parsons, JT. A minority stress-emotion regulation model of sexual compulsivity among highly sexually active gay and bisexual men. Health Psychol. 2015;34(8):829–840. https://psycnet.apa.org/doi/10.1037/hea0000180

128. Lundberg, Patric et al. "Poor mental health and sexual risk behaviours in Uganda: a cross-sectional population-based study." *BMC public health* vol. 11 125. 21 Feb. 2011, doi:10.1186/1471-2458-11-125

129. Stonewall. LGBT in Britain: Health report. 2018 [accessed 10 Dec 2020]. Available from: https://www.stonewall.org.uk/lgbt-britain-health

130. Williams A. Health inequalities among LGBTQ+ communities. The British Student Doctor Journal. 2021;5(2):88–94. DOI: http://doi.org/10.18573/bsdj.267

131. Baele, J., Dusseldorp, E., & Maes, S. Condom use self-efficacy: effect on intended and actual condom use in adolescents, Journal of Adolescent Health. 2001, 28(5): 421-431. DOI: 10.1016/s1054-139x(00)00215-9

132. Tarkang, E. Factors Influencing Consistent Condom Use among Secondary School Male Students in Limbe Urban City, Cameroon. Journal of Scientific Research and Reports, 2015; 4(2), 101-113. DOI: 10.9734/JSRR/2015/11334

133. Vieux, CR. The role of health belief model constructs in condom use among early young adults. Electronic Theses, Projects, and Dissertations. 2017; 604. https://scholarworks.lib.csusb.edu/etd/604

134. Paz-Bailey, Gabriela; Mendoza, ET AL. Trends in condom use among MSM in the United States, AIDS, 2016; 30(12) p1985-1990 DOI: 10.1097/QAD.0000000000001139

135. Sidebottom, D., Ekström, A.M. & Strömdahl, S. A systematic review of adherence to oral pre-exposure prophylaxis for HIV – how can we improve uptake and adherence? BMC Infect Dis 18, 581 (2018). https://doi.org/10.1186/s12879-018-3463-4

136. Kellstedt PM, Zahran S, Vedlitz A. Personal efficacy, the information environment, and attitudes toward global warming and climate change in the United States. Risk Analysis: An International Journal. 2008;28(1):113-26. https://doi.org/10.1111/j.1539-6924.2008.01010.x

137. Corrigan P, Michaels PJ, Morris S. Do the effects of antistigma programs persist over time? Findings from a meta-analysis. Psychiatr Serv. 2015 1;66(5):543-6. DOI: 10.1176/appi.ps.201400291

138. Griffiths KM, Carron-Arthur B, Parsons A, Reid R. Effectiveness of programs for reducing the stigma associated with mental disorders. A meta-analysis of randomized controlled trials. World Psychiatry. 2014;13(2):161-75. DOI: 10.1002/wps.20129

139. Tsai, AC., & Venkataramani, AS. The causal effect of education on HIV stigma in Uganda: Evidence from a natural experiment. Social science & medicine, 2015;142, 37–46. https://doi.org/10.1016/j.socscimed.2015.08.009

140. Hendry, A, Snowden, A, Brown, M. When holistic care is not holistic enough: The role of sexual health in mental health settings. J Clin Nurs. 2018; 27: 1015– 1027. https://doi.org/10.1111/jocn.14085

141. Rachel Jewkes, R., & Dunkle, K. Drivers of ethnic disparities in sexual health in the UK. 2017; 2:10, p441-442, DOI: https://doi.org/10.1016/S2468-2667(17)30182-2

142. Sullivan PS, Khosropour CM, Luisi N, Amsden M, Coggia T, Wingood GM, DiClemente RJ. Bias in online recruitment and retention of racial and ethnic minority men who have sex with men. J Med Internet Res. 2011, 13(2):38. DOI: 10.2196/jmir.1797

143. Galdas, P. Revisiting Bias in Qualitative Research: Reflections on Its Relationship with Funding and Impact. International Journal of Qualitative Methods, 2017; 16(1). https://doi.org/10.1177/1609406917748992

144. Public Health Wales. Sexual Health in Wales Surveillance scheme: SWSv2. 2018, accessed 31 Aug 2022. Available from: http://www.wales.nhs.uk/sites3/Documents/457/SWS Guidance for clinic staff.pdf

145. European Committee on Antimicrobial Susceptibility Testing (EUCAST). Breakpoint tables for interpretation of MICs and zone diameters, Version 10.0 2020. Available from: https://eucast.org/clinical_breakpoints

146. Williams A, Nichols J, Couzens Z, et al P125 The journey of postal testing for HIV and sexually transmitted infections in Wales. Sexually Transmitted Infections 2022;98:A82-A83. DOI: http://dx.doi.org/10.1136/2022.170

147. Public Health Wales Health Protection Division (2023). Sexual Health in Wales: Sexually Transmitted Infections, Emergency and Long-Acting Reversible Contraception provision and Termination of Pregnancy - Annual report 2023. Cardiff, Public Health Wales

148. Tableau. Time Series Analysis: Definition, Types, Techniques, and When It's Used. 2023. [Article]. Available from: https://www.tableau.com/learn/articles/time-series-analysis

149. edX. Policy Analysis Using Interrupted Time Series. 2023. Available from: https://learning.edx.org/course

150. Devkaran and O'Farrell. The impact of hospital accreditation on quality measures: an interrupted time series analysis. BMC Health Serv Res 15, 137 (2015). https://doi.org/10.1186/s12913-015-0784-5

151. Durbin, J. & Watson, GS. Testing for serial correlation in least-squares regression, I, Biometrika 1950;37,409-428. https://doi.org/10.2307/2332391

152. Frost, J. Autocorrelation and Partial Autocorrelation in Time Series Data, Statistics by Jim, 2023. Available from: https://statisticsbyjim.com/time-series/autocorrelation-partial-autocorrelation/

153. IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp

154. RStudio Team. RStudio: Integrated Development for R. RStudio, 2020. Available from: http://www.rstudio.com/

155. Microsoft Corporation. Microsoft Excel. 2020. Available from: https://office.microsoft.com/excel

156. Apers, L., Vanhamel, J., Caluwaerts, S., Platteau, T., Kenyon, C., & Florence, E. Impact of PrEP on a STI clinic in a Belgian context: a provider's perspective, Acta Clinica Belgica, 2021:76:6,477-481, DOI: 10.1080/17843286.2020.1767995

157. Public Health Scotland. Gonococcal antibiotic surveillance in Scotland (GASS): prevalence, patterns and trends. 2019. Available from: https://publichealthscotland.scot/publications/gass

158. Senedd Research. Coronavirus timeline: Welsh and UK governments' response. May 2021 [accessed June 2021]. Available: https://research.senedd.wales/research-articles/coronavirus-timeline

159. British Association for Sexual Health and HIV (BASHH). Sex, Social Distancing and COVID-19, March 2020 [accessed June 2021]. Available: https://members.bashh.org/Documents/COVID-19.pdf

160. Hyndman I, Nugent D, Whitlock GG, et al. COVID-19 restrictions and changing sexual behaviours in HIV-negative MSM at high risk of HIV infection in London, UK. STI BMJ, 2021. DOI: 10.1136/sextrans-2020-054768

161. Gillespie D, Knapper C, Hughes D, et al. Early impact of COVID-19 social distancing measures on reported sexual behaviour of HIV pre-exposure prophylaxis users in Wales. STI BMJ, 2021; 97:85-87. DOI: 10.1136/sextrans-2020-054598

162. Hammoud MA, Maher L, Holt M, et al. Physical Distancing Due to COVID-19 Disrupts Sexual Behaviors Among Gay and Bisexual Men in Australia: Implications for Trends in HIV and Other Sexually Transmissible Infections, JAIDS, 2020; 85(3): 309-315 DOI: 10.1097/QAI.0000000000002462

163. Sheppard V. Research Methods for the Social Sciences: An Introduction. Vancouver: BC. 2020.

164. Fincham JE. Response rates and responsiveness for surveys, standards, and the Journal. Am J Pharm Educ. 2008 Apr 15;72(2):43. DOI: 10.5688/aj720243.

165. Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010;341:c4587. doi: https://doi.org/10.1136/bmj.c4587

166. Kyngäs, H. Inductive Content Analysis. In: Kyngäs, H., Mikkonen, K., Kääriäinen, M. (eds) The Application of Content Analysis in Nursing Science Research. 2020. Springer, Cham. https://doi.org/10.1007/978-3-030-30199

167. de Sousa, A.F.L.;de Oliveira, L.B.; Queiroz, A.A.F.L.N.;de Carvalho, H.E.F.; Schneider, G.;Camargo, E.L.S.; de Araújo, T.M.E.;Brignol, S.; Mendes, I.A.C.; Fronteira,I.; et al. Casual Sex among Men Who Have Sex with Men (MSM) during the Period of Sheltering in Place to Prevent the Spread of COVID-19.Int.J. Environ. Res. Public Health2021,18,3266 https://doi.org/10.3390/ijerph18063266

168. Shilo G, Mor Z. COVID-19and the Changes in the Sexual Behavior of Men Who Have Sex With Men: Results of an Online Survey. J Sex Med 2020; 17:1827-1834. https://doi.org/10.1016/j.jsxm.2020.07.085

169. Ariely, D. and Loewenstein, G. (2006), The heat of the moment: the effect of sexual arousal on sexual decision making. Journal of Behavioral Decision Making, 19: 87–98. https://psycnet.apa.org/doi/10.1002/bdm.501

170. Ousseine YM, Allaire C, Ringa V, Lydie N, Velter A. Health Literacy as a Mediator of the Relationship Between Socioeconomic Position and Pre-Exposure Prophylaxis Uptake Among Men Who Have Sex with Men Living in France. Health Lit Res Pract. 2023 Jan;7(1):61-70. DOI: 10.3928/24748307-20230224-01

171. Williams, A. All-Wales postal testing evaluation. Public Health Wales. 2020 [accessed June 2021]. Available from: https://fasttrackcardiff.files.wordpress.com/2021/06/postal-testing-report.pdf

172. World Health Organisation. Accelerating the global Sexually Transmitted Infections response: report on the first informal Think-Tank meeting. June 2020 [accessed June 2021]. Available from: https://www.who.int/publications/i/item/9789240022591

173. UKHSA. Mpox (monkeypox) outbreak: epidemiological overview. 2023 Available from: https://www.gov.uk/government/publications/monkeypox-outbreak

174. PHW. Sexual Health in Wales; Annual report, 2023. Available from: https://phw.nhs.wales/publications/sexual-health-annual-report-2023

175. UKHSA. Sexually transmitted infections (STIs): annual data tables. 2023. Available from: https://www.gov.uk/government/statistics/stis-annual-data-tables

176. Swaen, B. & George, T. 2022. What Is a Conceptual Framework? Tips & Examples. Scribbr. Available from https://www.scribbr.co.uk/research-methods/conceptual-frameworks/

177. Varpio, L., Paradis, E., Uijtdehaage, S., Young, M. The Distinctions Between Theory, Theoretical Framework, and Conceptual Framework. Academic Medicine 2020, 95(7):p 989-994, DOI: 10.1097/ACM.0000000000003075

178. Ferguson, K.D. et al. 2020. Evidence synthesis for constructing directed acyclic graphs (ESC-DAGs): a novel and systematic method for building directed acyclic graphs. International journal of epidemiology 49(1),322–329. https://doi.org/10.1093/ije/dyz150

179. Tennant P, Textor J, Gilthorpe M, et al. Dagitty and directed acyclic graphs in observational research: a critical review. J Epidemiol Community Health 2017; 71. http://dx.doi.org/10.1136/jech-2017-SSMAbstracts.86

180. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology 1999; 10:37–48. https://pubmed.ncbi.nlm.nih.gov/9888278/

181. Krieger, N., & Smith, G.D. The tale wagged by the DAG: Broadening the scope of causal inference and explanation for epidemiology. International Journal of Epidemiology, 206; 45(6),1787–1808. https://doi.org/10.1093/ije/dyw114

182. Morgan SL, Winship C. Counterfactuals and Causal Inference.2nd ed. Cambridge University Press, 2015.

183. Textor J, van der Zander B, Gilthorpe MS, Liśkiewicz M, Ellison GT. "Robust causal inference using directed acyclic graphs: the R package 'dagitty'." International Journal of Epidemiology, 2016; 45(6), 1887–1894. doi:10.1093/ije/dyw341.

184. Quaife M, MacGregor L, Ong JJ, et al. Risk compensation and STI incidence in PrEP programmes. Lancet HIV. 2020; 7(4):222-223. DOI:10.1016/S2352-3018(19)30333-9

185. Brenner PS, DeLamater J. Lies, Damned Lies, and Survey Self-Reports? Identity as a Cause of Measurement Bias. Soc Psychol Q. 2016; 79(4):333-354. https://doi.org/10.1177/0190272516628298

186. Demetriou, C., Ozer, BU., & Essau, CA. Self-Report Questionnaires. Encyclopedia of Clinical Psychology. 2015 https://doi.org/10.1002/9781118625392.wbecp507

187. Parry, D.A., Davidson, B.I., Sewall, C.J.R. et al. A systematic review and meta-analysis of discrepancies between logged and self-reported digital media use. Nat Hum Behav. 2021; 5,1535–1547. https://doi.org/10.1038/s41562-021-01117-5

188. Rao A, Tobin K, Davey-Rothwell M, Latkin CA. Social Desirability Bias and Prevalence of Sexual HIV Risk Behaviors Among People Who Use Drugs in Baltimore, Maryland: Implications for Identifying Individuals Prone to Underreporting Sexual Risk Behaviors. AIDS Behav. 2017; 21(7):2207-2214. DOI:10.1007/s10461-017-1792-8

189. Gillespie D, Couzens Z, de Bruin M, et al. PrEP Use, Sexual Behaviour, and PrEP Adherence Among Men who have Sex with Men Living in Wales Prior to and During the COVID-19 Pandemic. AIDS Behav. 2022; 26(8):2746-2757. DOI: 10.1007/s10461-022-03618-4

190. Coyer, L., Van Bilsen, W., Bil, J., et al. Pre-exposure prophylaxis among men who have sex with men in the Amsterdam Cohort Studies: Use, eligibility, and intention to use. PLoS ONE, 2018. 13(10), 1–10. https://doi.org/10.1371/journal.pone.0205663

191. Freeborn, K., Portillo, CJ., Martinez, JE., & Jonas, KJ. Pre-exposure prophylaxis sorting among men who have sex with men. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV, 2019;31(3), 3254–3265. https://doi.org/10.1111/jocn.13990

192. Sagaon-Teyssier, L., Suzan-Monti, M., Demoulin, B., et al. Uptake of PrEP and condom and sexual risk behavior among MSM during the ANRS IPERGAY trial. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV, 2016, 28, 48–55. https://doi.org/10.1080/09540121.2016.1146653

193. Rogstad KE. Sex, sun, sea, and STIs: sexually transmitted infections acquired on holiday. BMJ. 2004 Jul 24;329(7459):214-7. DOI: 10.1136/bmj.329.7459.214

194. Storholm, E.D., Fisher, D.G., Reynolds, G.L. et al. Hepatitis Vaccination of Men Who Have Sex with Men at Gay Pride Events. Prev Sci, 2010; 11, 219–227 https://10.1007/s11121-009-0164-7

195. Mdodo R, Thomas PE, Walker A, et al. Rapid HIV testing at gay pride events to reach previously untested MSM: U.S., 2009-2010. Public Health Rep. 2014; 129(4):328-34. DOI:10.1177/003335491412900407

196. Shuper, P. A., MacLachlan, D. J., Joharchi, N., Guimond, T. H., Maxwell, J., & Adam, B. D. (2018). HIV Risk and Protective Factors in the Context of Alcohol and Substance Use During Pride. AIDS and Behavior, 22, 2797–2806. https://doi.org/10.1007/s10461-018-2117-2

197. Fichtenberg CM, Muth SQ, Brown B, et al. Sexual network position and risk of sexually transmitted infections. STI, 2009; 85:493-498. http://dx.doi.org.abc.cardiff.ac.uk/10.1136/sti.2009.036681

198. Woods WJ, Binson D, Pollack LM, Wohlfeiler D, Stall RD, Catania JA. Public policy regulating private and public space in gay bathhouses. J Acquir Immune Defic Syndr. 2003;32(4):417-23. DOI: 10.1097/00126334-200304010-00011

199. Kenyon C, Wouters K, Platteau T, Buyze J, Florence E. Increases in condomless chemsex associated with HIV acquisition in MSM but not heterosexuals attending a HIV testing center in Antwerp, Belgium. AIDS Res Ther. 2018;15(1):14. https://doi.org/10.1186/s12981-018-0201-3

200. Flores Anato JL, Panagiotoglou D, Greenwald ZR, et al Chemsex and incidence of sexually transmitted infections among Canadian pre-exposure prophylaxis (PrEP) users in the l'Actuel PrEP Cohort (2013–2020) Sexually Transmitted Infections 2022;98:549-556. http://doi/10.1136/sextrans-2021-055215

201. Patel P, Borkowf CB, Brooks JT. et al. Estimating per-act HIV transmission risk: A systematic review. AIDS. 2014;28(10):1509-19. DOI:10.1097/QAD.0000000000000298

202. Moskowitz, DA, Rieger, G, & Roloff, ME. Tops, bottoms and versatiles, Sexual and Relationship Therapy, 2008;23:3,191-202 doi.org/10.1080/14681990802027259

203. Underwood, SG. Gay Men and Anal Eroticism. 2003. Routledge. DOI: https://doi.org/10.4324/9780203057216

204. Siconolfi DE, & Moeller RW. Prevalence of seroadaptive behaviours of men who have sex with men, San Francisco, 2004. Sex Transm Infect 2009; 85:469–476. DOI: 10.1136/sti.2009.036269

205. Chakrapani V, Newman PA, Shunmugam M, et al. PrEP eligibility, HIV risk perception, and willingness to use PrEP among high-risk men who have sex with men in India: A cross-sectional survey, AIDS Care, 2022, 34:3, 301-309, DOI: 10.1080/09540121.2021.1887801

206. Hill, LM., Maseko, B., Chagomerana, M., … Rosenberg, NE. HIV risk, risk perception, and PrEP interest among adolescent girls and young women in Lilongwe, Malawi: operationalizing the PrEP cascade. J Int AIDS Soc. 2020; 23(S3) https://doi.org/10.1002/jia2.25502

207. Plotzker R, Seekaew P, Jantarapakde J, et al. Importance of risk perception: predictors of PrEP acceptance among Thai MSM and TG women at a community-based health service. JAIDS. 2017 15;76(5):473-81. DOI: 10.1097/QAI.0000000000001536

208. Storholm, E.D., Volk, J.E., Marcus, J.L. et al. Risk Perception, Sexual Behaviors, and PrEP Adherence Among Substance-Using Men Who Have Sex with Men: A Qualitative Study. Prev Sci 2017;18,737–747 https://doi.org/10.1007/s11121-017-0799-8

209. Di Ciaccio, M., Sagaon-Teyssier, L., Protière, C., et al. Impact of HIV risk perception on both pre-exposure prophylaxis and condom use. Journal of Health Psychology, 2019, 1–12. https://doi.org/10.1177/1359105319883927

210. Escandón, K., Rasmussen, A.L., Bogoch, I.I. et al. COVID-19 false dichotomies and a comprehensive review of the evidence regarding public health, COVID-19 symptomatology, SARS-CoV-2 transmission, mask wearing, and reinfection. BMC Infect Dis 2021 21,710. https://doi/10.1186/s12879-021-06357-4

211. Or Z, Gandré C, Durand Zaleski I, Steffen M. France's response to the Covid-19 pandemic: between a rock and a hard place. Health Econ Policy Law. 2022(1):14-26. DOI: 10.1017/S1744133121000165

212. To, KW & Lee, S. A review of reported cases of HIV pre-exposure prophylaxis failure with resultant breakthrough HIV infections. HIV Medicine. 2021:22. DOI: https://doi.org/10.1111/hiv.12989

213. Berçot, B., Charreau, I., Rousseau, C., et al. High prevalence and high rate of antibiotic resistance of mycoplasma genitalium infections in men who have sex with men: A Sub study of the ANRS IPERGAY Pre-exposure Prophylaxis Trial, Clinical Infectious Diseases, 2021; 3(7):2127–2133. https://doi.org/10.1093/cid/ciaa1832

214. Kenyon, C., Baetselier, I. D., & Wouters, K. Screening for STIs in PrEP cohorts results in high levels of antimicrobial consumption. International journal of STD & AIDS, 2020; 31(12), 1215-1218. DOI: 10.1177/0956462420957519

215. Gisselquist D, Potterat JJ. Confound it: latent lessons from the Mwanza trial of STD treatment to reduce HIV transmission. International journal of STD & AIDS. 2003 Mar 1;14(3):179-84. https://doi/10.1258/095646203762869188

216. Rotheram-Borus MJ, Wu Z, Li L, Detels R, Liang LJ. Spontaneous remission of sexually transmitted diseases must be considered in randomised controlled trials. [Letter] Sexually transmitted infections. 2011. http://doi./10.1136-2011-050009

217. Kanny D, Jeffries IV WL, Chapin-Bardales J, et al. Racial/ethnic disparities in HIV pre-exposure prophylaxis among men who have sex with men. Morbidity and Mortality Weekly Report. 2019;68(37):801. doi: http://dx.doi.org/10.15585/

218. Mercer, C.H., Prah, P., Field, N. et al. The health and well-being of men who have sex with men (MSM) in Britain: Evidence from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). BMC Public Health 2016(16). DOI: https://doi.org/10.1186/s12889-016-3149-z

219. Young RM, Meyer IH. The trouble with "MSM" and "WSW": erasure of the sexual-minority person in public health discourse. Am J Public Health. 2005;95(7):1144-1149, https://doi.org/10.2105/AJPH.2004.046714

220. Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of gonorrhoea and chlamydia following human immunodeficiency virus preexposure prophylaxis among men who have sex with men: A modelling study. Clin Infect Dis. 2017;1;65(5):712-718. DOI: 10.1093/cid/cix439

221. Welsh Government. HIV Action Plan for Wales 2023-2026. Available from: https://www.gov.wales/hiv-action-plan-wales-2023-2026

222. Jenness SM, Sharma A, Goodreau SM, Rosenberg ES, Weiss KM, et al. Individual HIV Risk versus Population Impact of Risk Compensation after HIV Preexposure Prophylaxis Initiation among Men Who Have Sex with Men. PLoS ONE, 2017, 12(1):0169484. https://doi.org/10.1371/journal.pone.0169484

223. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot. 1997;12(1):38-48. DOI: 10.4278/0890-1171-12.1.38

224. Kwasnicka D, Dombrowski SU, White M, Sniehotta F. Theoretical explanations for maintenance of behaviour change: a systematic review of behaviour theories. Health Psychol Rev. 2016;10(3):277-296. doi: 10.1080/17437199.2016.1151372

225. Kapadia F, Latka MH, Wu Y, … Garfein RS. Longitudinal determinants of consistent condom use by partner type among young injection drug users: the role of personal and partner characteristics. AIDS Behav. 2011;15(7):1309-18. DOI:10.1007/s10461-009-9569-3.

226. Whiting W, Pharr JR, Buttner MP, Lough NL. Behavioral Interventions to Increase Condom Use Among College Students in the United States: A Systematic Review. Health Educ Behav. 2019;46(5):877-888. DOI: 10.1177/1090198119853008

227. Stewart, J., Bukusi, E., Sesay, F.A. et al. Doxycycline post-exposure prophylaxis for prevention of sexually transmitted infections among Kenyan women using HIV pre-exposure prophylaxis: study

protocol for an open-label randomized trial. Trials 2022;23, 495. https://doi.org/10.1186/s13063-022-06458-8

228. Molina JM, Charreau I, Chidiac C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: An open-label randomised sub study of the ANRS IPERGAY trial. Lancet Infect Dis 2018; 18: 308–17. DOI: 10.1016/S1473-3099(17)30725-9

229. Luetkemeyer AF, Donnell D, Dombrowski JC, …, Vittinghoff E. Postexposure doxycycline to prevent bacterial sexually transmitted infections. New England Journal of Medicine. 2023;388(14):1296-306. DOI:10.1056/nejmoa2211934

230. Reiter, PL., McRee, AL., Katz, ML., & Paskett, ED. Human papillomavirus vaccination among young adult gay and bisexual men in the United States. American journal of public health, 2015;105(1): 96-102. doi: 10.2105/AJPH.2014.302095

231. Wang, H, Kennedy JI, de Paulo, D, Gültzow, T, Zimmermann, HML and Jonas, KJ. Monkeypox self-diagnosis abilities, determinants of vaccination and self-isolation intention after diagnosis among MSM. Eurosurveillance, 2022;27(33) https://10.2807/1560-7917.

232. Wakefield, L. Gay, bi and queer people share their experiences with the monkeypox vaccine. Pink News, 2022. Available from: https://www.thepinknews.com/mpox-vaccine-uk

233. Tsai JY, Sussman S, Pickering T, and Rohrbach LA. Is online partner-seeking associated with increased risk of condomless sex and sexually transmitted infections among individuals who engage in heterosexual sex? A systematic narrative review. Archives of sexual behaviour, 2019;48:533-555. https://doi.org/10.1007/s10508-018-1235-2

234. Whiting W, Pharr JR, Buttner MP, Lough NL. Behavioural Interventions to Increase Condom Use Among College Students in the United States: A Systematic Review. Health Education & Behaviour. 2019;46(5):877-888. DOI: 10.1177/1090198119853008

235. Agénor M, Muzny CA, Schick V, Austin EL, Potter J. Sexual orientation, and sexual health services utilization among women in the United States. Prev Med. 2017;95:74-81. DOI: 10.1016/j.ypmed.2016.11.023

236. Blomquist PB, Mohammed H, Mikhail A, Weatherburn P, Reid D, et al. Characteristics and sexual health service use of MSM engaging in chemsex: results from a large online survey in England. Sex Transm Infect. 2020;96(8):590-595. DOI: 10.1136/sextrans-2019-054345

237. Fuzayloff, S. The Risk for Males of Contracting Various STDs through One-Time Unprotected Homosexual Sex. STD Centre (infographic), 2019. Available from: https://stdcenterny.com/articles/one-time-homosexual-contact-std-risk-men.html

238. Gale, N.K., Heath, G., Cameron, E. et al. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol 2013;13, 117. https://doi.org/10.1186/1471-2288-13-117

239. Hall, W. A., Long, B., Bermbach, N., Jordan, S., & Patterson, K. Qualitative teamwork issues and strategies: Coordination through mutual adjustment. Qualitative Health Research, 2005, 15, 394–410. DOI: 10.1177/1049732304272015

240. Epstein, S. Impure Science: AIDS, Activism, and the Politics of Knowledge. 1996. United Kingdom: University of California Press.

241. Dawson, S., Ruddock, A., Parmar, V. et al. Patient and public involvement in doctoral research: reflections and experiences of the PPI contributors and researcher. Res Involv Engagem, 2020;6,23. https://doi.org/10.1186/s40900-020-00201-w

242. Creswell, JW. and Plano Clark, VL. Designing and conducting mixed methods research. 2017. 3rd ed. Los Angeles: SAGE.

243. Hussein, A. The use of Triangulation in Social Sciences Research: Can qualitative and quantitative methods be combined? Journal of comparative social work, 2015;4(1). DOI: https://doi.org/10.31265/jcsw.v4i1.48

244. Hastings, SL. Triangulation. In: Salkind, N. ed. Encyclopaedia of research design. 2010. Thousand Oaks: SAGE Publications. DOI: http://dx.doi.org/10.4135/9781412961288.n96

245. Denzin NK. The research act: A theoretical introduction to sociological methods. New Jersey: Transaction Publishers, 1970. Available from: https://doi.org/10.4324/9781315134543

246. Johnson M, O'Hara R, Hirst E, et al. Multiple triangulation, and collaborative research using qualitative methods to explore decision making in pre-hospital emergency care. BMC Med Res Methodol 2017; 17:11. https://doi.org/10.1186/s12874-017-0290-z

247. Noble H, Heale R. Triangulation in research, with examples. Evid Based Nurs. 2019 Jul;22(3):67-68. DOI: 10.1136/ebnurs-2019-103145

248. Hassan, M. Triangulation in Research – Types, Methods, and Guide. 2022. Available from: https://researchmethod.net/triangulation/Limitations

249. Terrence Higgins Trust. Heterosexual HIV diagnoses overtake those in gay men for first time in a decade. 2022 [press release]. Available from: https://www.tht.org.uk/news/hetero-hiv.

250. UKHSA. HIV testing, PrEP, new HIV diagnoses, and care outcomes for people accessing HIV services. [Report]. 2022. Available from: https://www.gov.uk/statistics/hiv-2022-report

251. UKHSA. Gonorrhoea and syphilis at record levels in 2022. [Press release]. 2023. Available from: https://www.gov.uk/news/gonorrhoea-and-syphilis-at-record-levels-in-2022

APPENDICES

APPENDIX ONE

1.1 Survey ethical approval letter

1.2 Interviews ethical approval letter

1.3 Routine data NHS ethical approval

APPENDIX TWO

2.1 Search terms

APPENDIX THREE

3.1 Interview participant information sheet

3.2 Interview consent form

3.3 Interview schedule

3.4 Coding framework

APPENDIX FOUR

4.1 STI data variables

4.2 PrEP data variables

4.3 AMR data variables

APPENDIX FIVE

5.1 Full survey

APPENDIX ONE

1.1 Survey ethical approval letter

School of Medicine
Yr Ysgol Meddygaeth

Cardiff University
Main Building
Heath Park
Cardiff CF14 4XN
Wales, UK
Prifysgol Caerdydd
Prif Adeilad
Parc y Mynydd Bychan
Caerdydd CF14 4XN
Cymru, Y Deyrnas Unedig

Wednesday 13th May 2020

Adam Williams
Centre for Trials Research
School of Medicine
Cardiff University

Dear Adam

Research project title: Understanding the impact of Covid-19 on the sexual behaviours and attitudes of MSM in Wales.
SREC reference: SMREC 20/56

The School of Medicine Research Ethics Committee ('Committee') reviewed the above application electronically on Wednesday 6th May 2020.

Ethical Opinion
The Committee gave a favourable ethical opinion of the above application on the basis described in the application form, protocol and supporting documentation, **subject to the conditions** specified below.

Conditions of the favourable opinion
The favourable opinion is subject to the following conditions being met prior to the start of the research project.

1. Provide confirmation as to why the ethical concerns section of the application form was left blank. If all ethical concerns have been addressed elsewhere in the application then please confirm this.
2. Please ensure that the University logo is used on all Participant Information Sheets and Consent Forms.
3. Review the data retention schedule as all non-clinical studies are required to be kept for 5 years following the completion of the study or 2 years post-publication (as opposed to 15 years).
4. Review Question 8 in *Section B Questions About You* as the Committee queried if all potential participants will understand the definitions of each choice.
5. Correct the wording and phrasing of question 5 in *Section B Questions about Risk and Sexual Health Testing* on the survey.

Whilst the Committee does not propose to conduct a further review of your application/revised research project documents following implementation of the conditions above, you should notify the Committee once all conditions have been met and provide copies of any revised documentation with updated version numbers before the research commences.

Please submit a response to the matters listed above and/or revised documentation to the Committee Secretary, Claire Evans via email (EvansCR9@cardiff.ac.uk). Please underline or highlight the changes which have been made and provide revised version numbers and dates.

Additional approvals
This letter provides an ethical opinion only. You must not start your research project until all appropriate approvals are in place.

Amendments
Any substantial amendments to documents previously reviewed by the Committee must be submitted to the Committee via email to Claire Evans (EvansCR9@cardiff.ac.uk) for consideration and cannot be implemented until the Committee has confirmed it is satisfied with the proposed amendments.
You are permitted to implement non-substantial amendments to the documents previously reviewed by the Committee but you must provide a copy of any updated documents to the Committee via email to Claire Evans (EvansCR9@cardiff.ac.uk) for its records.

Monitoring requirements
The Committee must be informed of any unexpected ethical issues or unexpected adverse events that arise during the research project. In addition to this, the Committee request an end of project report sent to the Committee via email to Claire Evans (EvansCR9@cardiff.ac.uk). This must be sent along with confirmation that your research project has ended and sent within the three months of the research project completion.

Documents reviewed by Committee
The documents reviewed by the Committee were:

Document	Version	Date
Application Form	V1	22/04/20
Project Proposal	V1	22/04/20
Brief Participant Information Sheet	V1	22/04/20
Full Participant Information Sheet	V1	22/04/20
Survey	V1	22/04/20

Complaints/Appeals

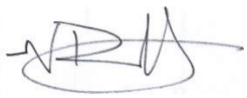
If you are dissatisfied with the decision made by the Committee, please contact the Chair of the Committee via the Committee Secretary (EvansCR9@cardiff.ac.uk) in the first instance to discuss your complaint. If this discussion does not resolve the issue, you are entitled to refer the matter to the Head of School for further consideration. The Head of School may refer the matter to the University Research Integrity and Ethics Committee (URIEC), where this is appropriate. Please be advised that URIEC will not normally interfere with a decision of the Committee and is concerned only with the general principles of natural justice, reasonableness and fairness of the decision.

Please use the Committee reference number on all future correspondence.

The Committee reminds you that it is your responsibility to conduct your research project to the highest ethical standards and to keep all ethical issues arising from your research project under regular review.

You are expected to comply with Cardiff University's policies, procedures and guidance at all times, including, but not limited to, its Policy on the Ethical Conduct of Research involving Human Participants, Human Material or Human Data and our Research Integrity and Governance Code of Practice.

Yours sincerely,



Dr Ned Powell
Acting Chair, School of Medicine Research Ethics Committee

CC: Professor Kerry Hood, Dr David Gillespie

1.2 Interviews ethical approval letter

School of Medicine
Yr Ysgol Meddygaeth

Cardiff University
Main Building
Heath Park
Cardiff CF14 4XN
Wales, UK
Prifysgol Caerdydd
Prif Adeilad
Parc y Mynydd Bychan
Caerdydd CF14 4XN
Cymru, Y Deyrnas Unedig

Monday 3rd February 2020

Adam Williams,
Centre for Trials Research,
School of Medicine,
Cardiff University,
Heath Park.

Dear Adam

Re: Understanding the relationship between pre-exposure prophylaxis, sexually transmitted infections, and antimicrobial resistance in Wales (UPrEP)

SMREC Reference Number: 20/21

This application was reviewed by the Committee in January 2020.

Ethical Opinion

On review, the Committee have asked for the following issues to be addressed:

1. Provide clarification as to what is meant by referral sampling. If this is via the NHS, then the study will require approval via NRES.
2. Review and revise the Information Sheet. The Committee have suggested that the information sheet be presented in two stages: the first being a general invitation via social media platforms' and the second being more detailed. Also, please confirm if the questionnaire will be provided with the Information Sheet.
3. Review the Information Sheet for acronym usage and ensure that it is understandable for all participants.
4. Include a statement in the Participant Information Sheet to acknowledge that there will also be discussions around sexual history as this would likely be an important consideration for participants.
5. Pilot the questionnaire so that you can provide a more accurate time estimation for completion to participants.
6. Clarify if the uPrEP study mentioned in the Interview Schedule is the same as the Do-PrEP study as referenced in the Consent Form.
7. Include information in the Participant Information Sheet informing participants that they can withdraw from the study or refuse to answer questions they find uncomfortable.

Please send the resubmitted application to the Committee Secretary, Mrs Claire Evans, via email. To be considered for the February meeting, the resubmitted application must be received by 4pm on 13th February.

Documents Considered

Document Type:	Version:	Date Considered:
Application	V1.2 07/01/2020	January 2020
Project Proposal	V1.2 07/01/2020	January 2020
Participant Information Sheet	V1.2 07/01/2020	January 2020
Consent Form	V1.2 07/01/2020	January 2020
Interview Schedule	V1.2 07/01/2020	January 2020

Yours sincerely,

Dr Jonathan Hewitt
Chair, School of Medicine Research Ethics Committee

CC: Prof Kerry Hood, Dr David Gillespie

1.3 Routine data NHS ethical approval letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr David Gillespie
Centre for Trials Research
Heath Park
Cardiff
CF14 4YS

Email: Wales.REC1@wales.nhs.uk

02 September 2020

Dear Dr Gillespie

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Understanding the relationship between HIV pre-exposure prophylaxis, sexually transmitted infections and antibiotic resistance in Wales.**
IRAS project ID:	**281194**
Protocol number:	**SPON1816-20**
REC reference:	**20/HCRW/0026**
Sponsor	**Cardiff University**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The *"After HRA Approval – guidance for sponsors and investigators"* document on the HRA website gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **281194**. Please quote this on all correspondence.

Yours sincerely,
Carl Phillips
Approvals Specialist

Email: Wales.REC1@wales.nhs.uk

Copy to: *Ms Helen Falconer*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]	N/A	26 August 2020
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Insurance]	N/A	01 August 2020
IRAS Application Form [IRAS_Form_19082020]	N/A	19 August 2020
IRAS Application Form [IRAS_Form_27082020]	N/A	27 August 2020
IRAS Checklist XML [Checklist_27082020]	N/A	27 August 2020
IRAS Checklist XML [Checklist_19082020]	N/A	19 August 2020
IRAS Checklist XML [Checklist_26082020]	N/A	26 August 2020
Letter from funder [Funder Letter]	N/A	27 September 2019
Letter from sponsor [Sponsor Letter]	N/A	05 June 2020
Organisation Information Document [OID]	2	27 August 2020
Research protocol or project proposal [Protocol]	3	15 June 2020
Schedule of Events or SoECAT [Schedule of Events]	1	07 July 2020
Summary CV for Chief Investigator (CI) [D Gillespie]	N/A	08 June 2020
Summary CV for student [A Williams]	N/A	08 July 2020

APPENDIX TWO

2.1 Search terms

Category	#	Search terms
Pre-exposure prophylaxis	1	PrEP
	2	HIV PrEP
	3	Pre-exposure prophylaxis
	4	HIV pre-exposure prophylaxis
Men who have sex with men	5	MSM
	6	GBMSM
	7	Heterosexual MSM
	8	Men who have sex with men
	9	Gay and bisexual men who have sex with men
	10	Gay / gay men
	11	Bisexual / bisexual men
	12	Heterosexual-identifying men who have sex with men
Sexually transmitted infections	13	STI/s
	14	Sexually transmitted infection/s
	15	Chlamydia / Chlamydia trachomatis
	16	Gonorrhoea / Neisseria gonorrhoeae
	17	Syphilis / Treponema pallidum
	18	HIV/AIDS
	19	HIV / Human immunodeficiency virus
	20	HPV / Human papilloma virus / genital warts
	21	HSV / herpes simplex virus / genital herpes
Antimicrobial resistance	22	AMR
	23	Antimicrobial resistance
	24	Antibiotic resistance
	25	Gonorrhoea resistance
	26	Super gonorrhoea
Risk compensation	27	Risk compensation
	28	Risk perception
	29	Decision making
	30	Risk decision-making
	31	Risk behaviour
Behaviour change	32	Behaviour change
	33	BCT / Behaviour change theory
	34	Health behaviour
	35	Health belief model
	36	Theory of planned behaviour
Location	37	United Kingdom
	38	Wales
	39	England
	40	Scotland

*Searches included a mix of terms

APPENDIX THREE

3.1 Interview participant information sheet

[BRIEF] PARTICIPANT INFROMATION SHEET

CALL FOR PARTICIPANTS

Cardiff University will be running an interview study to understanding the relationship between pre-exposure prophylaxis, sexually transmitted infections, and antibiotic resistance in Wales. This study is for **gay or bisexual men** who are currently or have previously used **PrEP** to prevent HIV to interview. Interviews are expected to last between 45 minutes to an hour and participants will be reimbursed with a **£20 gift voucher** for their time. Interviews will take place online via the platform Zoom.

For more information or to express your interest please email: UPREP@cardiff.ac.uk

The purpose of this study is to understand the relationship between PrEP and sexually transmitted infections, and how this relationship may impact antibiotic resistance. This study aims to interview 20 gay and bisexual males from three specific groups: 10 PrEP users, 5 previous PrEP users and 5 non-PrEP users. Interviews are expected to last between 45 minutes to an hour and participants will be reimbursed with a **£20 gift voucher** for their time. Interviews will take place online via the platform Zoom.

For more information or to express your interest please email: UPREP@cardiff.ac.uk

---

[FULL] PARTICIPANT INFROMATION SHEET

Understanding the relationship between pre-exposure prophylaxis, sexually transmitted infections, and antibiotic resistance in Wales

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and if you have any questions you can contact the research team using the details provided at the end.

Why are we doing this study?

The purpose of this study is to understand the relationship between PrEP (prevention medication for HIV) and sexually transmitted infections, and how this relationship may impact antibiotic resistance. This study aims to interview 20 gay and bisexual males. 10 PrEP users, 5 previous PrEP users and 5 non-PrEP users.

Why have I been chosen?

You have been chosen to take part because you fall within one of the three groups needed for this study:

- You identify as male
- You identify as gay or bisexual
- **ONE** of the 3 statements below applies to you:
    - You are currently using PrEP to prevent HIV
    - You have previously used PrEP but are currently not taking it (not used PrEP for one month or longer)
    - Have never taken a medication to prevent HIV

Individuals cannot participate if they are not a fluent English speaker or lacking the capacity to consent for themselves.

15/06/20 v3.0

Do I have to take part?
It is up to you to decide whether or not to take part. If you do decide to take part, you will be required to sign a consent form. If you agree to take part you are still free to withdraw at any time, without giving a reason and may refuse to answer any questions you find uncomfortable.

What do I have to do?
Participation will include an interview with the researcher (Adam Williams). The interview will include a discussion relating to your awareness and concerns of using PrEP, sexually transmitted infections and antimicrobial resistance. The interview will take place online via Zoom and will be audio-recorded. It is estimated to last between 45 minutes to one hour. Participants will receive a £20 gift voucher for their time.

Are there any risks?
Participating in the research is not anticipated to cause you any disadvantages or discomfort. If you feel uncomfortable with any of the questions asked you can refuse to answer and we can move on.

What if there is a problem?
Complaints: If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (contact details are at the end of this information sheet). If you remain unhappy and wish to complain formally, you can contact Cardiff University, who are sponsoring this study. Prof Kerry Hood can be contacted on 02920 687163 or hoodk1@cardiff.ac.uk
Harm: If something does go wrong and you are harmed during the research which is as a result of someone's negligence, you may have grounds for a legal action against Cardiff University but you may have to pay your legal costs.
General sexual health information and advice: If you feel affected by any of the discussions during the study, we would encourage you to discuss these with your sexual health clinician or a sexual health charity (e.g. Terrence Higgins Trust, which has two centres within Wales: Cardiff (telephone number 02920 666465) and Swansea (telephone number 01792 477540)).

What about confidentiality?
All information that you give to us as a part of this study will remain confidential, and we will store it securely in locked cabinets or secure computers. The audio recording of the interview will be transcribed (a record of the interview will be typed up). We may use quotes from your interview in reports, presentations or publications. If we do this, you will not be identified and we would change all names or places that you mention so that it is not possible for someone to identify you.
There are circumstances in which we would not be able to keep confidential something that you say. If you mention during the interview any information that suggests you, or someone in your care has been subject to/is at risk of harm, the researcher would have a duty to report this information to your GP or the appropriate authorities.
In line with the regulations, at the end of the study your data will be securely archived for 15 years – in case any questions arise about the study. Arrangements for confidential destruction will then be made.

Who is responsible for looking after my information?

Cardiff University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller (you can contact the data protection officer at: inforequest@cardiff.ac.uk). This means that we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. You have a right to lodge a complaint with the information commissioner's office (https://ico.org.uk/make-a-complaint/). The legal basis for processing your data will be a task in the public interest. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information https://www.cardiff.ac.uk/public-information/policies-and-procedures/data-protection

What will happen to the results of the research study?

Results of this research will aim to be published in medical and scientific literature. A summary of the results will be made available on Cardiff University websites. Results will also be reported at academic meetings, shared with non-academic groups (including policy makers, advocacy groups and charities) and be provided to participants on request.

Will I be identifiable in the results?

No, we take your confidentiality very seriously and any results published will not identify you.

Who is organising and funding the research?

The study is being organised by Cardiff University and the Chief Investigator is Adam Williams. The research is funded by KESS 2 East in conjunction with Public Health Wales.

Contact for Further Information

Adam Williams, MSc, BSc
Centre for Trials Research,
5th Floor Neuadd Meirionnydd,
Heath Park
Cardiff CF14 4YS
Email: WilliamsAD7@cardiff.ac.uk

1.2 Interview consent form

Consent Form for Interviews

Date: 03/07/20, version: 3.0

Title of Project: Understanding the relationship between pre-exposure prophylaxis, sexually transmitted infections and antibiotic resistance in Wales

Name of Researcher: ADAM WILLIAMS

Participant ID: .....

	Please initial
I confirm that I have read and understand the information sheet dated 15/06/20 (version 3.0) for the above study and have had the opportunity to ask questions.	
I understand that my participation is voluntary and that I am free to withdraw at any time.	
I agree that the interview can be audio recorded via Zoom.	
I agree that anonymised quotations can be used in reports, presentations and publications.	
I understand that personal details I provide (name and email) will be stored securely at Cardiff University and that no personal information will be used in the study report or other publications.	
I agree to participate.	

_____	_____	X _____
Name of Participant [PRINT]	Date [00/00/00]	Signature
ADAM WILLIAMS	_____	X _____
Name of Researcher [PRINT]	Date [00/00/00]	Signature

3.3 Interview schedule

UPrEP Qualitative Interviews: Interview Schedule

Introduction:
Hello my name is Adam, I am the lead investigator of the UPrEP study. Thank you for agreeing to speak to me today. I am looking to gain an understanding of your awareness and any concerns around PrEP, STIs and antibiotic resistance. The interview should take about 30 to 60 minutes to complete. Please remember that everything you say to me will be kept strictly confidential. If you find any of the topics difficult please let me know. If you wish to decline an answer you may do so. Any questions before we start?
To begin can you please say your name and the date? And do you consent to being audio recorded.
Okay first can we go through some demographic questions?

Question	Response
What is your PrEP situation?	Currently use / Previously used / Never used
How old are you?	
What is your sexuality?	Gay / Bisexual / Straight / Other
What is your ethnicity	White / Black / Asian / Other
What is your highest level of education?	None / GCSEs / A-levels or equivalent / Undergraduate / Postgraduate
What is your current relationship status?	Single / Dating / Open relationship / Exclusive relationship / Married
What is your employment status?	Unemployed / Full time employed / Part-time employed / Student

(START AUDIO RECORDER)
This is interview (study ID#) on (date) commencing (time). The participant is aware that this interview is being recorded and consents, is that correct?

Topic 1:
First, I would like to discuss PrEP.

- How did you first hear about PrEP?
- What encouraged your decision to take/not take PrEP?
  [For those who have stopped PrEP]
  - What informed your decision to stop taking PrEP?
- What benefits do you believe there are to PrEP?
- Can you think of any issues PrEP use may cause?

15/06/20 v3.0

Topic 2:
Some health professionals have suggested that PrEP use would reduce condom use.

- What do you think of their suggestion?
- In your opinion, how important do you think condom use is to gay and bisexual men?
- Do you think most gay and bisexual men are concerned with protection from sexual infections?

Topic 3:
Now I would like to discuss sexually transmitted infections.

- How knowledgeable do you think you are about STIs and how they can be passed on?
- How would you describe your level of safety during sexual encounters?
- Are you concerned about catching an STI?
    - What do you think informs your level of concern?
- What impact, if any, do you think PrEP may have on STIs, other than HIV?

Topic 4:
Finally, I would like to talk about antimicrobial resistance.

- Are you aware of the term antimicrobial or antibiotic resistance?
    - [If yes] could you explain your understanding of it?

The world health organisation defines antimicrobial resistance as the ability of a microorganism like bacteria, viruses, and some parasite to stop an antimicrobial such as antibiotics, antivirals and antimalarials from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others. It is serious concern and most countries are implementing procedures to slow the spread. One infection that has become increasingly resistant to multiple antibiotics is gonorrhoea.

- Do you think being made aware of antibiotic resistance would alter sexual practices among gay and bisexual?
- What do you think would be the best way to inform gay and bisexual men about antibiotic resistant sexual infections?
- Can you think of any ways to reduce STI rates among these groups?

Closing:
I appreciate the time you've taken to give this interview. Is there anything else you think would be helpful for me to know about?
Thanks – I should have all of the information I need. Would it be alright to email you if I have any more questions?
(STOP AUDIO RECORDER)

3.4 Coding framework

UPREP Coding Framework

CODE	Description
1. Base	
Age	18-30 / 30-39 / 40-50 / 50+
Location	Barry / Cardiff / etc
Methods/methodology	
Memorable quotes	
Taking PrEP	YES / NO / PREVIOULSY USED
2. PrEP	
Benefits	To PrEP use, self, others, and society
Impact on condoms	Impact of PrEP on condom use, self, others, and society
Impact on STIs	How PrEP impacts STI rates/spread
Impact on behaviour	Changes or lack of change to other behaviours
Knowledge	Participant knowledge/awareness of PrEP
Others knowledge	Such as HCP, friends, family knowledge and awareness of PrEP
Where find info	How did they find out about PrEP
Negatives to use	Side effects
Stigma	PrEP related stigma
Why stop using PrEP	Reasons for ever stopping using PrEP
Why not use PrEP	Reasons for not using PrEP
Why use PrEP	Reason for starting PrEP
3. STIs	
Clinic	Attending sexual health clinic, anything clinic related
Concern	Personal concern for STIs
Others concern	Other people's concern towards STIs/sexual health
Fear	Mentions of fear related to HIV
STI testing	Frequency of testing, how comfortable, do they get tested
Knowledge	Knowledge of various STIs
Postal testing	References to postal testing
Reducing STIs	Suggestions of how to reduce sti rates
Risk perception	Mention of their own views about their risk
Sexual encounters	
Views on condoms	
4. AMR	
Awareness/knowledge	Knowledge of antibiotic resistance and awareness of relationship to STI
Public awareness	Views on public awareness of issue
Suggestions	Suggestions of how to tackle the issue
What not work	What interventions will not work
5. Mental Health	References to mental health and how it impacts sexual behaviours
6. Covid-19 / Pandemic	
Behaviour change	How it has or has not changed behaviour
External judgement	Role external judgement plays on behaviour and references to being secretive about sexual encounters

APPENDIX FOUR

4.1 STI data variables

SWS records

Patient	PatientID	Patient clinic ID number
	Gender	Patient sex, in this case all male
	Age at attendance	In years
	Ethnicity	
	Sexuality	Homosexual or bisexual
	MSM	Patient identified as MSM
	GenderSexuality	Patient gender and sexuality, all coded as MSM
Practice	attlocationdescr	Sexual health clinic location
	reslhbla	Health board of clinic
	resla	Region of clinic location
Flagged codes	Aged1524	Patient aged between 15 and 24
	SexAbroadEver	Patient reports of sex in countries outside the UK
	Sexabroadcountry	Location that patient has had sex outside the UK, all list unknown
	IDUEver	Patient reports of injecting drug use
	HIVstatus	
Consultation	Att_date	Consultation date
	Att_year	Consultation year
	Diagnosis	Codes relating to consultation; PN, T4, P1A, A1, etc.
	Diagnosisdescr	Codes description relating to various testing, diagnosis, PrEP, other consultation reasons.

4.2 PrEP data variables

SWS records

Patient	PatientID	Patient clinic ID number
	Gender	Patient sex, in this case all male
	Age at attendance	In years
	Ethnicity	
	Sexuality	Homosexual or bisexual
	MSM	Patient identified as MSM
	GenderSexuality	Patient gender and sexuality, all coded as MSM
Practice	attlocationdescr	Sexual health clinic location
	reslhbla	Health board of clinic
	resla	Region of clinic location

Flagged codes	Aged1524	Patient aged between 15 and 24
	SexAbroadEver	Patient reports of sex in countries outside the UK
	Sexabroadcountry	Location that patient has had sex outside the UK, all list unknown
	IDUEver	Patient reports of injecting drug use
	HIVstatus	
Consultation	Planned/ Planneddescr	Type of attendance; appointment (booked), drop in, unknown
	Att_date	Consultation date
	Att_year	Consultation year
	Diagnosis	Codes relating to type of consultation i.e., O48W, O31W, PREPD
	Diagnosisdescr	Codes description relating to type of consultation i.e., started, regimen: daily, declined, eligible 1

4.3 AMR data variables

GRASP records

Patient	Clinic	Patient clinic ID number
	Patid	Patient ID: encrypted unique identifier given to a patient
	Age	In years
	Sex	Patient sex, in this case all male
Practice	Location	Clinic from which sample was collected
	Health board	Health board of clinic
Sample	Labspecn	Laboratory specimen number: unique identifier given to each sample
	Date collected	Date of sample collection
	Organism	Organism to be tested, only Neisseria gonorrhoeae
Antimicrobial tested	AZI	Azithromycin sensitivity
	CFM	Cefixime sensitivity
	CIP	Ciprofloxacin sensitivity
	CRX	Ceftriaxone sensitivity
	DOX	Doxycycline sensitivity
	PEN	Penicillin sensitivity
	SPE	Spectinomycin sensitivity
	TET	Tetracycline sensitivity

4.4 Demographic data

		All MSM [N=11415]		No PrEP cohort [N=10262]		PrEP cohort [N=1153]	
		Freq	%	Freq	%	Freq	%
Age	Mean	34 (years)	.	33 (years)	.	34 (years)	.
	Range	13-86	.	13-86	.	15-74	.
	<18	219	1.9	208	2.0	11	1.0
	18-25	3980	34.9	3666	35.7	314	27.2
	26-34	3278	28.7	2897	28.2	381	33.0
	35-44	1763	15.4	1531	14.9	232	20.1
	45-54	1261	11.0	1116	10.9	145	12.6
	55-64	653	5.7	593	5.8	60	5.2
	>65	261	2.3	251	2.4	10	0.9
Sexuality	Homosexual	9155	80.2	8158	79.5	1005	87.2
	Bisexual	2260	19.8	2104	20.5	148	12.8
Ethnicity	White British	7418	65.0	6700	65.3	718	62.3
	White Irish	618	5.4	567	5.5	51	4.4
	Other White	1539	13.5	1318	12.8	221	19.2
	White and Asian	19	0.2	16	0.2	3	0.3
	White and Black African	7	0.1	7	0.1	0	0.0
	White & Black Caribbean	9	0.1	9	0.1	0	0.0
	Other Mixed	122	1.1	106	1.0	16	1.4
	African	44	0.4	38	0.4	6	0.5
	Caribbean	12	0.1	12	0.1	0	0.0
	Other Black	47	0.4	39	0.4	8	0.7
	Chinese	47	0.4	42	0.4	5	0.4
	Pakistani	25	0.2	22	0.2	3	0.3
	Indian	23	0.2	20	0.2	3	0.3
	Bangladeshi	5	0.0	3	0.0	2	0.2
	Other Asian	52	0.5	42	0.4	10	0.9
	Any other	169	1.5	142	1.4	27	2.3
	Not stated	1259	11.0	1179	11.5	80	6.9
Health Board	Aneurin Bevan	2467	21.6	2190	21.3	277	24.0
	Betsi Cadwaladr	1640	14.4	1494	14.6	146	12.7
	Cardiff & Vale	4512	39.5	4065	39.6	447	38.8
	Cwm Taf	744	6.5	698	6.8	46	4.0
	Hywel Dda	843	7.4	790	7.7	53	4.6
	Powys Teaching	16	0.1	16	0.2	0	0.0
	Swansea Bay	1193	10.5	1009	9.8	184	16.0

APPENDIX FIVE

5.1 Full Survey

Understanding the Impact of Coronavirus on the Sexual Behaviours and Attitudes of men who have sex with men in Wales

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

Why are we doing this study? The purpose of this study is to understand how the lockdown measures imposed by the government have altered sexual behaviour of gay, bisexual and other men who sex with men and if the virus has potentially changed attitudes to other infections.

Can I take part? To take part you must:

- be a man who has sex with other men
- be aged 18 or over
- currently live in Wales
- have had sex with another man in the last 12 months

Do I have to take part? No, taking part is voluntary and you can stop at any time.

What do I have to do? Participation will include answering a series of questions relating to sexual behaviours and attitudes. We are interested in the impact Coronavirus has had on you personally, particularly relating to sexual behaviour and attitudes.

What are the possible benefits and disadvantages of taking part? Your participation will be help improve the understanding of how government measures have affected the lives of gay, bisexual and other men who have sex with men. The disadvantage is the time taken to complete the survey - it usually takes about 15 minutes and there are some personal questions.

What if there is a problem? ***Complaints:*** If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (contact details are at the end of this information sheet). If you remain unhappy and wish to complain formally, you can contact Cardiff University, who are sponsoring this study. Prof Kerry Hood can be contacted on 02920 687163 or hoodk1@cardiff.ac.uk ***General sexual health information and advice:*** If you feel affected by any of the discussions during the study, we would encourage you to discuss these with your sexual health clinician or a sexual health charity (e.g. Terrence Higgins Trust, which has two centres within Wales: Cardiff (telephone number 02920 666465) and Swansea (telephone number 01792 477540)).

What about confidentiality? All information that you give to us as a part of this study will remain confidential, and we will store it securely on University servers. No personal data will be collected so your results are fully anonymous and cannot be linked to you. In line with the regulations, at the end of the study your anonymised data will be securely archived for 5 years – in case any questions arise about the study. Arrangements for confidential destruction will then be made.

Who is responsible for looking after my information? Cardiff University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller (you can contact the data protection officer at: inforequest@cardiff.ac.uk). This means that we are responsible for looking after your information and using it properly. Your rights to

access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. You have a right to lodge a complaint with the information commissioner's office (https://ico.org.uk/make-a-complaint/). The legal basis for processing your data will be a task in the public interest. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information https://www.cardiff.ac.uk/public-information/policies-and-procedures/data-protection

What will happen to the results of the research study? We will aim to publish the results of this research in medical and scientific literature. A summary of the results will be made available on Cardiff University websites. Results may also be reported at academic meetings, shared with non-academic groups (including policy makers, advocacy groups and charities) and be provided to participants on request.

Who is organising and funding the research? The study is being organised by Cardiff University and has ethical approval from the School of Medicine Research Ethics Committee. The Chief Investigator is Adam Williams. The research is funded by KESS 2 East in conjunction with Public Health Wales.

Contact for Further Information

Adam Williams, MSc, BSc

Tel: +44 (029) 20879989
Email: WilliamsAD7@cardiff.ac.uk

CONSENT TO PARTICIPATE To take part in this study you must fit the criteria below:

- **I am 18 years or older**
- **I am a man who has sex with other men**
- **I currently live in Wales**
- **I have had sex with another man in the last 12 months**

Do ALL the listed items describe yourself?

Yes

No

I agree to participate and for my answers to be used in this survey.

Yes

No

Section A) About You

1. **How old are you?** [open text]

2. **How would you describe your ethnicity?**

Black /African/Caribbean	Arab	Asian	White
Mixed/multiple ethnic groups		Other ethnic group	Prefer not to say

3. **What region of Wales do you live in?**

Bridgend	Caerphilly	Cardiff	Carmarthenshire
Ceredigion	Conwy	Denbighshire	Flintshire
Gwynedd	Isle of Anglesey	Merthyr Tydfil	Monmouthshire
Neath Port Talbot	Newport	Pembrokeshire	Swansea
Powys Blaenau Gwent	Rhondda Cynon Taf	Torfaen	Vale of Glamorgan
Wrexham			

4. **What is your highest qualification?**

I have no educational qualifications.	GCSEs or equivalent
A -Levels or equivalent	BTEC/NVQ/diploma or equivalent
University degree or higher	Other (please state)

5. **What is your relationship status?**

Single	Relationship with a male
Relationship with a female	Open relationship with a male
Open relationship with a female	Polyamorous relationship
Married / Civil partnership with a male	Married / Civil partnership with a female
Other	

6. **How would you best describe your gender?**

Man	Non-Binary	Trans	Other

7. **Which best describes your sexuality?**

Gay	Bicurious	Bisexual	Straight
Pansexual	Queer	Other	

8. **In the last 12 months, who have you had sex with? (Tick all that apply)**

Men	Trans men	Trans women	Women
Genderqueer/Non-Binary individuals			

9. **What is your HIV status?**

HIV negative and tested in last year	HIV Negative but tested longer than a year ago
HIV Positive	Unknown
Prefer not to say	

10. Are you currently taking PrEP (daily or event based) or PEP?

Yes PrEP Yes PEP No No, receiving ART

11. Have you been diagnosed with HIV or STIs in the last 12 months?

	No (1)	Yes (2)
Chlamydia (1)	☐	☐
Gonorrhoea (2)	☐	☐
Syphilis (3)	☐	☐
Hepatitis C (4)	☐	☐
HIV (5)	☐	☐
Other (6)	☐	☐

12. In the last 12 months, have had sex with multiple people at the same time? E.g. threesome, gangbang, sex party. YES/NO

13. In the last 12 months, have you had sex whilst using a drug (e.g., mephedrone, crystal meth etc.) or alcohol?

Both drugs and alcohol Only drugs Only alcohol Neither

14. Which best describes the main reason for your last visit to a sexual health clinic?

Regular check up I had symptoms
I had been at risk of HIV A sexual partner told me they had an infection
I had a new sexual partner For a PrEP Review
Other (Please Specify) _____

15. When was your last STI test?

In the last month 2 to 3 months ago 4 to 12 months ago
More than a year ago I have never previously tested for STIs

16. How often do you get a check-up for STIs, assuming you have no symptoms?

Every month Every 3 months Every 6 months
Once a year Less than once a year

17. If there was a time when you were more at risk of STIs (e.g., when you had more sexual partners), would this change how often you would be tested? YES/NO

18. Has the lockdown stopped you from getting tested?

Yes (If yes, why?) _____ No

19. Are you aware that Wales recently started STI/HIV at-home testing? YES/NO

Sexual partners fall into 2 categories:

1. Regular sexual partners – a person you are in a relationship with e.g. boyfriend/husband *or* a person you have repeated sex with but are not in a relationship e.g. friends with benefits
2. Casual sexual partners – such as hook-ups, one-night stands, people met at saunas etc.

20. How many sexual partners would you have in an average month? (Before Coronavirus and lockdown)

Regular partners _____[OPEN TEXT]
Casual partners _____[OPEN TEXT]

21. What is your sexual position with sexual partners?

	Top [insertive]	Bottom [receptive]	Versatile [both]
Regular partner	☐	☐	☐
Casual partner	☐	☐	☐

22. What percentage of the time will you use condoms with your sexual partners?

0 10 20 30 40 50 60 70 80 90 100

Regular partners	
Casual partners	

23. Do you know the HIV status of your sexual partners before having sex?

	Always	Most of the time	About half the time	Sometimes	Never
Regular partners	☐	☐	☐	☐	☐
Casual partners	☐	☐	☐	☐	☐

24. Where do you usually meet CASUAL partners? (Tick all that apply)

Friends Grindr Apps (not Grindr) Bars
Cruising Sex in venues (saunas)
Other (where?) _____

We would like to discuss your sexual activity during lockdown. Please remember this is **fully anonymous** so please answer honestly. The lockdown measures started on March 23rd, 2020. For this survey, we define sex activity as any activity between two or more people that induces sexual arousal, including masturbation and all oral and anal activities. This does not include virtual sex.

25. Have you had sex during lockdown? YES/NO

26. Whom are you having sex with?

regular partner/s I knew before the lockdown
regular partner/s I met during the lockdown
casual partner/s I knew before the lockdown
casual partner/s I met during the lockdown

27. Do you live with the sexual partners you have had during lockdown?

Yes, all of them
Some of them
No, none of them
We moved in together for the lockdown
Other [free text]

28. Below is a list of each week of lockdown. Please indicate the number of new causal sexual partners you have had each week. If you met the same person multiple times, please only count them once (Put zero for none). [open text]

23rd March – 29th March _____
30th March - 5th April _____
6th April - 12th April _____
13th April - 19th April _____
20th April - 26th April _____
27th April - 3rd May _____
4th May - 10th May _____
11th May - 17th May _____
18th May - 24th May _____
25th May - 31st May _____
1st June - 7th June _____
8th June - 14th June _____
15th June - 21st June _____

29. What are your reasons for not having sex?

No privacy at where I live
No one else wants to meet
I don't want sex
Trying to limit social interaction
Self-isolating due to showing symptoms/someone in household has symptoms
Other _____

30. Have the number of sexual partners you have per week/month changed due to lockdown?

No, same number of partners as before lockdown
Yes, less partners now than before lockdown
Yes, more partners than before lockdown

31. How have your behaviours on the following changed because of the Coronavirus lockdown?

	Stopped completely	Less than before	Same as before	More than before	Started since lockdown	Didn't do before or now
Chatting via dating apps/ websites	○	○	○	○	○	○
Hookup via dating apps/ websites	○	○	○	○	○	○
Virtual sex (including sharing photos and video)	○	○	○	○	○	○
Oral sex	○	○	○	○	○	○
Masturbation	○	○	○	○	○	○
Mutual masturbation	○	○	○	○	○	○
Penetrative sex with condoms	○	○	○	○	○	○
Penetrative sex without condoms	○	○	○	○	○	○
Group sex	○	○	○	○	○	○
Using PrEP	○	○	○	○	○	○
Sex with toys	○	○	○	○	○	○
Sharing sex toys	○	○	○	○	○	○
Sex with payment (Receiving or giving)	○	○	○	○	○	○
Chemsex (e.g., use of illicit substances during sex)	○	○	○	○	○	○
BDSM (e.g., bondage, dominance, and submission)	○	○	○	○	○	○
Public sex with casual partner(s) (e.g., cruising)	○	○	○	○	○	○

32. Please explain some of the reasons why these behaviours have changed? [open text]

_____

33. **Have you received a letter about shielding from the Government due to being part of the high-risk group?** YES/NO
34. **Are you, or have you previously, self-isolating because you or someone in your household have symptoms of Coronavirus?** YES/NO
35. **Are you a key worker?** YES/NO
36. **Have you experienced any changes to physical or mental health due to the lockdown measures?**

Yes (please provide a brief explanation) _____ No

37. **How concerned are you with catching Coronavirus?**

Extremely concerned Somewhat concerned Not concerned

Don't think about it

38. **What do you think is your level of risk of catching Coronavirus?**

Extremely likely Somewhat likely Neither likely nor unlikely

Somewhat unlikely Extremely unlikely

39. **Do you agree with the lockdown measures used?**

Strongly agree Somewhat agree Neither agree nor disagree

Somewhat disagree Strongly disagree

40. **Do you wear a face covering when leaving the house?** YES/NO
41. **Prior to the lockdown (23rd March), did you alter any of your behaviours (e.g., start to limit social interactions) when you heard Coronavirus cases were rising in Wales?** YES/NO
42. **Has the Coronavirus made you more concerned about other contagious diseases/infections?**

YES/ SOMEWHAT/ NO

43. **What infections do you now have higher concern for? (please tick all that apply)**

Flu/Common cold Pneumonia

Severe acute respiratory syndrome (SARS) Sexually transmitted infections (STIs)/HIV

Other (please state) _____