Changes in sexual behaviour, pre-exposure prophylaxis use and HIV incidence among gay, bisexual, and other men who have sex with men in England

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Declaration

I, Nadia Hanum, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

The identification of longitudinal changes in sexual behaviour over time, pre-exposure prophylaxis (PrEP) use, the incidence of HIV infection among HIV-negative GBMSM, and risk behaviours among HIV-positive GBMSM shortly after diagnosis is needed to improve HIV prevention efforts and is crucial to assess the potential risk of HIV spread in the community. Data from UK prospective studies are lacking.

Data from two prospective studies were used in this thesis. The AURAH2 (*Attitudes to, and Understanding of, Risk of Acquisition of HIV over time*) study recruited GBMSM who were HIV-negative from three large sexual health clinics in England with four-monthly online follow-up (2013 – 2018, 1,162 men completed baseline questionnaire, 622 men completed at least one follow-up questionnaire). The Guy's and St. Thomas' study enrolled newly diagnosed people from an HIV clinic in London and followed them up at weeks 12, 24, and 48 (2015 – 2018, 90 GBMSM included in analyses).

Among all men enrolled in AURAH2, past three months condomless anal sex with two or more partners (CLS2+, 46% to 47%, *p-trend*=0.010) increased slightly between 2013 and 2018. PrEP use in the past year also increased from 0% in 2013 to 43% in 2018 ($p<0.001$). HIV incidence declined from 1.47 per 100 PYs in 2013/2014 to 0.25 per 100 PYs in 2018/2019. Among a subset of men in AURAH2 with at least two consecutive questionnaires during follow-up, men reporting CLS2+ had an overall 78% probability of reporting CLS2+ in the subsequent questionnaires, and of men who reported none or one CLS partner, 88% reported the same in the subsequent period.

Among GBMSM newly diagnosed with HIV in the Guy's and St. Thomas study, the within-individual tendency for reporting CLS was that men reduced their behaviours from baseline (62%) to week 12 (45.2%), then increased again by 48 weeks (62%). The greatest increase at week 48 was seen in the frequency of CLS with serodiscordant partners (CLS-D; 14% at week 12 to 36% at week 48). The proportion of men having CLS-D with the most recent documented plasma viral load (VL) > 200 copies/mL at week 12 was almost 11%.

With HIV incidence declining among GBMSM in England and coinciding with a substantial increase in the use of PrEP, there is a clear need to focus prevention efforts on potential transmission risk. HIV providers should emphasize the importance of knowledge of viral suppression in decision making about CLS among newly diagnosed GBMSM.

Impact Statement

Detailed longitudinal data on the incidence and predictors of new infections among HIV-negative gay, bisexual, and other men who have sex with men (GBMSM) at risk of HIV infection would be helpful to inform the development of future HIV prevention strategies in England and the United Kingdom (UK). Data on emerging risk behaviours that may be linked to HIV acquisition in GBMSM, changes in sexual behaviour over time within people, and trends in pre-exposure prophylaxis (PrEP) use would also be crucial to inform and support health care professionals and clinical services in the provision of HIV promotion measures tailored to GBMSM and to inform mathematical models used to assess the impact of different prevention strategies (1-3). Among HIV-positive GBMSM, longitudinal data on changes following HIV diagnosis would be helpful to inform HIV transmission risk and prevention methods from HIV-positive to HIV-negative GBMSM.

Within academia, one published result of my thesis provided important data regarding longitudinal trends in PrEP use between 2013 and 2018 and predictors of PrEP initiation among GBMSM attending sexual health clinics in England, before PrEP was made freely available through the National Health Service England (NHSE) (4). The results highlighted the need for a free PrEP programme, as indicators of socioeconomic disadvantage were associated with a lower rate of PrEP initiation. Another published results of my thesis provided current data (2013 – 2019) in HIV incidence and characteristics predictive of HIV acquisition among GBMSM in England (5), which highlighted the decline in HIV incidence coincided with a significant increase in the proportion of men reporting prior 12-month PrEP use, consistent with previous data from the UK Health Security Agency (UKHSA) (6).

Furthermore, one of the results in my thesis, which is also the novel evidence from this thesis, demonstrated that the majority of GBMSM were low risk for HIV acquisition between 2015 and 2018, though they experience short periods in which they are at higher risk. The results highlighted that these men might benefit from PrEP as a tool that can be used for that short period of the enhanced risk, and the markers of transitions might be used to identify GBMSM who are likely to increase their risk and to ensure these men are informed about the available HIV prevention measures. Finally, my last results chapter provided data on changes in sexual behaviour post-HIV diagnosis among GBMSM in London. The results demonstrated that a high proportion of GBMSM with new HIV diagnoses continued to have sex, with the majority having CLS, highlighting the need for HIV providers to emphasize the importance of knowledge of viral suppression in decision making about CLS.

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List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
AUDIT-C	Alcohol Use Disorders Identification Test-Consumption
AURAH	Attitudes to and Understanding Risk of Acquisition of HIV
AURAH2	Attitudes to and Understanding Risk of Acquisition of HIV over time
BHIVA	British HIV Association
CAGE	Cut-annoyed-guilty-eye questionnaire
cART	Combination Antiretroviral Therapy
CI	Confidence Interval
CLS	Condomless Anal Sex
GAD-7	General Anxiety Disorder scale-7
GBMSM	Gay, Bisexual, and other Men who have Sex with men
HANDD	HIV and AIDS New Diagnosis and Deaths
HARS	HIV and AIDS reporting system
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
IRR	Incidence Rate Ratio
LTFU	Loss-To-Follow-Up
MSM	Men who have Sex with Men
OR	Odds Ratio
PHE	Public Health England
PHQ-9	The 9-question Patient Health Questionnaire
PrEP	Pre-exposure prophylaxis
PEP	Post-exposure prophylaxis
PYs	Person-Years
STI	Sexually Transmitted Infections
TasP	Treatment as Prevention
UCL	University College London
UKHSA	UK Health Security Agency
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Chapter 1: Introduction

This PhD thesis investigates the longitudinal changes and predictors of sexual risk behaviour, the use of pre-exposure prophylaxis (PrEP) and occurrence and predictors of new HIV diagnosis among HIV-negative gay, bisexual and other men who have sex with men (GBMSM) attending sexual health clinics in England during the period 2013 to 2018. This thesis also describes changes in sexual behaviour following HIV diagnosis and associated factors among newly diagnosed with HIV GBMSM attending a London clinic between 2015 and 2018.

This thesis will provide comprehensive longitudinal data on HIV incidence and predictors of new HIV infections among HIV-negative GBMSM who are at risk of HIV infection. It will also provide some of the first data on within-person changes in sexual behaviour and uptake of PrEP. These are crucial to inform and support health care professionals and clinical services in the provision of HIV prevention services among GBMSM in England and the United Kingdom (UK). Data on within-person changes in behaviour are also needed to inform mathematical models used to assess the impact of different prevention strategies (1-3). The findings will also be relevant to national policies targeted at reducing HIV incidence and increasing HIV testing in the UK among GBMSM. Longitudinal data on changes following HIV diagnosis will help to inform HIV transmission risk and prevention methods from HIV-positive to HIV-negative GBMSM.

This thesis uses data from two prospective cohort studies from the United Kingdom (UK): **The** '*Attitudes to, and Understanding of, Risk of Acquisition of HIV over time'* **(AURAH2)** study of HIV-negative GBMSM, and **The Guy's and St. Thomas'** study of people newly diagnosed with HIV.

This introduction chapter describes the thesis objectives, outlines the contents of each chapter and provides the background information to the thesis.

1.1 Thesis aims

This thesis has two specific objectives.

The first is to examine, among initially HIV-negative GBMSM attending sexual health clinics in England between 2013 and 2018:

(i) Trends over calendar year in sexual behaviour measures
(ii) Within-person changes in frequency and patterns of condomless anal sex with two or more partners and transition probabilities between sexual behaviour risk levels
(iii) Predictors of transitions between sexual behaviour risk levels and factors associated with reporting condomless anal sex with two or more partners
(iv) Trends over calendar year in the use of PrEP and post-exposure prophylaxis (PEP)
(v) Predictors of PrEP initiation and factors associated with reporting PrEP use
(vi) Trends over calendar year in HIV incidence
(vii) Baseline and time-updated factors associated with subsequent HIV infection

The second is to examine, among GBMSM newly diagnosed in an HIV clinic in London between 2015 and 2018:

(viii) Trends over one year of follow-up since baseline in the prevalence of sexual behaviour measures
(ix) Within-person changes in sexual behaviour measures
(x) Factors associated with sexual behaviour measures in the initial period after an HIV diagnosis and factors associated with stopping condomless sex

1.2 Thesis outline

The complete thesis structure is detailed as below:

Chapter 1 describes the thesis objectives (Section 1.1), the contents of each chapter (this section) and the background information to the thesis (Section 1.3). The background section provides an overview of HIV (including how HIV is transmitted, HIV treatment and prevention, and global HIV epidemiology). This section then focuses on GBMSM in the UK, describes risky sexual behaviours among GBMSM in the context of HIV and provides a brief review of major studies on temporal trends in sexual behaviour among GBMSM in the UK from 2000 to 2018 (when I embarked on my PhD).

Chapter 2 contains results from a systematic review and three scoping reviews that were designed to gather global information regarding within-person changes and temporal trends in sexual behaviour, PrEP use, and incidence of HIV among HIV-negative GBMSM, and to determine changes in sexual behaviour following HIV diagnosis among HIV-positive GBMSM, in the era of combination antiretroviral therapy (cART). The first literature review (systematic review) focuses on the global data concerning sexual behaviour changes (within-individual and trends over time) among HIV-negative GBMSM published between January 1998 and December 2018. It also presents data from articles that assess trends in HIV incidence and PrEP use and determine sexual behaviour changes following HIV diagnosis. The three additional scoping reviews collate three specific areas of literature published until August 2020 from observational studies among GBMSM in high-income countries, particularly the UK, on (i) recent evidence on HIV incidence, (ii) the use of PrEP and (iii) changes in sexual behaviour post-HIV diagnosis. This chapter also outlines the rationale for this PhD thesis.

Chapter 3 describes the design and methodology of the AURAH2 study used to address aims (i) to (vii). This includes recruitment routes, completion of AURAH2 questionnaires, the AURAH2 participants, the data linkage process between the AURAH2 data and the national HIV surveillance data managed by the UK Health Security Agency (UKHSA, formerly Public Health England) and the data management for the AURAH2 study that I completed as part of this thesis (including variable derivation and managing linked data from the UKHSA). The methodology of the second study used in this thesis is presented together with the results in Chapter 8.

The following Chapters (4 to 8) present the thesis results. Each of these chapters finishes with a discussion section, in which the results are discussed in the context of relevant previous studies, including studies published subsequent to the formal literature reviews presented in Chapter 2. The limitations of the finding are also discussed in the discussion sections.

Chapter 4 describes the baseline characteristics and risk factors for loss to follow-up among participants in the AURAH2 study. This chapter details the definition of non-participation and loss to follow-up, the measures and statistical analysis used to estimate the AURAH2 study attrition rates and associations of factors with non-participation or loss to follow-up.

Chapter 5 addresses specifically the Objectives (i), (ii) and (iii) of this thesis (see Section 1.1), relating to within-person changes in sexual behaviour among participants in the AURAH2 study. Results included in this chapter are trends between 2013 and 2018 in the prevalence of sexual behaviour measures, within-individual changes in the frequency of

reporting condomless anal sex with two or more partners during follow-up (2015 – 2018), the overall estimates of transition probabilities from higher-risk to lower-risk behaviour and vice versa and the predictors of transition probabilities in sexual behaviour, and factors associated with reporting higher-risk sexual behaviour.

Chapter 6 addresses specifically the Objectives (iv) and (v) of this thesis (see Section 1.1) regarding trends in PrEP and PEP use among participants in the AURAH2 study. First, the trends over time in awareness of PrEP and PEP at baseline are described, followed by longitudinal trends in the use of PrEP and PEP over the entire study period (2013 – 2018) among all participants enrolled in the AURAH2 study. The chapter then identifies predictors of PrEP initiation during follow-up limited to men who did not report the use of PrEP at baseline and compares the predictors of PrEP initiation with cross-sectional factors associated with reporting the recent use of PrEP among all men.

Chapter 7 addresses specifically the Objectives (vi) and (vii) of this thesis (see Section 1.1) concerning trends in HIV incidence among all participants enrolled in the AURAH2 study. First, the ascertainment process of incident HIV in the study is detailed, followed by the description of trends in HIV incidence between 2013 and 2019 and the association of baseline demographic, socioeconomic, health, lifestyle, and behavioural factors with subsequent incident HIV among all men enrolled in the study. This chapter then describes the association of time-updated factors with subsequent incident HIV among men who completed at least one online follow-up questionnaire and the overall HIV incidence rate among men in the online cohort.

Chapter 8 addresses specifically Objectives (viii), (ix) and (x) of this thesis (see Section 1.1), presenting the methods and results from analysis of changes in sexual behaviour post-HIV diagnosis using data from the Guy's and St. Thomas' study of people with newly diagnosed HIV. The methods section describes the study design, recruitment and data collection, data management, definitions of variables used, and statistical analysis. The results section presents the characteristics of participants included in the analysis, the overall prevalence and trends over one year of follow-up since baseline in sexual behaviour measures, and the factors associated with sexual behaviours at week 12 and week 48 after enrolment in the study.

Chapter 9 summarises the main findings from all results chapters, explains the strengths and weaknesses of the study design along with the interpretation of the results, discusses the potential implications of the thesis, and gives recommendations for public health policy and health care providers and future research. This chapter also outlines the publications and presentations arising during this PhD thesis.

1.3 Background to the thesis

1.3.1 Human Immunodeficiency Virus (HIV)

AIDS (Acquired Immune Deficiency Syndrome) first manifested clinically in the early 1980s in Los Angeles after cases of unusual opportunistic infections were reported, predominantly among previously healthy gay men (7). The first reports of this syndrome in the UK appeared in late 1981 (8). AIDS is caused by Human Immunodeficiency Virus (HIV), a retrovirus that can spread by sexual, percutaneous, and perinatal routes. However, HIV is primarily a sexually transmitted infection as 80% of adults with HIV acquire the virus through exposure to genital mucosal surfaces (9-11).

Continuous high-level HIV replication in the human body leads to virus and immune-mediated destruction of the key immune effector cell, the CD4 lymphocyte (12). Over time, the decline in CD4 lymphocytes leads to opportunistic infection, defining AIDS (13). Shortly after infection, individuals become viraemic, and at this stage, HIV is detectable in the plasma. About four to six weeks after infection, antibodies to HIV become detectable. Most infected individuals seroconvert by three months and become HIV antibody-positive. Initially, there are high levels of circulating HIV resulting from rapid replication in infected cells, and patients can be symptomatic with features of primary HIV infection. After a specific antibody has developed, viral levels decline to reach a steady state, and patients generally remain asymptomatic for several years (14). Over time, CD4 lymphocyte numbers gradually decline because of viral killing, eventually to a point where cell-mediated immunity is affected, and the individual is susceptible to opportunistic infections, HIV-associated nephropathy (deterioration of kidney function), dementia and cancers (15, 16).

There are two types of HIV: HIV-1 and HIV-2, with HIV-1 being the prevalent virus globally (11). HIV-2 is only responsible for comparatively few infections confined mainly to West Africa. HIV-2 causes a similar illness to HIV-1, but immunodeficiency progresses more slowly, and the virus is less transmissible (11, 17). From this point onwards, unless stated otherwise, the term HIV refers to HIV-1.

1.3.1.1 HIV transmission and risk

Different transmission routes and risk behaviours play essential roles in facilitating HIV transmission (18). HIV is transmitted through direct contact with bodily fluids (blood, semen, vaginal secretions, breast milk). Babies born to HIV-infected women may become infected before or during birth or through breastfeeding after birth (19). Heterosexual transmission is responsible for nearly 70% of HIV infections worldwide, with the remainder mainly attributable to sex between men, maternal-infant infection, and injection drug use (18).

The number of copies per millilitre (mL) of plasma HIV ribonucleic acid (RNA) or viral load is a significant factor in determining the risk of HIV sexual transmission (20). Among HIV discordant couples, a two and half-fold increase in transmission probability was observed for every ten-fold increase in viral load (21, 22). The clinical-stage of infection (acute, middle, late) in the transmitting partner can also play a key role in defining the efficiency of transmission due to variation in viral load levels during the different stages, with the risk of transmission from individuals with acute or early infection being higher than that in established infection (23, 24).

Other factors that can modulate HIV transmission in the absence of treatment include sexually transmitted infections (STIs), particularly those that result in genital inflammation and ulcers, as they can elevate HIV shedding into the genital tract and can increase infection susceptibility by two- to 11-fold (25); pregnancy, during which a greater than two-fold increase in HIV acquisition risk has been observed (26); and circumcision, which in three large clinical trials have been shown to reduce the acquisition of HIV in the male partner by between 38% and 66% over 24 months (27).

1.3.1.2 HIV treatment and prevention

Early access to antiretroviral therapy (ART) and support to remain on treatment is critical to prevent the progression of HIV (28, 29). Current ART does not cure HIV infection but highly suppresses viral replication within a person's body and allows an individual's immune system to recover and regain the capacity to fight off opportunistic infections and some cancers (28). Overall life span has lengthened for individuals with HIV, with data suggesting that individuals with HIV who initiate ART at high CD4 cell counts may reach a similar life span as individuals without HIV (30, 31).

ART also plays a vital role in reducing the transmission of HIV. People with HIV taking ART who are virally suppressed do not transmit HIV to their sexual partners (32-34). Since 2016, the World Health Organization (WHO) has recommended that all people with HIV be provided with lifelong ART, regardless of clinical status or CD4 cell count ('treat all' strategies) (35, 36). In addition, the WHO recommends a rapid ART initiation by offering ART on the same day as diagnosis ('test and treat' strategies) to decrease community viral load (28). Besides the use of ART for HIV prevention, other vital approaches to reduce the risk of HIV transmission, which are often used in combination, including condom use (male and female) (37), testing and counselling for HIV (38), STIs treatment and linkages to tuberculosis (TB) care, voluntary medical male circumcision (VMMC), harm reduction for people who inject and use drugs, elimination of mother-to-child transmission of HIV (39) and use of PrEP (40).

PrEP is the use of ART by HIV-negative individuals to prevent the acquisition of HIV and is highly effective (40-42). The principle of PrEP is that if the person taking PrEP is exposed to HIV, the anti-HIV drugs in their body stop the virus from entering cells and replicating (43). PrEP prevents HIV from establishing itself and stops the person from acquiring HIV (43). Research shows that PrEP works for heterosexual men and women (44), cisgender and transgender people (45), and gay, bisexual, and other men who have sex with men (40). It has been more than a decade since the first evidence of the efficacy of daily oral PrEP was published (46). PrEP is now a valuable additional option for people at higher risk of HIV. Increased PrEP provision is contributing to reductions in new HIV infections. Besides the widespread use of ART as HIV prevention, steep drops in new HIV diagnosis in the United Kingdom (UK) and Northern Ireland (6), Australia (47) and the United States of America (US) (48) during 2012 – 2016 have been associated with the population-level impact of PrEP use. The global uptake of PrEP has continued to increase, despite the COVID-19 pandemic, with country data showing that in 2020 there was a 43% increase since 2019 in the number of people who received PrEP globally (49, 50). However, access is still poor in many countries (51), and even in countries with widespread PrEP availability, such as the US, inequalities are apparent in PrEP use, with disparities according to ethnicity and socioeconomic, geographic, and demographic factors (52).

1.3.1.3 Global epidemiology of HIV

HIV is a significant contributor to the global burden of disease. In 2020, there were 37.7 (30.2–45.1) million people living with HIV, including 10.2 (9.8–10.2) million who were not on treatment, 1.5 million new HIV infections (1.0–2.0), and 680,000 (480,000–1 million) AIDS-related deaths (50). Among those not on treatment, about 4.1 million did not know their HIV-positive status, and 6.1 million knew their HIV status but did not access treatment (50). The global ART coverage at the end of 2020 was 73% (56-88%), which equates to 27.5 (26.5–27.7) million people living with HIV who were receiving ART (50). The 90-90-90 UNAIDS targets were missed globally, with 84% of people living with HIV knowing their HIV status, 87% of people living with HIV who knew their HIV status taking ART, and 90% of people on treatment virally suppressed (49).

The global roll-out of ART has saved millions of lives, with an estimated 16.6 (11.7–24.2) million AIDS-related deaths have been averted over the last two decades, including a 47% decline in AIDS-related mortality since 2010 (50). Efforts to prevent HIV infections, however, have been less successful. The annual number of new infections among adults globally has hardly changed, and total new infections have declined by just 31% since 2010 (50). Many countries have failed to implement the combination of structural, behavioural and biomedical

approaches to HIV prevention focused on those at most significant risk (49). For example, consistent condom use, although possible, has proved difficult to achieve among all populations; coverage of PrEP and VMMC in 2020 also was well below the targets set five years earlier (49). Overall, key populations (people who inject drugs, transgender people, female sex workers, and gay men and other men who have sex with men) and their sexual partners accounted for 65% of HIV infections worldwide in 2020 and 93% of infections outside of sub-Saharan Africa (50). Key populations continue to be marginalized and criminalized for their gender identities and expression, sexual orientation and livelihoods (53).

In the UK specifically, the HIV epidemic is relatively small and concentrated, with an estimated 105,200 (103,300–108,500) people living with HIV by the end of December 2019 (54). Undiagnosed patients accounted for 6,600 (4,900–9,800) of the totals, or 6% (5–9%). From a peak of 6,312 new HIV diagnoses reported in 2014, the overall number of people newly diagnosed with HIV declined by 34% in 2019, to 4,139 (54). For the third year in a row, in 2019, the UK met the UNAIDS 90-90-90 target nationally, with 94% of people living with HIV being diagnosed, 98% of those diagnosed being on treatment and 97% of those on treatment having an undetectable viral load. In London, the equivalent figures were 95%, 98% and 97%, meeting the 2030 95-95-95 target for the second consecutive year (55). The continued drop in new HIV diagnoses is positive, and the widespread use of ART and subsequent viral suppression is a significant achievement. However, there are still twice as many people living with HIV outside of London as in the city.

1.3.2 Gay, Bisexual, and other Men who have Sex with Men (GBMSM) and HIV

Men who have sex with men (MSM) is a term introduced in HIV literature since the 1990s used to describe men engaging in sexual activity with other men, regardless of how they identify themselves (56). Therefore, this encompasses men who self-identify as gay or bisexual as well as men who do not (57, 58). Although men who have sex with men is a neutral term commonly used in public health discourse, it has received criticism for its potential to undermine the self-labelling of gay, and bisexual people, its failure to capture relationships holistically and its inadequacy in conveying variations in sexual behaviour (59). Therefore, the term gay, bisexual, and other men who have sex with men (GBMSM) is used throughout this thesis.

GBMSM is a key population group affected by HIV. The risk of acquiring HIV is 25 times higher among GBMSM than the general population (60). In 2019, an estimated 23% of new adult HIV infections were among GBMSM globally (61). HIV has become endemic in GBMSM populations in many high-income settings, including the UK, the US, the

Netherlands and Australia (62). This population accounted for nearly 64% of new infections in Western and Central Europe and North America (61). Data suggest that individual-level, network-level, biological, and community drivers are crucial to understanding why HIV transmission rates have stayed high in this population (58, 63).

Individual-level behaviours that are particularly linked to HIV acquisition risk include anal intercourse without a condom (condomless sex), a high number of sex partners, HIV status of partners, treatment and viral load in the index partner, and whether PrEP is being used (64-67). In terms of sexual practices, role reversal, whereby individuals practise both insertive and receptive anal sex, is practised by significant proportions of GBMSM (68-70). Role reversal can aid HIV transmission by overcoming the low HIV acquisition probability from receptive to insertive partners because an individual can be infected through receptive sex and transmit through insertive sex. Systematic reviews and meta-analysis of HIV transmission risks with anal sex reported a 138 per 10,000 per-act probability for unprotected receptive anal sex compared to 8 per 10,000 exposures for unprotected receptive vaginal sex (71, 72). The sexual network-level risk is also crucial as HIV can be transmitted through large GBMSM networks at great speed (73-75).

STIs have also been associated with biological risk for HIV infection in GBMSM, notably syphilis and gonorrhoea. Several biological mechanisms cause the synergy between HIV and STI epidemics (76, 77). Infections that disrupt the epithelial surface of the genital tract may boost acquisition by facilitating the access of HIV to target cells under the epithelial surface, thus increasing the probability that HIV can establish a systemic infection. Ulcers in both partners can facilitate blood to blood contact and thereby transmission, while STIs in the HIV infected partner can increase viral shedding in the genital tract (76, 77). One retrospective study in London observed early syphilis as a risk factor for HIV acquisition among 206 GBMSM who received a diagnosis of primary, secondary or early latent syphilis in a large sexual health clinic in 2014, predicting an HIV incidence of 8.3 per 100 person-years (PYs) in a real-life setting (78). Syphilis as an independent predictor of HIV acquisition has also been found in a cohort of 8,925 GBMSM in San Diego between 2008 and 2014 (Hazard Ratio, HR 4.67) (79), among 2,805 GBMSM between 2000 and 2010 in New York City (HIV incidence 5.6 per 100 PYs) (80), and among 2,499 GBMSM who participated in the multinational iPrEX study, where an HIV incidence of 8.0 per 100 PYs was discovered, and an HR of 2.6 was estimated versus no syphilis (81). Infection with herpes simplex virus type 2, anal infection with human papillomavirus, and hepatitis C virus also have been found to be associated with HIV infection among GBMSM (82-84).

In many settings, stigma and discrimination related to homosexual activities have also been major barriers against GBMSM seeking essential HIV and health services (63). Homosexuality is illegal in many countries, with the risk of imprisonment or even death (85). In the United Kingdom, findings from the people living with HIV Stigma Survey UK in 2015 reported that compared to heterosexual men, gay men were significantly more likely to report worrying about workplace treatment concerning their HIV, worrying about HIV-related sexual rejection, avoiding sex because of their HIV status, and experiencing HIV-related sexual rejection in the past 12 months (86). The study also found that, in a multivariate logistic regression controlling for other socio-demographic factors, being gay was a predictor of reporting HIV-related sexual rejection in the past 12 months (86). The ethnic and racial minorities within the GBMSM community also carry a disproportionate burden of HIV (87). These groups may have particular barriers to accessing health care, thus limiting the potential effectiveness of prevention strategies, such as ART and PrEP. According to a 2014 poll of Black GBMSM Africans living with HIV in the UK, a third reported having faced discrimination due to their HIV status (88). Half of those facing discrimination said health care professionals, including doctors, dentists and hospital staff, had discriminated against them. As a result, some people have lost faith in health care confidentiality.

1.3.2.1 Treatment as Prevention among GBMSM

Treatment as Prevention (TasP) refers to the use of ART to prevent HIV transmission by prescribing antiretroviral (ARV) drugs to those who are living with HIV in order to reduce the amount of virus in their blood to undetectable levels so that there is effectively no risk of transmission of HIV (89, 90). TaSP has solid biological reliability, with studies in the UK demonstrating that effective ART is associated with a marked reduction in virus activity in blood, semen and cervical mucosa (91, 92). Results from the second phase of the PARTNER study (PARTNER2), a large prospective observational study conducted in 14 European countries, were published in 2019. The study that enrolled 972 serodiscordant gay couples who reported condomless sex during 2010-2018 reported no phylogenetically linked within-couple transmissions, suggesting the risk of HIV transmission in gay couples through condomless sex when HIV viral load is suppressed is effectively zero (33). During 2012-2016, the Opposites Attract study, an observational longitudinal cohort study of male homosexual serodiscordant couples conducted in clinics throughout Australia, Brazil and Thailand also found no phylogenetically linked HIV transmissions between 343 gay couples where the HIV-positive partner had a viral load under 200 copies/ml, the negative partner was not taking PrEP, and they did not use a condom (34). In doing so, these studies added the evidence that people with HIV who had an undetectable viral load were not infectious or,

to quote the campaign that has become a global brand, **undetectable = untransmittable (U=U)** among gay men (93).

1.3.2.2 Use of Pre-exposure prophylaxis among GBMSM

PrEP consisting of oral tenofovir-emtricitabine (TDF-FTC) taken daily or on-demand prior to potential risk exposure is highly efficacious in preventing HIV infection in GBMSM (40, 41, 46). The iPrEx multinational trial, conducted among 2,499 men or transgender women who have sex with men in Peru, Ecuador, Brazil, Thailand, South Africa and the US during 2007-2009, reported the efficacy of daily dose of FTC-TDF at 43%, as compared to placebo (46). In 2015, the PROUD trial, an open-label trial done at 13 sites in England among 544 HIV-negative GBMSM, observed the highly protective effect of PrEP at 86%. This created momentum for PrEP related work in Europe, especially as the study also showed high adherence to the use of PrEP (40). The third trial to show a significant reduction in HIV infections with PrEP was the multi-centre IPERGAY randomized trial, conducted among 414 GBMSM in France and Canada during 2012–2014 (41). The trial also showed the efficacy of on-demand oral PrEP at 86%.

Data are emerging on the uptake of PrEP within PrEP programmes from high-income countries other than the UK, usually available through prescription data and health service data. In the US, an analysis of electronic prescription data from approximately 80% of retail pharmacies between 2012-2016 by Gilead (manufacturer of Truvada) found that 98,732 people started PrEP during this period and estimated that 136,000 people in the US were on PrEP by the end of the second quarter of 2017 (did not include non-retail pharmacy prescriptions) (94). Uptake of PrEP within the population was characterized by slow initial uptake, followed by an acceleration and then a steady state (94). Data from the cross-sectional National HIV Behavioural Surveillance (NHBS) System in 20 US cities in 2014 found that only 4% of surveyed GBMSM reported using PrEP, but more than half reported that they would be willing to take it and that PrEP use was higher among White compared with Black GBMSM and among those with greater education and income levels (95). A PrEP programme in New South Wales in Australia has enrolled over 6,500 participants over 70 weeks with steady enrolment (96). While in France, 2,805 people had started on PrEP in the first year of the programme in 2017 (97).

1.3.3 HIV among GBMSM in the UK

1.3.3.1 Decline in new HIV diagnosis and incidence among GBMSM in the UK

Since the 1980s, GBMSM has remained the group most at risk of acquiring HIV infection, and one of the key groups for which controlling the HIV epidemic remains a public health priority in the UK (98, 99). Of the 4,139 new HIV diagnosis in the UK in 2019, 1,700 (41.1%) new HIV diagnoses were among GBMSM. In 2017, an estimated 48,900 GBMSM were living with HIV in the UK, with around 4,200 with undiagnosed HIV. This means roughly 83 out of every 1,000 GBMSM (aged 15-74) were living with HIV. It is an even greater number in London, with 134 out of every 1,000 living with HIV (100).

The decline in new HIV diagnosis in recent years in the UK is primarily driven by a steep fall in diagnoses among GBMSM, from a peak of 3,214 in 2014 to 1,700 diagnosed in 2019 (a 47% drop) (54). Those of White ethnicity (2,550 in 2014 and 1,107 in 2019), born in the UK (1,869 in 2014 and 715 in 2019), aged 15 to 24 (449 in 2014 and 222 in 2019), and living in London experienced the most considerable reductions (1,542 in 2014 and 702 in 2019). Incidence trends estimated using a CD4 back-calculation model (101) among GBMSM show a sustained decline since 2011, preceding the steep fall in new HIV diagnoses. During this time, the projected number of incidents of HIV infections in England fell by 80%, from a high of 2,700 in 2011 (95% credible interval (Crl) 2,520-2,850) to a low of 540 in 2019 (95% Crl 180-1,810).

An 18% increase in GBMSM tested for HIV was observed from 103,296 in 2015 to 122,010 in 2019 (54). This represented 12% of everyone tested at specialist sexual health services (SHS). The 794 GBMSM who tested positive in 2019 at SHS accounted for 52% of all new HIV diagnoses in this setting. HIV positivity among tests done in GBMSM has continued to fall (0.7% in 2019), with most (85%) GBMSM newly diagnosed with HIV having not been tested in the previous year.

1.3.3.2 HIV prevention among GBMSM in the UK

HIV elimination in the UK can be achieved by combining preventative strategies such as high levels and frequency of HIV testing, PrEP programme, rapid linkage to care and treatment, and support to ensure that people with HIV attain viral suppression (102). Treatment as prevention strategies based on ‘test and treat’ were enhanced between 2011 and 2015 to manage the HIV epidemic among GBMSM in England (103).

Economic modelling has suggested that TasP is a cost-effective approach and is likely to be cost-saving over 15 years in GBMSM, due to the resulting reductions in transmission and, therefore, people needing treatment (2). Analysis undertaken by the UKHSA in developing

the TasP policy has shown that 1,800 new HIV infections will be prevented, with an overall saving of between £500-647 million to the National Health Service (NHS) (104). In the UK, an HIV test every three months (rather than every six months) for the most at-risk GBMSM was recommended in 2012 (105), and new guidelines were issued to offer ART to those with a CD4 count of less than 350 cells per µL (106), followed in 2013 by a position statement recommending that healthcare professionals discuss the use of ART to reduce the risk of transmission with all people living with HIV (107). In 2015, immediate ART initiation was recommended for all people newly diagnosed with HIV infection (108, 109).

Following evidence on the efficacy of PrEP in GBMSM when taken consistently from the PROUD trial (40), in 2015, internet sites were established to facilitate the self-purchase of PrEP from abroad. An online survey of GBMSM indicated that PrEP usage quadrupled during 2016, with an estimated 3000 GBMSM taking PrEP by the end of the year (110). The British HIV Association / British Association for Sexual Health and HIV (BHIVA/BASHH) guidelines on the use of HIV PrEP recommend that PrEP with on-demand or daily oral TDF-FTC should be offered to HIV-negative GBMSM who are identified as being at elevated risk of HIV acquisition through condomless anal sex in the previous six months and ongoing condomless anal sex, and/or GBMSM having condomless anal sex with partners who are HIV positive (unless the partner has been on ART for at least six months and their plasma viral load is <200 copies/mL (111). Daily PrEP is recommended as one effective option for GBMSM at substantial risk of HIV acquisition (112). A modelling study in the UK, in which 40,000 men who have sex with men initiated event-driven PrEP during a 15-year period, showed that 25% of new HIV infections could be averted by this cost-effective and ultimately cost-saving program (113). Overall, the cost-effectiveness was observed to be highly dependent on HIV incidence of the population taking up PrEP, HIV prevalence, PrEP drug cost, PrEP efficacy, rate of HIV diagnosis in the population and cost of antiretroviral treatment for the HIV-positive population (111).

In England, from October 2017 to July 2020, PrEP was only available freely as part of the PrEP Impact Trial (114). During the trial, over 24,000 people had access to PrEP, most of whom were GBMSM (96%). Data from February 2020 showed that participants in the trial were more likely to be White (76%) and aged 25 to 39 years (median age 33 years), with just under 3% identifying as women and 1.5% Black African (115). Routine PrEP availability began in the autumn of 2020 through specialist sexual health services (116); however, due to the COVID-19 pandemic, some services have been delayed. Community surveys indicate that a minority of gay and bisexual men stopped taking PrEP because of reduced sexual activities during COVID-19 social restrictions (117).

In Scotland, PrEP has been rolled out across the country by the NHS Scotland since July 2017, while in Wales, a three-year pilot began in July 2017 via Genito Urinary Medicine (GUM) clinics (118). The results on the first eight months of PrEP implementation in Scotland (July 2017 – February 2018) showed that providing PrEP in sexual health clinics is feasible with higher than expected uptake and reaches people at high risk who were previously not engaging in care (119). Among 117,000 individuals who attended SHS (8,082 were gay and bisexual men), 2,517 PrEP prescriptions were provided to 1,295 individuals, of which 96% were GBMSM.

1.3.4 Risky sexual behaviours among GBMSM in the context of HIV

Condomless anal sex (CLS) and high numbers of sexual partners are common among GBMSM, which I describe in Sections *1.3.4.1* and *1.3.4.2* below. GBMSM also report serosorting, meaning selecting partners perceived to be the same HIV serostatus. Compared to consistent condom use, serosorting presents a higher risk of HIV infection if men do not know they are infected with HIV (120, 121).

There is also evidence that the use of recreational drugs is common among GBMSM and associated with risky sexual behaviour (122, 123). In particular, 'chemsex', a term used to describe intentional sex under the influence of specific psychoactive drugs (mephedrone, γ-hydroxybutyrate (GHB), γ-butyrolactone (GBL), and methamphetamine), may facilitate sexual sessions lasting several hours or days with multiple sexual partners (124). The publication of "The Chemsex study" in 2014 provided the first paper to describe chemsex in the UK comprehensively (125). The results of this study among 15,423 European MSM Internet Survey (EMIS) respondents between 2013 and 2014 who were resident in England highlighted that whilst chemsex was only engaged in by a minority of GBMSM (10% of GBMSM in Lambeth, Southwark and Lewisham (LSL) had used GHB/GBL and 10% had used mephedrone, <5% had used crystal methamphetamine, all in the last four weeks), the complex array of issues to men's health, including potential for increased HIV/STI transmission, psycho-social issues, mental health and well-being, and physical harms related to individual drugs used in chemsex, were of significant concern (125). The report noted that there were few services in place for GBMSM in sexual health services that were competent to address the psychosocial aspects of health and harm arising from chemsex, and that there was a lack of harm reduction information relating to chemsex in gay men (123).

1.3.4.1 Patterns in sexual behaviour among GBMSM over time

Among GBMSM, sexual behaviour has been influenced by important population episodes. After the HIV outbreak in the early 1980s, a reduction in sexual risk behaviour, for example, condomless anal sex and high number of sexual partners, was observed (126, 127). Following that, a resurgence in risk behaviour was reported after the introduction of cART in the mid-1990s (128, 129). A systematic review of studies conducted in high-income countries that examined behavioural trends from 1990 to 2013 indicated increasing sexual risk behaviours, including condomless anal sex and high numbers of partners, over time among GBMSM, with the increases seen in North America, Australia, and Europe (130), in the trends of CLS with casual partners, main partners and partners of unknown or discordant HIV status. During the period 1980 to 2010, while the scale-up of early detection and treatment might make the end of the HIV epidemic possible, there was evidence that reductions in condom use might jeopardize the population-level benefits of cART (131). Data at the individual level on sexual behaviour changes among GBMSM is limited, with few studies suggesting a variation within-individual (132, 133).

Studies suggest that the prevalence of high-risk sexual behaviours in GBMSM increased after cART was available because of optimism about HIV treatment, relating to the reduced morbidity and mortality and the reduced risk of transmission (134, 135). Condom fatigue, personal preferences about condoms, complacency about HIV, availability of other prevention options, and the adoption of serosorting strategies may have eroded consistent condom use and increased CLS (136-138). Other potential correlates of CLS that have been examined in the literature include drug and alcohol use, depression, and increased access to the internet and mobile app for seeking sexual partners (139-142).

In the era of **U=U**, the effectiveness of the TasP strategy would hinge on the inter-play among high-risk behaviours, viral load suppression and changes in the sexual connections among GBMSM before and after HIV diagnosis. Over the years, new infections through male-to-male sexual contact are ongoing, implying that condomless sex remains prevalent also among HIV-positive GBMSM, especially those with non-suppressed viral load. A thorough understanding of the pattern of risk behaviours among HIV-positive GBMSM, both before and after their diagnosis, would be crucial to assess the potential risk of HIV spread in the community. Some studies have reported reductions in sexual behaviours associated with HIV transmission after HIV diagnosis, including declines in number of sexual partners, increases in condom use, and declines in condomless anal sex (143-145). Transmission risk to HIV-negative persons should theoretically become lower with these behavioural changes adopted by newly diagnosed GBMSM. However, both the prevalence and persistence of

reduced risk behaviours among HIV-positive GBMSM remain unclear in light of ongoing HIV transmission in some countries, including the UK.

1.3.4.2 Trends in sexual behaviour among GBMSM in the UK

To gain insight into the trends in sexual behaviour among GBMSM after the availability of cART, I summarize previous UK studies published between 2000 and 2018 that examined trends (data for at least two-time points) in sexual behaviour among GBMSM. Relevant sexual behaviours included are condomless anal sex with any partners, casual partners, main or regular partners, and condomless anal sex with serodiscordant or unknown HIV status partners. As shown in Table 1.1, these studies were primarily cross-sectional studies from convenience sample surveys, which observed increases in condomless anal sex in the UK, England and Scotland from 1990 until 2016.

Between 1990 and 2000, data from two large-scale, probability sample surveys of the general population; the National Surveys of Sexual Attitudes and Lifestyles ('Natsal') (N=6,000 in 1990 and N=4,762 in 2000), provided evidence that among British GBMSM (n=100 in 1990 and n=175 in 2000), the prevalence of CLS with any partners increased (32% versus 59.8%) (146). Between 1996 and 2000 in London, a series of five cross-sectional surveys of men attending selected gay community venues reported that the proportion of men having CLS increased significantly each year from 30% in 1996 to 42% in 2000 (147). Between 1998 and 2003, the percentage of gay men using London gyms reporting CLS with a casual partner of unknown or discordant HIV status also increased (6.8% to 16.1%), with patterns seen for HIV-negative, positive, and never tested men alike regardless of age (148). There was no significant change in the percentage of men reporting condomless anal sex with a main partner alone (7.8% to 5.6%) (148). Annual health surveys conducted among gay men in London in 1996, 1999 and 2002 reported that CLS with any partners, CLS with partners of unknown/discordant HIV status, and CLS with more than one partner increased significantly in 1999 and 2002 compared to 1996 (149). Between 1998 and 2008, also among GBMSM who used London gyms surveyed annually, Lattimore and colleagues reported an increase in CLS with partners of the same status, particularly in HIV-negative GBMSM, from 12% in 1998 to 21% in 2008 (150).

In the period of 2001 – 2008, using data from the large internet-recruited surveys in England, an increase in CLS among men with diagnosed HIV and an increase in insertive CLS with HIV-positive men among men never tested for HIV were also observed (151). Over the period 2000 – 2013 in London, A serial cross-sectional study by Aghaizu and colleagues that recruited GBMSM from gay social venues showed that irrespective of the positive changes

in testing uptake, risk behaviour has increased over 14 years, characterised by increased CLS and numbers of sexual partners, particularly in HIV-negative men (152). Finally, cross-sectional data from two studies that recruited HIV-negative GBMSM from sexual health clinics in England, the 2013 – 2014 AURAH cross-sectional study (153) and baseline data (2014 – 2016) from the AURAH2 prospective study analysed in this thesis (154) observed a higher proportion of men reported CLS and CLS with two or more partners in the AURAH2 study compared with the AURAH study (155).

The increasing trends were also described in Scotland. Data from three waves of cross-sectional surveys that took place in Glasgow and Edinburgh between 1999 and 2002 reported that high-risk sexual behaviour among homosexual men in Scotland increased (156). Another cross-sectional data from eight self-report surveys between 1996 and 2008 in commercial gay venues in Glasgow and Edinburgh also reported that the percentage of CLS with two or more partners reported in the previous 12 months increased significantly between 2000 and 2002, adjusted for age group; however, the behaviour did not change significantly between 2002 and 2008 (157).

Data from the studies above have provided important insight regarding the increasing trends in condomless anal sex measures since cART was available in the UK among GBMSM. However, given their study designs, none of these studies provided longitudinal data at the individual level. To study more about within-person changes and patterns in sexual behaviour among GBMSM, I further conducted a systematic review on this topic. I summarize the systematic review findings and outline my PhD thesis's rationale based on my literature review findings in the next chapter, Chapter 2.

Table 1.1 Summary of studies on temporal trends in condomless anal sex among GBMSM in the UK published during 2000 – 2018

First author (year); location	Study design; sampling method	Years of data collection	Sample characteristics	Results
Dodds (2004); London	5 cross-sectional surveys; gay venues-based recruitment	1996 – 2000 (annually)	N total: 8,052 GBMSM Median age: 32 years 89% White ethnicity HIV +: 10.9% (in 2000)	• CLS in the past year increased from 30% in 1996 to 42% in 2000 (p<0.001) • CLS with discordant partners did not change (~16%)
Mercer (2004); the UK	2 stratified probability sample surveys of the general population	1990 and 2000	N 1990: 6,000 (100 GBMSM) N 2000: 4,762 (175 GBMSM) Mean age: 31.5 years No info on HIV prevalence	• CLS in the past year increased from 32% in 1990 to 59.8% in 2000 (OR 2.08, 95% CI 1.08-4.00) • 46% GBMSM reported five or more partners in the past 5 years
Elford (2004); London	Annual behavioural surveillance; gay venues-based recruitment	1998 – 2003 (annually)	N total: 4,264 GBMSM HIV +: 654 (15.3%) HIV -: 2652 (62.2%) never tested: 958 (22.5%)	• CLS in the past 3 months with casual partners increased from 6.7% in 1998 to 16.1% in 2003 (p<0.001) • CLS with main partners did not change (7.8%, 5.6%, p=0.7)
Hart (2005); Glasgow, Edinburgh	repeated cross sectional studies; gay venues-based recruitment	1996, 1999, 2002	N total: 6,508 GBMSM N 1996: 2,276; N 1999: 2,498; N 2002: 1,734 No info on HIV prevalence	CLS with casual partners increased from 10.7% to 18.6% over the period 1996 – 2002 (p<0.001)
Williamson (2006); London	sex health surveys; gay venues-based recruitment	1996, 1999, 2002	N total: 4,588 GBMSM N 1996:1,895, m age: 30 years N 1999: 1,368, m age:32 years, HIV +: 13% N 2002: 1,325, m age: 33 years HIV +: 11%	CLS with any partners, partners of unknown or discordant HIV status, and CLS with more than one partners increased in 1999 and 2002 versus 1996: • OR any CLS: 1999: 1.43 (95% CI 1.23-1.66), 2002: 1.60 (95% CI 1.37-1.86) • OR CLS with discordant HIV status: 1999: 1.28 (95% CI 1.05-1.55), 2002: 1.41 (95% CI 1.16-1.71) • OR CLS with more than one partner: 1999: 1.64 (95% CI 1.32-2.04), 2002: 1.76 (95% CI 1.42-2.19)
Knussen (2011); Glasgow, Edinburgh	8 cross-sectional surveys; gay venues-based recruitment	1996, 1999, 2000, 2002, 2005, 2008	N total: 10,223 GBMSM 1996: N: 2,184. 1999: N: 2,244. 2000: N: 713. 2002: N: 2,106 2005: N: 1,646.	CLS with 2 or more partners increased between 2000 and 2002, but not between 1996 and 2002 and between 2002 and 2008: • aOR 1996–1999: 0.93 (95% CI 0.75 - 1.15) • aOR 1999–2000: 0.98 (95% CI 0.73 - 1.32) • aOR 2000–2002:1.68 (95% CI 1.26 - 2.23)

First author (year); location	Study design; sampling method	Years of data collection	Sample characteristics	Results
			2008: N: 1,330 (no data on HIV prevalence, age or other demographic)	• aOR 2002–2005:1.05 (95% CI 0.87 - 1.26) • aOR 2005–2008:1.06 (95% CI 0.86 - 1.32)
Lattimore (2012); London	Annual surveys as part of behavioural surveillance program; gay venues-based recruitment	1998 – 2005 (annually), 2008	N total: 6,064 GBMSM HIV +: 16.5% Median age increased from 35 to 41 years (HIV +), from 33 to 37 years (HIV -) during 1998-2008	• CLS with partners of the same status increased from 12% in 1998 to 21% in 2008 among HIV-negative (p<0.05) • CLS increased from 24.3% in 1998 to 36.6% in 2008 (p = 0.07)
Hickson (2012); England	2 annual sexual health surveys (*The Gay Men's Sex Survey*); recruitment through booklet and the internet	2001, 2008	N 2001: 3,517 GBMSM; HIV +: 3.4 %; median age: 29 years; 94.1 % White ethnicity N 2008: 1,382 GBMSM; HIV +: 9.1 %; median age: 36 years; 92.4% White ethnicity	• CLS in the past year increased from 89.2% in 2001 to 90.3% in 2008 (p<0.05) • number of sexual partners did not change • serosorting did not change
Aghaizu (2016); London	10 cross-sectional surveys (*The Gay Men's Sexual Health Survey*); venue-based recruitment of GBMSM at bars, clubs, and saunas.	2000 – 2013 (annually)	N total = 11,876 GBMSM HIV + =13% (8% - 17%). Median age = 33 years (range 16–82 years) 86% White ethnicity.	• CLS in the past year increased from 43% in 2000 to 53% in 2013 overall, among HIV-negative men from 42% to 51% • CLS with partners of unknown or discordant status decreased from 22% in 2000 to 17% in 2013, from 22% to 16% in HIV-negative men • serosorting increased from 18% in 2000 to 28% in 2013; in HIV-negative men from 18% to 27%.
Sewell (2018); London and Brighton	Cross sectional assessments comparing two studies (AURAH and baseline AURAH2); recruitment through sexual health clinics	AURAH: 2013 – 2014 baseline AURAH2: 2014 – 2016	N total: 2,022 GBMSM (AURAH: 991, AURAH2: 1,031) White ethnicity: AURAH 81.0%, AURAH2 80.5%; <25 years: AURAH 14.8%, AURAH2 24.5%	• CLS with one or more partners in the past 3 months increased in the AURAH2 study as compared with the AURAH study (aPR 1.14 95% CI 1.05 to 1.24) • CLS with two or more partners also increased (aPR 1.22 95% CI 1.05 – 1.41)

CLS condomless anal sex, OR odds ratio, aOR adjusted odds ratio, CI confidence interval, aPR adjusted prevalent ratio

Chapter 2: Literature review

2.1 Introduction

2.1.1 Background

Relatively little research exists regarding variability at an individual level in sexual behaviour over time among HIV-negative gay, bisexual, and other men who have sex with men (GBMSM). There are also relatively few studies investigating predictors of within-person changes in sexual behaviour. To better understand these issues, systematic documentation of data from studies that have assessed individual patterns in sexual behaviour and identified predictors of changes at the individual level is needed.

This chapter presents the results of a systematic review and three additional scoping reviews I conducted on longitudinal studies among initially HIV-negative GBMSM. The reviews were conducted at the beginning of my PhD in 2018 – 2019 and updated in 2020, and therefore presents the body of literature that was relevant to informing the development of my thesis objectives related to within-person changes in sexual behaviour (Section 1.1, points (ii) and (iii)) and the corresponding data analysis), trends in pre-exposure prophylaxis (PrEP) use (Section 1.1, points (iv) and (v)) and HIV incidence (Section 1.1, points (vi) and (viii)), and changes in sexual behaviour post-HIV diagnosis (Section 1.1, points (viii), (ix) and (x)).

2.1.2 Chapter aims

The primary objectives of this chapter are, among HIV-negative GBMSM in the era of combination antiretroviral therapy (cART), to perform a systematic review of worldwide literature in the period 1998 to 2018 to:

(i) investigate within-person changes in sexual behaviour over time among HIV-negative GBMSM
(ii) assess trends over time (over calendar year or follow-up period) in sexual behaviour

This chapter also presents the literature related to the following secondary objectives as the background information to Chapters 6,7 and 8 of this thesis, which is to:

(iii) assess trends over time in PrEP use and associated factors
(iv) assess trends over time in HIV acquisition and associated factors
(v) determine changes in sexual behaviour following HIV diagnosis

2.2 Methodology for literature review

The systematic review approach was used to address the primary objectives (Points (i) and (ii)). The major advantage of taking a systematic review approach to accessing all relevant studies is that it aims to minimise bias in assessing the questions under investigation, thus enhancing the reliability of the conclusions drawn (158, 159). In addition, to my knowledge, no previous systematic review investigating within-person changes in sexual behaviour among GBMSM existed.

To identify the most relevant studies on trends in HIV incidence, PrEP use, and changes in sexual behaviour post-HIV diagnosis (secondary objectives, points (iii), (iv) and (v)), three additional scoping reviews were also done (160). It was not possible to rely on the results of a single systematic search or do multiple systematic reviews on different topics given the time constraints of this PhD.

2.2.1 Systematic review

2.2.1.1 Study design, settings and population

As the research questions concern individual changes and incidence, only data from longitudinal studies were included in this literature review. Information from these studies on temporal trends was also extracted. Longitudinal studies, either observational or interventional, employ continuous or repeated measures to follow particular individuals over specific periods (161, 162). Because data are collected repeatedly among individuals within a predefined group, appropriate analysis can be employed to examine changes over time for the cohort as a whole or a particular individual (within-person changes). Using longitudinal studies makes it possible to gain insight into cause-and-effect relationships because the temporality of the event is known. Unlike cross-sectional studies, which provide no information about the sequence of factors in time, it is possible to establish whether the potential causative agent occurred prior to the outcome in longitudinal studies. Temporal trends evidence also comes from repeated cross-sectional studies; however, in this literature review, I limited only to longitudinal studies to obtain information not only at an aggregate level but also on who has changed, or how and why.

Longitudinal study designs included in this literature review were prospective observational studies (including cohorts and representative panels where data is regularly collected from a specific sample of a population), retrospective observational studies, and interventional studies (including randomized controlled trials).

Studies from high-income, middle-income and low-income countries were included, as the main objective was to collect as much evidence available on within-person changes in

sexual behaviour as possible. The population being studied was initially HIV-negative or undiagnosed GBMSM. Eligible studies included gay men, bisexual men, and transgender individuals. No restrictions were made according to the type or characteristic of GBMSM (age and ethnicity), nor to the sampling method (probability or non-probability methods), data collection design (online, self-completed, interview), and further inclusion and exclusion criteria of the studies.

2.2.1.2 Search strategy

I followed the PRISMA standards for reporting systematic reviews (163), although because I was the only reviewer, I only did a single screening rather than a double screening (i.e. including at least two reviewers screening independently of one another). All longitudinal studies that collected repeated information on sexual behaviour on the same individuals over time among GBMSM were included. I searched the following databases: Web of Science, PubMed, and Ovid to locate articles. Search terms were combinations of medical subject heading (MeSH) terms and free text, reflecting the following categories:

(i) Keyword terms related to sexual risk behaviour ("sex" OR "intercourse" OR "condom" OR "serosorting" OR "chemsex"); **AND**

(ii) keyword terms related to GBMSM descriptors (“MSM” OR "homosexual" OR "homosexuality" OR "men who have sex with men" OR "gay" OR "gay men" OR "bisexual men"); **AND**

(iii) Keyword terms related to longitudinal study ("longitudinal" OR "cohort" OR "prospective" OR "trial")

I limited the search to English-language peer-reviewed articles published between January 1998 and December 2018. A publication cut-off of 1998 was chosen because it covered 20 years before the original search date and focused on the sexual behaviour trends in the era of combination antiretroviral therapy (cART) that has been available to people living with HIV/AIDS starting in 1996. I carried out the search between November 2018 and February 2019.

2.2.1.3 Selection criteria

Articles were included in this review if they:

(i) reported data on GBMSM who were HIV-negative or of unknown serostatus; **AND**

(ii) utilized a longitudinal repeated measures study design on the same individuals (in which data were collected at least two-time points); **AND**

(iii) collected information on relevant sexual behaviours (see measures of sexual behaviour below), even if within-person data on these behaviours were not reported; **AND**

(iv) had a sample size of at least 30; **AND**

(v) length of follow-up was at least six months

The measures of sexual behaviour considered in this review were:

(i) condomless anal sex (CLS), defined as any measure of anal sex without condom use. CLS-based measures were regarded as the most important measures of risk behaviour for the HIV-negative GBMSM population due to relatively low PrEP use during this review period

(ii) CLS with regular or casual partners

(iii) CLS with partners of unknown or discordant HIV status

(iv) CLS with multiple partners

(v) number of (any) sexual partners

(vi) serosorting (restricted CLS to partners known to have the same HIV status)

(vii) any measures of individual changes in sexual behaviour, including recreational drugs use, serosorting, PrEP use, or aggregate of several sexual behaviours (based on scores)

Apart from measures of sexual behaviour above, I also documented findings from the articles on the points below, if reported together with at least one of the findings on measures of sexual behaviour:

(viii) trends over time in HIV and other sexually transmitted infections (STIs) incidence and associated factors

(ix) trends over time in PrEP use and related factors

(x) any measures of changes in sexual behaviour post-HIV-diagnoses

Please note that additional scoping reviews were also done to add more relevant literature on the topics (viii) - (x) (see Section 2.2.2).

2.2.1.4 Data extraction

Full-text articles were obtained for articles determined to meet the criteria above for further content review. Articles were excluded if they failed to report findings among HIV-negative GBMSM (i.e., studies among HIV-positive GBMSM or both HIV-positive and negative but no separated data for only HIV-negative).

Data extracted included:

(i) study characteristics (name, author, settings, and years of the study)
(ii) design and method/intervention descriptions (including statistical analyses used)
(iii) inclusion and exclusion criteria
(iv) sample characteristics
(v) outcome measures
(vi) main findings

If more than one article from the same study fulfilled the inclusion criteria, I grouped articles according to the study. Three articles that reported findings only on PrEP use were still included in the review because their data were from the same studies that provided data on measures of sexual behaviour (but published in different articles). For studies that reported multiple sexual behaviour outcomes, for example, trends in CLS and the number of sexual partners, I extracted all findings to examine all available data in the literature.

2.2.2 Scoping reviews

In the systematic review, the search term focused mainly on sexual behaviour measures among HIV-negative GBMSM; therefore, studies that reported trends in PrEP use, trends in HIV incidence, and sexual behaviour change post-HIV diagnosis might have been missed. In the scoping reviews process, I aimed to explore the recent state of evidence (studies published after the 2000s until August 2020, 20-year period) from observational studies in the UK or other high-income countries.

To do this, I searched PubMed and Ovid for English-language peer-reviewed articles using key search terms:

(i) keyword terms related to trends in HIV incidence:
("HIV") **AND** ("MSM" OR "homosexual" OR "men who have sex with men" OR "gay" OR "bisexual men") **AND** ("incidence" OR "diagnosis" OR "prevalence" OR "predictors") **AND** ("longitudinal" OR "cohort" OR "prospective" OR "trial").

(ii) keyword terms related to trends in PrEP use:
("pre-exposure prophylaxis" OR "PrEP") **AND** ("HIV") **AND** ("MSM" OR "homosexual" OR "men who have sex with men" OR "gay" OR "bisexual men") **AND** ("longitudinal" OR "cohort" OR "prospective" or "trial")

(iii) keyword terms related to changes in sexual behaviour post-HIV diagnosis:
("sex" OR "sexual behaviour") **AND** ("HIV") AND ("incidence" OR "diagnosis" OR "after diagnosis") **AND** ("MSM" OR "homosexual" OR "men who have sex with men", "gay" OR "bisexual men") **AND** ("longitudinal" OR "cohort" OR "prospective")

Study populations, selection criteria and data extraction process were all the same as the systematic review process. As for the study setting, I only included longitudinal observational studies (interventional studies were excluded) from high-income countries.

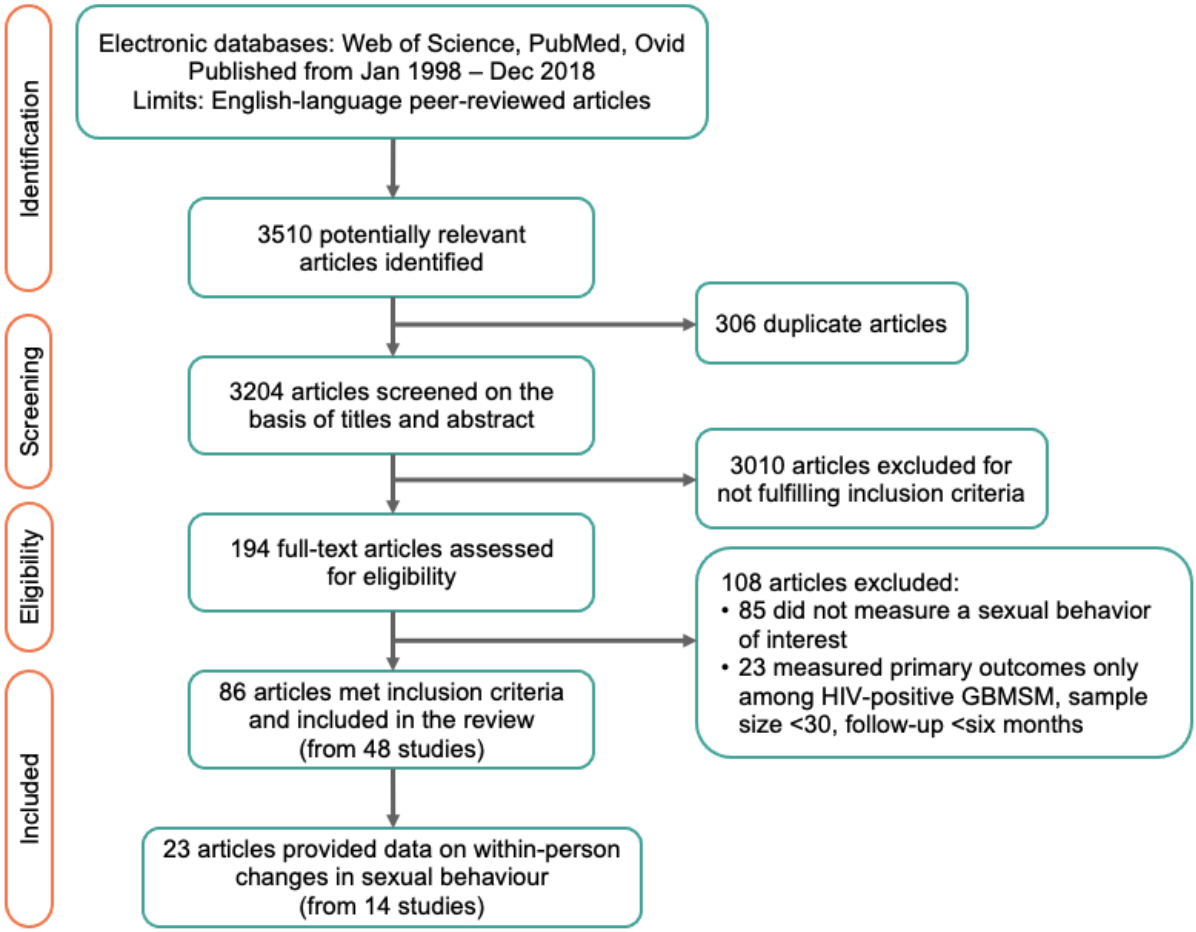
2.3 Results

2.3.1 Included studies from the systematic review process

Figure 2.1 summarizes the study selection process. In total, after removing duplicates, 3,204 articles were identified and screened, of which 3,010 were initially excluded because they were non-longitudinal, did not provide relevant sexual behaviour outcomes, did not target GBMSM, or were not original research contributions (for example, commentaries, review, opinion and letters). The remaining 194 articles were subject to full-manuscript review. One hundred and eight articles were excluded at the full-report level because they did not measure a sexual behaviour variable of interest (see Section *2.2.1.3*) or did not include results from an HIV-negative GBMSM population. Eighty-six full-text articles representing 48 studies were determined to be eligible for this review.

Among the 86 included articles that published behavioural data between 1998 and 2018, 75 were articles from studies conducted in high-income countries and only 11 in non-high-income countries. Of the 75 in high-income countries, the majority were conducted in the US (n=44), nine in Canada, eight in Australia, eight in the Netherlands, four in France and Canada, one in France, and one in the UK. Among those conducted in non-high-income countries, three were conducted in China, two in Thailand, and one each in India, Brazil, Romania, Russia and Hungary, Kenya, and the Central African Republic. The majority of the 86 were observational cohort studies (n=52, summarised in Appendix 1), while the other 34 were interventional studies (summarised in Appendix 2).

Figure 2.1 Flow diagram of study selection in inclusion process



2.3.2 Studies that have investigated within-person changes in sexual behaviour

Of the 86 articles, only 23 from 14 studies reported changes in sexual behaviour at the individual level. I updated the search in January 2021 to include additional studies published after December 2018 and identified two more articles from two different studies. The updated review was only done to investigate whether other more recent studies had reported within-person changes; therefore, I did not include them in Figure 2.1. In total, 25 papers from 16 different studies were reviewed.

Table 2.1 summarises articles that provided data on within-person changes in sexual behaviour. All studies were conducted in high-income settings: one in the Netherlands (164), two in Canada (165, 166), two in France and Canada (167, 168), two in Australia (169, 170), and 18 in the United States (US) (132, 133, 171-186). Studies are described according to their recruitment settings, year of data collection, sample size, outcome measures, and main findings.

Table 2.1 Summary of 25 articles providing data on within-person changes in sexual behaviour among HIV-Negative GBMSM at enrolment globally, 1998 – 2020

Name of the study; study settings; recruitment settings	First author (year)*; data collection	Sample characteristics	Outcome measures; *Statistical analysis*	Main findings
ACS; Amsterdam; STI clinic, adverts in gay scene (convenience sampling), by other participants (chain referral)	Basten (2018) (164); 2007 – 2017	N=803 men; Mean age 35.6 years (SD 9.6); 76% Dutch; 75% highly educated	Sexual behaviour trajectories and associated factors; *Latent class growth mixture modelling*	• Three trajectories identified: Low-risk (90%), Falling high-risk (7%), Rising high-risk (3%). • Men in Falling high-risk (21%) and Rising high-risk (25%) groups were more likely to acquire HIV during follow-up • Falling high-risk group associated with younger age at sexual debut, fewer steady partnerships, substance use; Rising high-risk group associated with substance use
VPCNSS; Melbourne; sentinel surveillance from health clinics	Wilkinson (2015) (169); 2007 – 2013	N=4,685 men; 516 for analysis individual transitions Mean age 37.6 years (30.2 – 45.5); 76% Australia-born; no data on education	Sexual behaviour classes, individual transitions, and associated factors; *Latent class and latent transition modelling*	• Four classes identified: monogamous (26%), risk minimizer (31%), risk potential (28.5%), risk taker (14.5%) • Probability of remaining in the same class between visits was 70%, except for monogamous class (50%) • Age associated with membership in the risk potential class, STIs associated with risk potential, risk minimizer, and risk taker classes
MACS; Baltimore, Pittsburgh, Chicago and Los Angeles; gay organizations, gay media, health care professionals	1) Pines (2014) (171); 2003 – 2011	N=419 men enrolled between 2001 – 2003 and had completed data until 2011; Mean age 38.3 years (SD 9.8); 38% White; 42% Black; 15% Hispanic; 43% college degree	Sexual behaviour trajectories, probability, and associated factors; *Nagin's group-based trajectory modelling*	• Three trajectories identified: low-risk (63%), moderate-risk (23%), high-risk (14%) • Probability of engaging in high-risk behaviours over time for the high risk group was 71% • High risk group associated with younger age, being White, depression, substance use
	2) Lim (2012) (172); 2003 – 2008	N=2,389 men; Mean age 47 years (SD 10) 64% Caucasian; 52% college degree	Drug use trajectories and associated factors; *Individual and group based growth curve modelling*	• Three trajectories identified: consistent users of stimulant drugs over time (10%), men whose use increased over time (5%), men whose use declined over time (7%), abstinent or rarely-using men (78%) • Men whose used increased or decreased reported congruent changes in number of unprotected receptive anal sex partners
IPERGAY Trial; France and Canada; gay venues	1) Sagaon-Teyssier (2016) (168); 2012 – 2014	N=400 men; Median age 34.9 (29–43) years; 72.3% had a high school/higher diploma; Median follow-up 9.3 months (4.9 – 20.6)	Frequency of condom and PrEP use reported during the last sexual intercourse; *test for trend*	• 29% men reported both PrEP and condom use, 12% reported condom use only, 17% reported no PrEP or condom use, no change during follow-up • 70% and 69% of participants reported, respectively, CLS and receptive CLS last sex, no change during follow-up • 83% of participants protected themselves by PrEP or condom or both during the trial, and no increase in at risk sexual practices
	2) Sagaon-Teyssier (2018) (167);	N=332 (from double blind + OLE); Median age 36 years (29 – 43)	Behavioural trajectories for condom and PrEP use, changes over time	• Two condom trajectories identified: low level users (53%), high level users (47%)

Name of the study; study settings; recruitment settings	First author (year)*; data collection	Sample characteristics	Outcome measures; *Statistical analysis*	Main findings
	2012 – 2015	73% high school or higher	in PrEP use trajectories and associated factors; *Group-based trajectory modelling*	• Four PrEP trajectories identified: systematic adherence (50%), high adherence (19%), declining adherence (15%), low adherence (16%) • Among the low level condom users group, 24% also belonged to the low PrEP adherence group (most at risk group, 13% of all participants) • Low level condom users group associated with knowing most recent partner's HIV serology and perceiving high risk during anal intercourse
Young Men Study; Los Angeles; public venues (stratified probability sampling)	Wong (2012) (173); 2005 – 2009	N=526 men; Mean age 22.15 years; 24% Black, 40% Hispanic, 36% White; 35% post-secondary education	Transitions in sexual risk behaviour over time and associated factors; *Hidden Markov Model*	• 35-52% of individuals who practiced protected anal intercourse at any one wave were predicted to transition to a different risk group by the next wave. • 46-53% of individuals at highest risk were predicted to transition out of that group by the next wave • Men with primary partners were more likely to engage in CLS
CSS; Chicago, Denver, San Francisco; no data on recruitment	1) Romero Severson (2012) (132); 1992 – 1995	N=882 men; No data on demographics	Within and between-person variation in sexual behaviour and transitions; *Poisson and negative binomial modelling*	• Number of sexual contacts highly variable between individuals (mean 1.55/month) and heterogeneous at the individual level over time • There was a high level of transition between dichotomous sexual roles (insertive/receptive, protected/unprotected, anal/oral, and HIV status of partners)
	2) Romero-Severson (2015) (133); 1992 – 1995		Dynamic variation in individual sexual contact rates; *Iterated filtering modelling*	• High levels of both between-person and within-person variability • The average duration of time for which an individual has a constant average contact rate is approximately 2 years
P18 Cohort Study; New York City; active sampling (direct recruitment) and passive sampling (flyers, youth or dating websites)	1) Halkitis (2015) (174); 2009 – 2013	N=598 men; Mean age 18.23 (SD 0.43); 38% Latino, 29% White non-Hispanic, 15% Black non-Hispanic, 13% mixed, 5% Asian; 86% enrolled in school	Latent construct of sexual behaviour over time; *Latent class modelling*	• There was considerable variability within-person and over time in CLS • CLS increased from baseline to 18-months follow-up
	2) Kapadia (2015) (175); 2009 – 2013		Within and between-individual changes in sexual activity and associated factors; *Latent growth curve modelling*	• There was a positive growth in the number of reported episodes of receptive oral sex by 18 months' follow-up • Black, Hispanic/Latino, and those self-identifying as some other race engaging in fewer episodes of condomless sex relative to White ethnicity • Condomless sex among Black young GBMSM declined over time compared to White
	3) Halkitis (2017) (176); 2009 – 2014		Patterns of growth in drug use and CLS and associated factors; *Latent growth curve modelling*	• Insertive and receptive CLS, drug use, and inhalant use increased over time • Alcohol use was associated with receptive CLS
	4) Cook (2018) (177); 2009 – 2014		Transitions and variation in CLS behaviour, and associated factors; *Zero-inflated Poisson growth modelling*	• Young GBMSM participated in more CLS as they aged • CLS episodes differed significantly across men, and there was variability in initial levels of receptive CLS • Perceptions of greater romantic relationship control increased the likelihood of CLS

Name of the study; study settings; recruitment settings	First author (year)*; data collection	Sample characteristics	Outcome measures; *Statistical analysis*	Main findings
The Vanguard Project; Vancouver; gay venues, gay media (community outreach)	Piaseczna (2001) (165); 1995 – 2001	N= 130 men who had completed all four annual follow-up questionnaires; Median age 26 years (24-28) 79% White ethnicity; 85% high school degree	Frequency of CLS with regular and casual partners; *Cochran-Armitage test*	• >70% of men reported 1 or more regular male partners in the past year over a 5-year follow-up • During each of the five successive 1-year periods: 34%-40% of men reported having had receptive CLS with regular partners, 29%-39% reported having had insertive CLS with regular partners, 13%-25% insertive CLS with casual sex partners and 9%-18% receptive CLS with casual sex partners
The Omega Cohort Study; Montreal; gay pride week, gay media	George (2006) (166); 1997 – 2003	N=579 men who had complete data for eight follow-up visits; 53% older than 30 years 56% Quebec-born 70.4 % highly educated	Frequency of CLS with any type, casual, and seroconcordant partners; *Trend analysis per visit*	• Increase in CLS with seroconcordant partners, from 21% to 31% • Increase in CLS with any type of partner, from 32% to 44% • Increase with casual partners, from 7% to 10%
HIM cohort; Sydney; gay community	Mao (2006) (170); 2002 – 2005	N=302 men who had completed all four interviews, no data on demographics	Total number of CLS casual partners; *Trend analysis per visit*	• Decrease in the mean number of CLS with casual partners over 4-years • Increase in the mean number of CLS with HIV-negative casual partners
RADAR study; Chicago; gay venues, peer recruitment and online	Janulis (2021) (178); 2015 – 2020	N=804 men; Mean age 21.2 years (SD 2.95) 35% Black, 30% Hispanic, 24% White, 11% other	Within and between-person variation in one-time partnership contact rates and associated factors; *Hybrid random effects modelling*	• 42% men never reported a one-time partner, 73% reported no one-time partners during most visits • Number of one-time partners associated with age, casual partners, main partners
Project Q2; Chicago – The U.S; outreach and chain-referral sampling	1) Newcomb (2010) (179); 2007 – 2010	N=144 men; Mean age 18.53 (SD 1.21); 48.4% Black African American	Within-person variability in substance use; *Hierarchical linear modelling*	Sensation seeking was a moderator of the relationship between frequency of alcohol use prior to sex and frequency of unprotected sex
	2) Mustanski (2011) (180); 2007 – 2010	N=122 men; Mean age 18.53 (SD 1.21); 48.4% Black African American;	Effects of partner and relationship characteristics on the frequency of unprotected sex within relationships; *Hierarchical linear modelling*	• On average, men had 5.74 episodes of CLS in each partnership • CLS associated with considering relationship with partners to be serious, older partners, drug use prior to sex, physical violence, forced sex, and partnership lasting more than 6 months
	3) Beidas (2012) (181); 2007 - 2010	N=119 men; Mean age 18.51 (SD=1.22); 48.4% Black African-American	Within-person and between-person correlates of sexual risk taking; *Hierarchical linear modelling*	• Men had an average of 1.37 – 2.47 CLS acts and 1.25 – 1.36 partners per 6 months • Ethnicity related to number of total partners; African-American participants had 34% fewer partners than non-African American; African-American participants had 50% fewer CLS acts • PTSD was a moderator between CLS acts and psychological distress
	4) Newcomb (2016) (182); 2007 – 2010		Main effects of partner and relationship characteristics on CLS; *Hierarchical linear modelling*	• Serious sexual partnerships associated with an approximate 12-fold increase in rate of CLS relative to casual partnerships • Partner age differences and violence were associated with more CLS

Name of the study; study settings; recruitment settings	First author (year)*; data collection	Sample characteristics	Outcome measures; *Statistical analysis*	Main findings
SF PEP Study; San Francisco; community-based organizations, media, and STI clinics or hospitals	Martin (2004) (183); 1997 – 2000	N=397 men; Median age 32 years (17-72); 69% white; 59% college educated	Changes in number of high risk sexual acts following receipts of PEP; *The sign test*	76% of men reported a decrease in number of times they had performed any high-risk act with a high-risk partner, 11% no change and 13% an increase at 12 months following receipts of PEP
Rhode Island PrEP Study; Rhode Island; STI/HIV prevention clinic	Oldenburg (2017) (184); 2013 – 2016	N=61 men; Median age 31 years (26 - 46); 24.6% Hispanic, 4.9% African American 73.8% highly educated	Changes in number of sex partners and CLS partners after PrEP initiation; *Mixed-effect models*	An increase in mean number of CLS partners at 6 months (mean increase 1.31 partners) with association stronger in an analysis restricted only to individuals who reported multiple partners in the previous 3 months at a given time point (n=55).
Relationship dynamics longitudinal study; San Francisco; active recruitment by field staff and passive recruitment through gay communities and media	Darbes (2013) (185); 2005 – 2010	N=556 gay couples; Median age 42 years (18-83); 47% interracial, 45% White	Associations of within-couple differences with sexual behaviour; *random coefficient modelling*	Couples with higher levels of positive relationship dynamics (e.g., commitment, satisfaction) were less likely to engage in CLS with outside partners of serodiscordant or unknown HIV status
EXPLORE Project; San Francisco; outreach, gay venues. gay media, community, referrals	Colfax (2005) (186); 1999 - 2003	N=386 men; 42% between 26 – 35 years; 69% white, non-Latino; 37% had a college degree	Within-person patterns in drugs use and predictors of baseline use and changes in use of the drugs; *conditional logistic regression*	Compared with periods of no drug use, periods of both light drug use (less than weekly use of drugs) and heavier drug use (at least weekly use of at least one drug) associated with engaging in serodiscordant CLS, characterized by higher composite drug use scores

*year of paper publication

CLS condomless anal sex, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis

Most (nine) of the 16 studies used mixed recruitment strategies to recruit participants (active and passive samplings), including the combination of recruitment through gay venues and gay media, community outreach, chain referral, or STI clinics. One study (two articles) did not report recruitment settings (132, 133), one observational study used data from sentinel surveillance from health clinics (169), three studies recruited participants via convenience sampling through the gay communities, venues or media (166, 167, 170), one study recruited participants who started PrEP at an STI clinic (184), and one study recruited men using a stratified probability sampling in public venues (173).

The sample size varied from 61 men in an observational study among men initiating PrEP (184) to more than 4,000 participants in a study using data from sentinel surveillance from health clinics (169). Length of follow-up also varied from as short as six months in trial studies to ten years in observational cohorts. The full explanation of the studies, including detailed sample characteristics and inclusion and exclusion criteria, are described in Appendices 1 and 2.

Overall, how within-person sexual behaviour was reported in the literature varied across studies, with no consistent approach apparent. Statistical analyses used also differed across the studies. Each study described within-person changes using a different outcome measure, including condomless sex, number of partners, recreational drug use, PrEP use, or the composite of several variables to define ‘high-risk’ or ‘low-risk’ behaviours. Therefore, the classification of study findings was somewhat complicated because these studies investigated different sexual behaviour measures.

To facilitate classification and synthesis of study results, I then grouped these articles based on the outcome measures and main findings reported into four sub-findings:

(i) individual or group-based trajectories of sexual risk behaviour (Section *2.3.2.1*)
(ii) transitions in sexual risk behaviour (Section *2.3.2.2*)
(iii) changes in the prevalence or patterns of sexual behaviour over time (Section *2.3.2.3*)
(iv) factors associated with changes in sexual behaviour (Section *2.3.2.4*)

2.3.2.1 Individual or group-based trajectories of sexual risk behaviours

Five publications from three observational cohorts and one PrEP trial summarised behavioural trajectories among GBMSM. They used different approaches and modelling techniques (164, 167, 169, 171, 172) (Table 2.1). The major findings in these studies showed that although GBMSM differed in their risk level, low-risk behaviour predominated.

In the Netherlands, longitudinal data from 803 GBMSM recruited via convenience sampling (e.g. brochures at the STI clinic, advertisements in the gay scene) and 'chain referral sampling' (participants recruited by other participants) in the Amsterdam Cohort Studies on HIV and AIDS (ACS) between 2007 and 2017 identified three typical trajectories of sexual risk behaviour during the life course of GBMSM (164). Based on a sexual behaviour risk score that was predictive of HIV seroconversion (including the following variables: total number of receptive anal sex partners, three combined variables of the number of receptive anal sex partners and condom use per partner type [i.e. one-night stands, multiple-time casual partners and sex buddies], total number of condomless insertive anal sex partners with unknown or positive HIV status and anal sex during group sex), this study estimated linear trajectories of sexual risk behaviour predictive of HIV acquisition from age at sexual debut (with a man) onwards. The three trajectories were labelled as 'low-risk' (90% of the sample) - a trajectory of low sexual risk behaviour with a slight increase over time; a 'falling high-risk' trajectory (6.5%) with very high levels of sexual risk behaviour during the first years after sexual debut and a decrease to low risk in 30 years' period; and a 'rising high-risk' trajectory (3.3%) with low levels of sexual risk behaviour in the first years after sexual debut and a rapid increase over time.

In Australia, data from surveillance among 4,685 HIV-negative GBMSM attending general practices for sexual health screening between 2007 and 2013, The Victorian Primary Care Network for Sentinel Surveillance on Bloodborne Viruses and STIs (VPCNSS), identified four distinct classes of sexual risk based on patterns of behaviour over time, labelled as 'monogamous' (26%), 'risk minimizer' (31%), 'risk potential' (28.5%), and 'risk taker' (14.5%) (169). Members of the 'monogamous' class reported one or no anal partners, no casual partners, inconsistent condom use with regular partners, and not meeting partners at sex on-premises venues. Members of the 'risk minimizer' class had a high probability of reporting two to ten sexual partners in the past six months, consistent condom use with casual and regular partners, and meeting partners through social networks/venues. Members of the 'risk potential' class had greater probabilities of reporting inconsistent condom use with casual and regular partners and meeting partners at sex on-premises venues and through the Internet. In comparison, members of the 'risk taker' class (highest risk) had greater probabilities of reporting more than ten sex partners in the past six months, inconsistent

condom use with casual and regular partners, and meeting partners at sex on-premises venues or through the Internet.

In the US, two publications from the Multicenter AIDS Cohort Study (MACS), a 35-year study of HIV infection in gay and bisexual men that ran between 1984 and 2019 in four US cities, showed that GBMSM exhibited different patterns of sexual behaviour and stimulant drug use over time (171, 172). MACS participants differed somewhat in each of the four locations. Participants in Baltimore were recruited from gay and metropolitan newspaper stories and personal communication between the investigators and the leaders of the gay communities in both Baltimore and Washington, DC. In Chicago, a clinic founded by and for homosexual men provided a familiar focal point. The investigation could draw upon deep existing roots in the clinic's established patient population and, more specifically, upon participants in an existing cohort study of hepatitis B vaccine efficacy. In Los Angeles, homosexual men drawn from a pre-existing AIDS study cohort, numerous organisations, referrals by other health professionals, and announcements in gay media were recruited without extraordinary recruitment efforts. In the Pittsburgh area, a smaller and less visible population of homosexual men required the development of several active recruitment techniques. For example, clinical research staff made multiple visits to all known gay bars and baths to enrol men in a local screening study, from which men volunteered for the Multicenter AIDS Cohort Study.

Based on a comprehensive sexual risk behaviour score (variables included: condomless anal sex, condom serosorting, condom seropositioning and engaging in high-risk sex or no seroadaptive behaviours), Pines et al. identified three sexual risk trajectories among 419 GBMSM between 2001 and 2003: ‘low-risk’ (63%), ‘moderate-risk’ (23%, mean duration of consecutive high-risk periods approximately one year), and ‘high-risk’ (14%, mean duration of consecutive high-risk intervals approximately two years) (171). To identify subgroups of participants that followed different sexual risk trajectories, the study modelled sexual risk behaviour scores (<4 versus ≥4), of which the latter was considered high-risk. Lim et al. analysed data from 2,389 men in MACS between 2003 and 2008 and identified three drug use trajectories: consistent users of stimulant drugs over time (9.8%), men whose use increased over time (5.4%), men whose use declined over time (6.9%) and a group of abstinent or rarely-using men (77.9%) (172). Lim et al. also found that men who increased or decreased stimulant drug use over time reported congruent changes in sexual risk-taking: the decreasing group reported a reduction in the number of receptive CLS partners over time, and the increasing group reported a greater number of receptive CLS partners over time.

In France and Canada, a multicentre PrEP trial, the *Intervention Préventive de l'Exposition aux Risques avec et pour les Gays* (IPERGAY), identified four PrEP use trajectories and two condom trajectories among 332 GBMSM in the double-blind and open-label extension (OLE) phases of the trial between 2012 and 2015 (167). PrEP use trajectories were: 'systematic adherence users', 'high adherence users' (49.7%), 'declining adherence users' (15.3%), and 'low adherence users' (16%), while the two condom trajectories were 'low-level users' (53%) and 'high-level users' (47%). Among 53% of men who belonged to the low-level users of condoms, 24.4% also belonged to the low-adherence PrEP group. This most-at-risk group represented 13% of all participants.

2.3.2.2 Transitions in sexual risk behaviour

Six studies examined the probability of transitions or movement across different stages of behavioural risk-taking over time, of which four studies were conducted in the US, one in Australia, and one in France and Canada (132, 167, 169, 171, 173, 177). Most studies revealed that HIV-negative GBMSM in the cART period exhibited relatively consistent patterns of sexual risk behaviour across time (between data collection periods or throughout the follow-up period), with relatively little movement between risk classes.

In Australia, the VPCNSS found general stability across sexual risk classes among a subset of 516 out of 4,685 gay men with at least three complete visits between 2007 and 2013: men had an average of 70% probability of remaining in the same class between visits (every six months) for three groups ('risk minimizer', 'risk potential', and 'risk taker' groups). The 'monogamous' group had only a 51% probability of remaining in the monogamous behaviour (169). Prevalence within the classes remained relatively stable across the three time points, with the "risk minimizer" class having the highest prevalence (approximately 40%). From visit one to visit two, there was a relatively low probability of transitioning out of the 'risk minimizer', 'risk potential', and 'risk taker' classes; each had an approximate 75% probability of remaining in the same class. Stability in the 'monogamous' class was much lower; 51% probability of remaining in the same class at the next visit, with a relatively high probability of transitioning into the 'risk minimizer' class (37%, 95% confidence interval 15% - 59%). Between visit two and visit three, stability was generally lower, except for the 'monogamous' class, for which stability was comparatively higher (69% probability of remaining in the same class). There was some movement towards higher-risk classes among the 'risk minimizer' and 'risk potential' classes.

In the US, analysis from MACS also similarly demonstrated that men exhibit relatively stable yet distinct patterns of sexual risk behaviour over time (171). Over time, the predicted probability of engaging in high-risk behaviours for the 'low-risk' group was approximately

0.9% and 71% for the ‘high-risk’ group per semi-annual visits between 2003 and 2011. While for the ‘moderate-risk’ group, the probability started at 29% then declined to 17% at the end of the study follow-up.

In contrast with studies mentioned above, the Young Men’s Health Study, a study among 493 ethnically diverse young GBMSM (mean age 22 years) recruited at public venues using the stratified probability sampling design in Los Angeles between 2005 and 2006 (data collection 2005 – 2009), indicated substantial movement at the individual level transitions (173). The study predicted that 35-52% of individuals who practised protected anal sex at any one wave transitioned to a different risk group by the next wave (six months), and 46-53% of individuals at highest risk transitioned out of that group by the next wave. This study defined the risk group from a four-category index of past three months’ sexual risk score by combining variables of number of partners, consistent condom use regardless of the number of partners, CLS with a single partner whose HIV serostatus was reported by the respondent to be consistent with his own (i.e., seroconcordant), CLS with a serodiscordant partner and CLS with multiple partners. As for the illicit drug use risk, there was high stability in the lifetime non-use group, with the probabilities of remaining in that group in subsequent waves ranging from 83% to 93 %. The probability of staying as recent non-users also tended to be high (72% – 81%), suggesting this group represents individuals who previously experimented with drugs but no longer engage in drug use. This interpretation is supported by the relatively high proportion of individuals at each wave moving from recent light use to recent non-use (44% – 60%), again suggesting experimentation. However, 54% to 60% of recent frequent or heavy users remained so in subsequent waves.

Another prospective cohort among 598 young GBMSM (mean age 18 years) recruited through active and passive recruitment techniques in New York City between 2009 and 2014, P18 cohort study, reported that young GBMSM transitioned to more episodes of sexual risk behaviours (receptive and insertive CLS) as they aged (177). The CDC collaborative Seroincidence Study (CSS), a two-year prospective cohort of 882 gay men in three US cities between 1992 and 1995 (article published in 2012), also observed a high level of movement between dichotomous sexual roles: insertive or receptive, with or without condom, anal or oral, and HIV status of partners (132). The average periods of exclusively unprotected sexual contact lasted 16 months.

In France and Canada, data from the double-blinded and OLE phase of the IPERGAY trial examined changes over time in trajectories of adherence to PrEP (167). The trajectory of the ‘systematic adherence to PrEP’ group (49.7% of all 332 participants) remained stable during the whole follow-up, with probabilities of PrEP adherence oscillating between 95% and

100%. The trajectory of high adherence to PrEP group (19% of all 332 participants) was also relatively stable, with probabilities oscillating between 71% at month two (double-blind phase) and 74% at month 18 (OLE). Concerning the declining adherence to the PrEP group (15.3% of all 332 participants), substantial changes were observed in their adherence pattern. During the double-blind phase, the probability of PrEP adherence in this group oscillated between 83% and 94%, whereas during the OLE phase, it decreased from 84% at baseline (month 0, OLE) to only 8% at the end of the follow-up (month 18, OLE). The trajectory of 'low adherence to PrEP' group (16% of all 332 participants) included probabilities approaching 50% at month two in the double-blind phase that subsequently decreased rapidly. The lowest level observed in the double-blind phase was <10%.

2.3.2.3 Changes in the prevalence or patterns of sexual risk behaviour over time

Fifteen publications from ten studies examined changes in the prevalence or the amount of variation in sexual behaviour within-individual over time, of which two were conducted in Canada (165, 166), one in Australia (170), six in the US (132, 133, 174-178, 180, 181, 183, 184), and one trial in France and Canada (168). In terms of CLS episodes, the number of partners, and type of sexual encounters across time, these studies suggested there was within-person variability, with the construct of CLS activity among young GBMSM being less stable than that of older GBMSM.

In Canada, the Vanguard Project, a prospective cohort study in Vancouver, reported that among 130 men between 1995 and 2001 who were recruited through community outreach at gay community events, health clinics and mainstream media and completed all study follow-up, high-risk sexual behaviour remained relatively consistent over five years within individuals (165). During each successive one-year period, between 34% and 40% of respondents who had complete data for four annual follow-up visits reported having had insertive CLS with regular partners. Another Canadian cohort, the Omega cohort study, reported non-negligible and consistent increases in CLS with seroconcordant partners from the first until last follow-up visit (21.3% to 31.1%), any type (31.8% to 43.9%), and casual partners (7.3% to 9.6%) among 579 men in Quebec between 1997 and 2003 who had complete data for eight follow-up visits (166). In this cohort, recruitment was done through posters, the Internet, the gay print media, and the distribution of information cards during the annual gay pride week.

In Australia, the Health in Men (HIM) study, a prospective cohort study in Sydney that recruited GBMSM using community-based strategies, collected data from 302 men with complete data in four interviews between 2002 and 2005. It reported an increase in the mean number of CLS with casual partners within-individual (rate ratio per year 1.3) (170).

In contrast, the CSS that collected data in the US before cART was available, reported that the total number of sexual contacts made throughout the study were highly variable between individuals, and the types of contacts were also heterogeneous over time (132). On average, exclusively unprotected sex contact periods lasted 16 months (132). In 2015, another paper from CSS reported significant within-person behavioural variability even in relatively short time series. For most contact types, the average duration of time for which an individual had a constant average contact rate was approximately two years (mean 0.04 contacts per month) (133).

Among young GBMSM, three longitudinal cohort studies in the US reported various findings. RADAR study, a cohort of 804 young GBMSM (mean age at baseline 21 years) between 2015 and 2020 in Chicago who were recruited through venue-based, online, and peer recruitment, reported there was a substantial within-person variation in reporting one-time partners in the past six months (178). This study classified partnerships into three categories: main, casual, and one-time partners. A large minority of participants (42.1%) reported never having a one-time partner, and participants reported zero one-time partners during most visits (72.6%). These findings imply that having a one-time partner is prevalent but varies over time in this target population.

The P18 cohort study published four articles on within- and between-person variations (174-177). Halkitis et al. reported considerable variability in reports of sexual behaviours both within-person and across time and an increase in both insertive and receptive CLS over the first 18-month period of the study (the study was conducted during 2009 – 2014) (174). Kapadia et al. confirmed the finding that there was an increase in the number of reported episodes of receptive oral sex by an 18-month follow-up (175). In 2018, Halkitis et al. investigated growth patterns in drug use and CLS, including their associations and found significant growth in CLS frequencies, alcohol to intoxication, marijuana use, and inhalant nitrate use among participants (176). Cook et al. also suggested that CLS increased over the emerging adulthood period, and there was variability in initial levels of both insertive and receptive CLS (177).

Project Q2, a longitudinal study among 122 young GBMSM (mean age 18.5 years) between 2007 and 2010 in Chicago who were recruited through a combination of outreach (38%) and incentivized snowball sampling (62%), also published some findings on sexual behaviour changes. Mustanski et al. reported that, on average, young men had six episodes of CLS in each partnership (180), while Beidas et al. reported that men reported an average of 1.37 – 2.47 CLS acts and 1.25 – 1.36 male partners per six months (181).

Three studies reported changes in sexual behaviours following PrEP or post-exposure prophylaxis (PEP) initiation (168, 183, 184). San Francisco PEP study evaluated the concern that the availability of PEP exposures might result in behavioural disinhibition among 397 men in San Francisco between 1997 and 2000 (183). The study reported that after 12 months following receipt of PEP, 76% of men reported a decrease, 11% no change, and 13% an increase compared with baseline in the number of times they had performed high-risk sexual acts. The Rhode Island PrEP study described changes in sexual behaviours among 61 MSM following PrEP between 2013 and 2016 and reported an increase of 1.31 in the mean number of CLS partners at six months after PrEP initiation (184). The IPERGAY trial assessed the frequency of condom and PrEP use reported during the last sexual intercourse among 400 men between 2012 and 2014 and reported that during the 24-month follow-up of the trial, the majority of MSM in the trial (83.3%) used at least one of its prevention tools (PrEP and condoms) during sexual acts and no increase in at-risk sexual practices was observed (168). There was a tendency towards a decrease in the median number of sexual partners over time within individuals.

2.3.2.4 Factors associated with changes in sexual behaviour

Seven studies (13 publications) reported factors associated with sexual risk-taking, using individual-level data, of which one was conducted in the Netherlands, one in Australia, and five in the US. These studies took varied approaches in identifying predictors or characteristics linked to transitions or memberships in specific sexual behaviour trajectories.

In the Netherlands, ACS characterized GBMSM following each trajectory by demographic and psychosocial factors and examined whether the identified trajectories were associated with these factors (164). The study reported differences among group trajectories in age at sexual debut, steady partnership, and substance use. GBMSM in the ‘falling high-risk’ trajectory were younger at their sexual debut than GBMSM in the ‘low-risk’ group (mean age 15.5 vs 18.4 years). At their first visit, they were less likely to have a steady partner than GBMSM in the ‘low-risk’ group (39.5 vs 62.9%), while at the last visit, no difference in steady partnership between groups was found. GBMSM in the ‘falling high-risk’ group more often used recreational drugs, poppers and erectile dysfunction drugs than GBMSM in the ‘low-risk’ group at both first visit and last visit. Regarding GBMSM in the ‘rising high-risk’ group, the study found that they were more likely to have a steady partnership at their first visit than GBMSM in the ‘low-risk’ group (90.0% vs 62.9%), while at the last visit, no difference was present. In the ‘rising high-risk’ group, increasing percentages of GBMSM using recreational drugs (57.9% at first visit vs 95.0% at last visit) and erectile dysfunction drugs (35.0% at first visit vs 70.0% at last visit) were found over time. At the last visit, they were more likely to use

recreational drugs, poppers and erectile dysfunction drugs than GBMSM in the 'low-risk' group. Differences between groups were examined by performing analysis of variance (ANOVA) for continuous variables and chi-squared tests for dichotomous variables. In addition, for each group, change in steady partnership and substance use over time were studied by comparing the first and last visit within the study window using exact binomial McNemar's tests. These analyses were performed in GBMSM with at least two visits.

In Australia, the VPCNSS (2007 – 2013) reported that older age was associated with reduced odds of membership in the 'risk potential' class (169). A positive test for syphilis, chlamydia, or gonorrhoea was associated with membership of the 'risk potential' and 'risk taker' classes compared with the 'monogamous' class, with a positive STI test being most strongly associated with the membership in the 'risk taker' class. Latent transition modelling was used to identify factors associated with each risk class.

In the US, using the longitudinal risk trajectories that had been defined, MACS reported that compared to 'low risk' group membership, 'high risk' group membership was associated with younger age, being White, earning an income ≥$20,000, distress or depression symptoms, and substance use (171). There were also significant differences between groups of drug use trajectory, that men who increased or decreased stimulant drug use over time reported congruent changes in sexual risk-taking (172). The EXPLORE study, a randomized behavioural intervention in San Francisco to determine whether ten individualized counselling sessions reduce HIV-infection rates compared with standard HIV testing and counselling, described patterns of drugs use among 736 GBMSM between 1999 and 2003. The within-person analysis found that CLS with an HIV-positive partner or unknown-status partner was more common during reported periods characterized by increased drug use, compared with periods of no drug use, periods of both light drug use (less than weekly use of drugs) and heavier drug use (at least weekly use of at least one drug) (186). A longitudinal study of 566 ethnically diverse gay couples between 2005 and 2010 in San Francisco revealed that couples with higher levels of positive relationship dynamics (e.g., commitment, satisfaction) were less likely to engage in CLS with outside partners of serodiscordant or unknown HIV status (185).

Among young GBMSM, the Young Men's Health study examined changes in developmental contexts that can impact young adults' choices to engage in risk behaviours, for example, entry into the workforce and the maintenance of more intimate romantic relationships, as predictors of HIV-risk behaviours. The study reported that young men with primary partners were more likely to engage in CLS than those without primary partners (173). Project Q2 reported that alcohol and drug use prior to sex, considering relationships with partners to be

serious, and being White were predictors of a higher frequency of CLS acts (179-182). P18 cohort identified that White and mixed-race young GBMSM reported more instances of CLS than other ethnic groups, with declining rates over time noted in Black young GBMSM (175). The study also found evidence of the co-occurrence of drug use with CLS acts (176), and perceptions of greater romantic relationship control increased the likelihood of having insertive and receptive condomless anal sex (177).

2.3.3 Studies that have investigated trends in sexual behaviour in the era of cART

Of the 86 articles identified in the systematic review, 43, from 36 different studies, provided results on trends (over calendar time or follow-up period) in sexual behaviour among HIV-negative GBMSM between 1998 and 2018. 13 of the 36 studies were observational cohort studies, while 23 were interventional studies. Table 2.2 shows observational cohort studies that have reported trends over time in sexual behaviour, while the interventional studies are shown in Table 2.3. For interventional studies with at least two arms (intervention and control), results were reported for both arms.

Most studies were conducted in high-income countries (n=26), with only ten studies conducted in non-high-income countries. Recall period differed across studies and variables, but most common was past six months for longitudinal cohorts and past three months for interventional studies. Sections *2.3.3.1* to *2.3.3.6* below summarise the temporal trends in CLS with any partner, CLS with regular or casual partners, CLS with HIV-positive partners, CLS with multiple partners, serosorting and number of partners. The reported trends could relate to temporal trends in the behaviour (such as over calendar year) or a type of cohort effect such as ageing and loss to follow-up in the cohort.

Table 2.2 Summary of 13 observational studies on temporal trends in sexual behaviour among HIV-negative GBMSM at enrolment globally, 1998 – 2018

Name of the study; study settings	First author (year); data collection period; sample size	Recall period (months)			Outcome measures*						Findings		
		3	6	12	CLS – any partners	CLS – reg / cas partners	CLS – discordant	CLS – multiple partners	sero sorting	number partners	increase	decrease	no change
High-income countries													
ACS; Amsterdam	1) Dukers (2001); 1984 – 2000; 877 men		√			√					√		
	2) Van der Bij (2005); 1984 – 2002; 863 men		√			√					√		
			√							√			√
	3) Jansen (2011); 1984 – 2009; 1,642 men		√		√						√		
			√			√					√		
	4) Van den Boom (2014); 2007 – 2011; 445 men		√						√				√
AmPrEP; Amsterdam	Hornenborg (2018); 2015 – 2016; 328 men	√			√						√		
		√								√			√
St Louis Hospital Study; Paris	Noret (2018); 2015– 2017; 1,049 men	√			√						√		
HIM; Sydney	1) Mao (2006); 2002 – 2005; 1,148 men		√			√					√		
			√						√		√		
	2) Zablotska (2008); 2003 – 2006; 1,427 men		√				√				√		
	3) Jin (2015); 2001 – 2007; 1,427 men		√						√		√		
Vanguard Project; Vancouver	Strathdee (2000); 1995 – 1998; 681 men			√	√						√		
	George (2006);		√		√						√		

Name of the study; study settings	First author (year); data collection period; sample size	Recall period (months)			Outcome measures*						Findings		
		3	6	12	CLS – any partners	CLS – reg / cas partners	CLS – discordant	CLS – multiple partners	sero sorting	number partners	increase	decrease	no change
Omega Cohort Study; Montreal	1997– 2003; 1,587 men		√			√					√		
Momentum Health Study; Vancouver	Moore (2017); 2012 – 2015; 556 men		√				√						√
Project Q2; Chicago	Newcomb (2016); 2007 – 2010; 114 men		√		√								√
P18 Cohort Study; New York	1) Halkitis (2015); 2009 – 2013; 598 men	past 30 days			√						√		
	2) Halkitis (2017); 2009 – 2014; 598 men	past 30 days			√						√		
HIV Seroadaptive Behaviours Study; San Francisco	McFarland (2011); 2007 – 2009; 732 men		√				√						√
PHSKC Cohort Study; Seattle	Montano (2018); 2014 – 2017; 183 men	past 30 days			√						√		
Non-high-income countries													
Beijing VCT study; Beijing	Lau (2015); 2009 – 2012; 228 men	√			√								√
		√					√						√
BMCS; Bangkok	1) Holtz (2015); 2006 – 2012; 1,569 men	past four months			√					√		√	
	2) VanGriensven (2015); 2006 – 2013; 1,259 men	past four months			√							√	

*CLS – reg / cas partners: condomless anal sex with regular or casual partners; CLS – discordant: condomless anal sex with HIV-positive partners of of unknown status; serosorting: restricted CLS to partners known to have the same HIV status

Table 2.3 Summary of 23 interventional studies on temporal trends in sexual behaviour among HIV-negative GBMSM at enrolment globally, 1998 – 2018

Name of the study; study settings	First author (year); data collection period; sample size	Recall period (months)			Outcome measures**						Findings*		
		3	6	12	CLS – any partners	CLS – reg / cas partners	CLS – sero-discordant	CLS – multiple partners	serosorting	number partners	increase	decrease	no change
High-income countries													
PROUD Trial; England	McCormack (2015); 2012 – 2014; 544 men	√						√			√		
		√								√			√
IPERGAY Trial; France and Canada;	Molina (2015); 2012 – 2014; 400 men	past two months			√								√
										√		√	
IPERGAY OLE; France and Canada	Molina (2017); 2014 – 2016; 361 men	past two months			√						√		
										√			√
PrELUDE study; Sydney	Zablotska (2018); 2014 – 2016; 320 men	√				√ **(regular)**							√
		√				√ **(casual)**					√		
		√					√				√		
CDC Safety Study; San Francisco	Liu (2013); 2005 – 2009; 400 men	√			√					√		√ √	
VISION/VAX004; The US, Canada, and The Netherlands	Bartholow (2005); 1998 – 2002; 3,924 men		√		√							√	
			√				√					√	
EXPLORE study; Boston, Chicago, Denver, New York, San Francisco and Seattle	Koblin (2004); 1999 – 2003; 4,295 men		√		√							√ √	
			√				√					√ √	
Project MIX;	Mansergh (2010);	√			√							√ √	

Name of the study; study settings	First author (year); data collection period; sample size	Recall period (months)			Outcome measures**						Findings*		
		3	6	12	CLS – any partners	CLS – reg / cas partners	CLS – sero-discordant	CLS – multiple partners	serosorting	number partners	increase	decrease	no change
Chicago, Los Angeles; New York, San Francisco	2004 – 2008; 1,686 men												
SF Repeat Testers Study; San Francisco	Dilley (2002); 1997 – 2000; 248 men	√					√					√ √	
NYMI Trial; New York	Morgenstern (2009); 2004 – 2007; 150 men	√					√						√
Hola en Grupos; North Carolina	Rhodes (2017); 2012 – 2015; 304 men	√			√							√	√
MINTS-II; The U.S (online)	Rosser (2010); 2007 – 2009; 650 men	√			√								√ √
3MV Project; New York	Wilton (2009); 2005; 338 men	√				√					√	√	
		√								√		√ √	
Get Real; Philadelphia	Lauby (2017); 2007 – 2010; 278 men	√								√			√ √
Keep It Up; Atlanta, Chicago, New York	Mustanski (2018); 2013 – 2017; 901 men	√			√							√ √	
Non high-income countries													
PrEP Brasil; Rio de Janeiro, Sao Paulo	Grinszteijn (2018); 2014 – 2017; 450 men	√								√		√	
Internet MSM Study; Hongkong	Lau (2008); 2005; 280 men		√			√							√ √
Nanjing HIV Counselling; Nanjing	Huan (2013); 2008 – 2010; 430 men		√		√							√	
			√							√		√	

Name of the study; study settings	First author (year); data collection period; sample size	Recall period (months)			Outcome measures**						Findings*		
		3	6	12	CLS – any partners	CLS – reg / cas partners	CLS – sero-discordant	CLS – multiple partners	serosorting	number partners	increase	decrease	no change
Pilot RCT Chennai; Chennai – India	Safren (2014); 2013; 96 men	√			√							√ √	
Coastal Kenya Cohort Study; Mtwapa	Moller (2015); 2005 – 2011; 469 men	past weeks			√							√	
		past weeks								√		√	
CNRIST/TAR; Bangui	Marcel (2018); 2010 – 2012; 99 men	√			√								√
		√								√			√
Romanian mHealth; Study; Bucharest	Weinberger (2018); 2015 – 2016; 43 men	√			√							√	
Russia–Hungary Trial; St. Petersburg and Budapest	Amirkhanian (2015); 2007 – 2012; 586 men	√			√							√	√
		√				√						√ √	
		√						√				√ √	

*** Green tick (√) is for the findings in control arms,**

Red tick (√) is the for the findings in intervention arms, or the overall results in studies with no control arms, or overall results in studies that reported intervention results without no separate results for control and intervention arms

** CLS – reg / cas partners: condomless anal sex with regular or casual partners; CLS – discordant: condomless anal sex with HIV-positive partners of of unknown status; serosorting: restricted CLS to partners known to have the same HIV status

2.3.3.1 CLS with any partners

Ten longitudinal observational cohort studies and 17 intervention trials examined trends over time in CLS with any partners between 1998 and 2018. In most observational cohort studies, including observational studies among men who initiated PrEP, an increase in this behaviour was reported. Findings from interventional studies were mixed.

(i) Observational studies

In the Netherlands, reports of CLS in the previous six months between 1984 and 2009 among 1,642 men in ACS increased from 38% to 55% (128). Among 328 GBMSM who participated in the Amsterdam PrEP project (AmPrEP), a prospective open-label demonstration PrEP study offering a choice of daily PrEP or event-driven PrEP regimen at the STI clinic of the Public Health Service of Amsterdam between 2015 and 2016 in an STI clinic, an increase in CLS (from median CLS acts of 11 at baseline to 14 at six months) was also reported (187).

In Canada, Vanguard Project (1995–1998, N=681) and the Omega Cohort study (1997–2003, N=1,587) both reported trends towards increasing levels of CLS from the late 1990s to early 2000s (166, 188).

In France, St. Louis Hospital Study in Paris, a single-centre prospective cohort study enrolling 1049 participants who started PrEP between 2015 and 2017, reported a significant increase in CLS in the previous three months' rates from 53% at baseline to 79% at 12 months (189).

In the US, data from the Public Health Seattle and King County (PHSKC) cohort in Seattle among 183 men who initiated PrEP between 2014 and 2017 reported an increase in the proportion who did not use condoms at 12 months after PrEP initiation (relative risk 1.5) (190). Among young GBMSM, two publications from the P18 cohort in New York (2009 – 2014 N=598) similarly reported an increase in the number of CLS acts in the past month from 0.4 at baseline to 0.6 and 18-month follow-up, and receptive CLS from 1.8 to 3 episodes per month (174, 175); while Project Q2 in Chicago (2007 – 2010, N=114) reported no change in the previous six months CLS during two years of follow-up (182).

In non-high-income countries, two publications from Bangkok MSM Cohort Study (BMCS) among 1,569 men between 2006 and 2013 reported that CLS decreased substantially between baseline and 36 months follow-up, from 36% to 19% (191, 192). The Beijing Voluntary Counseling and Testing (VCT) study conducted between

2009 and 2012 among 228 men reported no change in the proportion reporting CLS with any partners (193).

(ii) Interventional studies

Biomedical interventional studies:

The IPERGAY trial in France and Canada reported no between-group differences in the proportion of episodes of receptive CLS or the proportion of episodes of CLS during the most recent sex during the study period as compared with baseline (2012 – 2014) (41). The OLE phase of the trial between 2014 and 2016 among 361 men reported an increase in the proportion of participants reporting receptive CLS (77% at baseline vs 86% at 18 months) (42).

In the US, the VISION/VAX004 study (1998–2000, N=5,095), a phase 3 efficacy trial of a bivalent rgp120 HIV vaccine, reported that the proportion of men who reported engaging in CLS decreased from the baseline to the 36-month visit (194). Another PrEP trial, the CDC safety study (2005 – 2009, N=400), also reported that CLS declined during follow-up (195). The proportions were similar between the immediate versus delayed arm (p = 0.29) from baseline to months 3 – 9 and months 12 – 24.

Behavioural interventional studies:

For behavioural interventional studies, most data were from the US. Project MIX, a randomized cognitive-behavioural intervention that enrolled 1,686 MSM in four US cities between 2004 and 2008, reported a 32% decrease in CLS at 12 months follow-up; however, the decreases were not different between the intervention and control group (196). The *HOLA en Grupos* intervention, a Spanish-language small group behavioural HIV prevention intervention among 304 GBMSM between 2012 and 2015, reported increased consistent condom use (odds ratio 4.1 for intervention participants) (197). Finally, Keep it Up!, an online double-blinded randomized controlled trial (RCT) with a one-year follow-up enrolled 901 men in three US cities between 2013 and 2017, showed reductions in CLS over time in both the control and intervention participants at month 12 (198).

In non-high-income countries, the Nanjing HIV counselling study (2008-2010, N=430) in China reported a decrease in the reported CLS from 60.9% at baseline to 42.9% at 18 months (199). A decrease in CLS was also reported from a Kenyan trial of risk reduction counselling (2005 – 2011, N= 469) among participants at four years of follow-up among men in Mtwapa (no control arm) (200). In India, the Chennai RCT behavioural intervention among 96 GBMSM reported a decline in the rate of CLS in

the intervention versus control at six months (201). In Russia and Hungary, a two-arm trial of the social network intervention (2007-2012, N=586) where the intervention guided network leaders in giving personal HIV risk reduction advice to their friends, reported significant reductions between baseline, first follow-up, and second follow-up in the intervention versus comparison arm for the proportion of men engaging in any CLS (202). In Central African Republic, the *Centre National de Référence des Infections Sexuellement Transmissibles et de la Thérapie Antirétrovirale* (CNRIST/TAR) intervention study (2010-2012, N=99) reported that receptive CLS increased (60% at baseline vs 66% at 12 months) (203). In Bucharest, Romania mHealth study, a behavioural intervention among 43 young GBMSM (mean age 23 years) between 2015 and 2016 reported an increase in the number of protected sex acts from baseline to follow-up (mean 6.3 to 8.6) (204).

2.3.3.2 CLS with regular or casual partners

Three longitudinal observational cohort studies and four intervention trials examined trends over time in CLS with regular or casual partners.

(i) Observational studies

Articles based on longitudinal cohorts were all from high-income countries, three from ACS in the Netherlands between 1984 and 2009 (128, 205, 206), one from the HIM cohort in Australia between 2002 and 2005 (170), and one from the Omega Cohort Study in Canada between 1997 and 2003 (166). Similarly, with the trends over time in CLS with any partners, all these studies reported an increase in the prevalence of CLS with regular or casual partners. An increase in this behaviour was reported since 1995 in ACS.

(ii) Interventional studies

Biomedical interventional studies:

For biomedical interventional studies, data were only available from the PrELUDE study, an open-label, single-arm study that evaluated daily PrEP in 320 high-risk men in Australia between 2014 and 2016 (207). The trial reported that CLS with casual partners among participants increased, but no change in CLS with a regular partner (around 31.5%).

Behavioural interventional studies:

For behavioural interventional studies, a decrease in CLS with regular or casual partners was reported from Many Men, Many Voice (3MV) Project, a small RCT

behavioural intervention among 338 Black GBMSM in New York City in 2005 from baseline to six-month assessment (RR 0.34) (208), and from the Russia-Hungary network intervention trial (% of CLS with non-main sex partners in intervention versus comparison networks at baseline, first follow-up, and second follow-up 18% to 8% to 9% versus 23% to 21% to 21%, respectively) (202). One online RCT in Hongkong that evaluated the efficacy of an internet-based HIV behavioural intervention among 280 men in 2005 reported no change in CLS with regular partners (63% at baseline, 60% post-program at month six) (209).

2.3.3.3 CLS with a partner of unknown or HIV-positive status

Four longitudinal observational cohort studies (three in high-income countries and one in China) and five intervention trials in high-income countries examined trends over time in CLS with a partner of unknown or HIV-positive status.

(i) Observational studies

In Australia, the HIM cohort reported that the proportions of HIV-negative men with serodiscordant casual partners increased during 2003-2006 among 1,427 men, from 3% to 4% (210). In Canada, Momentum Health Study, a longitudinal study among 556 GBMSM in Vancouver between 2012 and 2015, reported no change (30% in period one, 27% in period six) (211). In the US, the HIV sero-adaptive behaviours study, a longitudinal study of sero-adaptive behaviours among 732 men in San Francisco between 2007 and 2009, also reported no change in this behaviour (212). In non-high-income countries, the Beijing VCT study in China (2009 – 2012, N=228 men) reported an increase in this risky behaviour at month 21 (193).

(ii) Interventional studies

Biomedical interventional studies:

The PrELUDE PrEP trial in Australia (2014 – 2016, N=320) reported that the levels of CLS with HIV-positive partners increased (207).

Behavioural interventional studies:

Four behavioural interventional studies in the US (all conducted before the PrELUDE trial) reported a decrease in this behaviour.

The San Francisco repeat-testers study, a randomized counselling intervention trial between 1997 and 2000 among 248 GBMSM, reported that CLS with non-primary partners of unknown or discordant HIV status at six and 12 months decreased from

66% to 21% at six months and to 26% at 12 months, as compared with a control group (213). Among subjects in the standard counselling control group, this behaviour decreased from 45% to 31% at six months then increased to 44% at 12 months. The VISION/VAX004 vaccine trial (1998 – 2000, N=5,095) also reported that CLS with HIV-positive partners declined during follow-up (36 months) (194). The EXPLORE trial reported that among 4295 men between 1999 and 2003, the occurrence of CLS with HIV positive and unknown-status partners was 20.5% lower in the intervention than in the standard group (214). In both arms, this behaviour decreased from baseline to months 12 – 18. Finally, the New York Motivational Interviewing Trial (NYMI) study, a randomized trial study among 150 men between 2004 and 2007 in New York City, reported a decrease, but not significant, in the number of unsafe sex acts across the 12 months study period compared with the education control (215).

2.3.3.4 CLS with multiple partners

No observational studies and two interventional studies (one biomedical and one behavioural interventional trial) reported trends in CLS with multiple partners over time (40, 202).

The PROUD trial reported that at 12 months among participants allocated to immediate PrEP, 21% reported receptive anal sex with ten or more partners without a condom in the last month compared to 12% in the deferred PrEP arm, no trends over time within-groups reported (40). In contrast, the Russia – Hungary behavioural network intervention trial (2007 – 2012) reported reductions between baseline, first follow-up, and second follow-up in the intervention versus comparison arm for the proportion of men engaging in CLS with multiple partners (14% to 2% to 5% versus 19% to 17% to 13%, respectively) (202).

2.3.3.5 Serosorting

Two longitudinal observational cohorts and no interventional studies reported trends in serosorting behaviour.

Two publications from the HIM cohort in Australia reported an increase in serosorting between 2001 and 2007 (170, 216), while data from ACS in the Netherlands showed no changes in serosorting between 2007 and 2011 (217). Between 2001 and 2007, the HIM cohort reported that the proportion of participants who practised serosorting with any sexual partners increased significantly from 48.2% to 71.5% (216). Between 2002 and 2007, the proportion of CLS with HIV-negative partners increased from 12% to 24% among men in the HIM cohort (170). Among 445 GBMSM with casual partners, ACS reported the proportions

of visits at which GBMSM reported serosorting remained relatively stable over time: 10.2%, 11.4%, 10.0%, 10.0%, and 13.9%, respectively, of the visits in the years 2007-2011 (217).

2.3.3.6 Number of partners

Three observational studies and four interventional studies reported temporal trends in number of partners.

(i) Observational studies:

In the Netherlands, the ACS reported that the number of sexual partners (total and casual partners) per six-month period did not change significantly over time, 11 and 10 in 1995 versus eight and eight in 2002 (205). The AmPrEP (2015 – 2016) also reported no evidence for a change in the number of partners after six months of PrEP use overall or the number of unknown casual partners among 328 men (187). In a non-high-income country, the BMCS in Thailand reported that over 36 months, the odds for having more than four sexual partners in the past four months decreased by 1% for each additional four-month visit study participants attended (191).

(ii) Interventional studies

Biomedical interventional studies:

In the US, the US CDC Safety PrEP trial (2005 – 2009) reported that mean numbers of sex partners in the past three months decreased significantly from 7.25 at baseline to 6.02 during months 3–9 and 5.71 during months 12-24, but did not differ in the delayed arm compared to the immediate arm (195)**.**

In the UK, the PROUD trial (2012 – 2014) reported that the total number of sex partners varied from baseline to one year in both arms, but the study detected no difference between groups at one year (p-value at baseline not reported) (40).

In France and Canada, the IPERGAY randomized trial phase (2012 – 2014) reported a slight but significant difference in the number of sexual partners within the past two months in the placebo group as compared with the TDF-FTC group (average over the study period 7.5 and 8 respectively) (41). The IPERGAY trial OLE phase (2014 – 2016) reported that the number of sexual partners in the last two months (frequency of visits) did not change during the study period (42).

In a non-high income country, PrEP Brasil, a 48 week, open-label demonstration study that assessed PrEP delivery in Rio de Janeiro and Sao Paulo among 375

GBMSM between 2014 and 2016, reported the mean number of sexual partners in the previous three months decreased from 11.4 at enrolment to 8.3 at week 48 (218).

Behavioural interventional studies:

For behavioural interventional studies, all data from high-income countries were from the US. The 3MV behavioural intervention (2005, N=338) reported that at the 3-month assessment, 3MV participants reported a 25% greater reduction in the number of main or casual male sex partners during the past three months than comparison participants (208). Get Real, a community-level intervention in Philadelphia and Baltimore from 2007 to 2010 among 278 young GBMSM, reported the number of partners in the past six months and number of non-main anal sex partners in the past three months did not differ significantly by the city at either baseline or 36-month follow-up (219).

In non-high income countries, two behavioural intervention studies in Africa, the CNRIST/TAR (2010 – 2012) (203) and the Coastal Kenya study (2005 – 2011) (200), also reported a decrease in the mean number of sexual partners following a behavioural intervention. In the CNRIST/TAR, the mean number of sexual partners showed a trend to decrease from 4.0 ± 3.0 per month at inclusion to 3.0 ± 3.1 after two years, but the variation was not significant (203), while in the Coastal Kenya study on risk reduction counselling, between baseline and four years of follow-up, the number of partners in the past week declined from 0.5 to 0.3 (200). In China, the Nanjing HIV counselling study (2008 – 2010) reported that the proportion of participants who had one or no partner significantly increased from 40.9% to 48.0% (199).

2.3.4 Studies that have investigated trends in HIV and other STIs incidence and associated factors

From the systematic review process, six longitudinal cohorts (eight publications; six from high-income countries and two from non-high-income countries) and 13 interventional studies (15 publications; ten from high-income countries and five from non-high-income countries) reported trends or overall estimates of HIV incidence. Among these studies, there were nine studies (eleven publications) that also reported factors associated with HIV incidence. Two longitudinal cohorts and 11 interventional studies reported trends in STIs incidence, and two longitudinal cohorts reported factors associated with STI incidence.

During the additional scoping review, I identified four other observational studies published in recent years (since 2012), one from the Netherlands, one in Australia, and two studies from

the UK. Table 2.4 shows observational studies investigating trends in HIV and STI incidence, PrEP use, and sexual behaviour post-HIV diagnosis identified from the systematic review and scoping review processes, while data from interventional studies are summarized in Table 2.5

2.3.4.1 Trends in HIV and other STIs incidence over time

(i) Observational studies:

In the Netherlands, ACS published five papers, of which four I identified through systematic review and one through scoping review. Dukers et al. reported that during the period of 1984 – 2000, among 877 HIV-negative men, the incidence of HIV-1 strongly decreased in the early years of the ACS (1984 – 1985) and then fluctuated between 1989 and 1999 (205). In 1999, the incidence rate was 2.0 per 100 person-years (PYs). The incidence of Gonorrhoea increased slightly after July 1996, but this increase was not statistically significant in univariate analyses, and the relative risk decreased with correction for potential confounders in multivariate analyses. Van der Bij et al. reported that among 863 men, between 1995 and 2002, there was a significant increase in syphilis (0 to 1.4/100 person-years (PYs) and gonorrhoea incidence (1.1 to 6.0/ 100 PYs), but no change in HIV incidence (1.1 and 1.3/100 PYs) (206). Jansen et al. reported that among 1,642 men, HIV incidence strongly decreased from 8.6/100 PYs in 1985 to 1.3/100 PYs in 1992; it remained relatively stable around 1.0/100 PYs between 1992 and 1996, then slowly increased to 2.0/100 PYs in 2009 (128). Van den Boom et al., between 2007 and 2011, reported a high overall HIV incidence rate among 445 GBMSM with casual partners participating in ACS, 2.8/100 PYs (217). Results from my scoping review yielded another article published by ACS in recent years (2009 – 2017) by van Bilsen et al. that reported HIV incidence decreased from 1.9/100 PYs to 0.5/100 PYs among 905 GBMSM, while the incidence of any bacterial STI increased from 16.8/100 PYs to 33.1/100 PYs (220). The AmPrEP demonstration study reported a stable prevalence of any STI (17% at baseline vs 17% at six months) (187).

In Canada, the Vanguard project reported a high HIV incidence rate among 681 men between 1995 and 1998, 1.7 per 100 PYs in Vancouver (188). The Omega Cohort study reported an overall HIV incidence rate of 0.6 per 100 PYs between 1996 and 2003 among 1,587 men (221).

In France, the St. Louis Hospital study in Paris reported an overall HIV incidence of 0.82 per 100 PYs among 1,049 men initiating PrEP between 2015 and 2017, with all HIV infections diagnosed occurring in poorly non-adherent patients, while the increase in bacterial STIs was modest in this study (14.6% at baseline vs 19.2% at month 12) (189).

In Australia, the HIM cohort reported an overall incidence rate of 0.8 per 100 PYs among 1,423 men between 2001 and 2007 (222). Through scoping review, I identified another study, a retrospective observational study in Melbourne Sexual Health Centre (MSHC study) between 2013 and 2017 reported that the proportion of GBMSM tested each year who were diagnosed with incident HIV infection fell from 0.83% in 2014 to 0.38% in 2017 among 12,180 GBMSM attending sexual health centres (223).

In the US, the PHSKC cohort study (2014 – 2017, N=183) reported that the percentage of patients diagnosed with any STI while using PrEP (49.2%) was higher than the percentage diagnosed in the 12 months prior to PrEP use (35%), no data on HIV incidence were given (190).

In the UK, no observational studies were identified through the systematic review that showed trends in HIV incidence from prospective cohort studies. Two publications using data from the Genitourinary Medicine Clinic Activity Dataset (GUMCAD) were identified through scoping review process. In this open national cohort study among GBMSM who tested HIV negative at any STI clinic in England, a high annual HIV incidence among 26,600 repeat testers, 2.0 per 100 PYs, was reported in 2012 (224). Between 2014 and 2016, another study using GUMCAD data reported that between 2014 and 2016, new HIV diagnoses among GBMSM fell by 17% in England and 25% in London (109).

In non-high-income countries, both Chinese (5.0/100 PYs to 14.3/100 PYs between 2009 and 2012 among 809 HIV-negative GBMSM) and Thai cohorts (overall incidence rate above 5.0 per 100 PYs among 8,176 GBMSM between 2006 and 2013) reported an increase in HIV incidence (192, 193).

(ii) Interventional studies

Biomedical interventional studies:

PrEP trials reported significant reductions in HIV incidence (in intervention arm versus control or placebo) or no change over time and low HIV incidence rates, while the incidence of other STIs remained high. On the other hand, PEP trials reported no change in HIV or other STIs incidence and high incidence rates for both HIV and other STIs.

In the UK, the PROUD trial reported a reduction of 86% or a rate difference of 7.8 per 100 PYs in HIV incidence between the immediate group and deferred groups, but the proportion of STIs, including rectal gonorrhoea or chlamydia, did not differ (57% vs 50%) (40). No data on trends over time were given.

In France and Canada, the IPERGAY trial also reported a 86% relative reduction in HIV incidence, while the proportions of participants with a new STI during follow-up were not significantly different (41% in the TDF-FTC group vs 33% in the placebo group) (41). The OLE phase of the IPERGAY trial confirmed the high efficacy of PrEP in GBMSM having frequent sex, with a relative reduction of HIV incidence of 97% compared with that of the placebo group during the randomised phase of the study (0.19 per 100 PYs vs 6.60 per 100 PYs), again in the context of the incidence of first bacterial STI not changing significantly compared with the randomised phase (59·0 vs 49.1/100 PYs, respectively, p=0.11) (42).

In Australia, the PrELUDE study reported that no HIV infections were observed in 18 months, while the incidence of STIs, including the incidence of three infections caused by *Neisseria gonorrhoeae* (gonorrhoea, any location), *Chlamydia trachomatis* (chlamydia, any location) and infectious *Treponema pallidum* (infectious syphilis) was high and stable (207). However, gonorrhoea infections were declining from 100.0 to 25.8 per 100 PYs between six and 15 months (207). In a non-high-income setting, PrEP Brasil (2014 – 2017) reported HIV incidence of 0.51/100 PYs (218), no data on trends over time were given.

Among men receiving PEP, two studies in the US reported findings. The San Francisco PEP study reported an HIV incidence rate of 1.2 per 100 PYs at 12 months among 397 men, equivalent to rates in San Francisco among all GBMSM during 1997 – 2000 (183). The assessment of STI incidence in this study was done by cross-referencing the database of STIs maintained by the San Francisco Department of Public Health for individuals who resided in San Francisco county. Overall, comparing the total number of STIs recorded in the year following study entry with that of the year before entry, most participants (85%) in the study had no change in STI incidence; 8.5% had a decrease and 6.8% an increase. The EXPLORE trial (1999 – 2003, N=4,295) also reported no change in HIV infections where non-occupational PEP courses were reported (hazard ratio = 0.91) (225).

Behavioural interventional studies:

Data from behavioural intervention studies, both in the US and non-high-income countries, either reported no change in HIV incidence after intervention, much lower reduction in HIV incidence than PrEP trials, or even higher incidence rates.

The EXPLORE trial reported an 18.2% lower rate of HIV acquisition in the intervention group consisting of ten one-on-one counselling sessions than the standard group (twice-yearly individual counselling) among 4295 men recruited between 1999 and 2001 (214).

A high overall incidence rate among 3764 men in the EXPLORE trial was also reported in 2011 (2.1 per 100 PYs), with Latinos having a higher incidence rate than non-Latino whites (2.99 vs 1.90/100 PYs) (226). Keep It Up! online trial (2013 – 2017, N=901) in Chicago reported the rate of self-reported incident HIV diagnoses of 2.1 per 100 PYs, with no difference between control (standard online HIV information, 2.0 per 100 PYs) and intervention arms (multimedia behaviour lessons 2.3 per 100 PYs) (204). STI diagnosis at month 12 was 40% lower for intervention participants in the intervention arm.

In non-high-income countries, China's Nanjing HIV counselling study reported a decrease in HIV incidence from 5.2 per 100 PYs at baseline to 3.8 per 100 PYs during 6-12 months, then to 1.1 per 100 PYs during 12-18 months between 2008 and 2010 (199). In India, the Chennai RCT in 2013 reported no incident HIV infections throughout the six-month follow-up, and the incidence of bacterial STIs was lower in the intervention group who received integrating risk-reduction counselling with counselling to foster self-acceptance (17.5%) than the control group who received only the standard of care (28.6%) (201). The CNRIST/TAR risk reduction counselling intervention (2010 – 2012) study in Central Africa showed that the prevalence of HIV, syphilis and hepatitis B increased significantly from 29% to 41%, 12% to 21% and 14% to 23%, respectively, between baseline and two-year follow-up among participants (203). Lastly, the Russia-Hungary pilot social network intervention trial (2007 – 2012) reported that HIV/STI incidence was lower in intervention networks than in the comparison networks (9.0 per 100 PYs vs 15.0 per 100 PYs) (202).

2.3.4.2 Factors associated with HIV incidence

Eight of 11 observational studies that reported factors associated with HIV incidence reported CLS as the main factor associated with incident HIV infection (188, 206, 217, 224, 227-229), two studies reported serosorting as a predictor (217, 222), two studies reported a lower level of education (128, 227), three studies reported younger age (188, 192, 227), and three studies reported drug use (188, 224, 228). Other factors that were reported as predictors of HIV acquisition included multiple sex partners (128) and gonorrhoea (128). Factors associated with STI incidence included CLS (206) and serosorting (230).

Two other observational studies that were identified through the scoping review reported additional results on associations of factors with HIV incidence. Desai et al. reported that among GBMSM in England in 2012, HIV incidence was higher among Black GBMSM (3.2 per 100 PYs) and those with a bacterial STI diagnosis at the initial attendance (3.2 per 100 PYs) (224). GBMSM with previous syphilis or gonorrhoea infection were at significantly greater risk of acquiring HIV in the subsequent year (224). In Australia, the MSHC cohort in

Melbourne reported that being newly-arrived and Asian-born was associated in the multivariable analysis with the odds of being diagnosed with incident HIV infection in the period July 2015–June 2017 (aOR 4.40 (2.38–8.15), $p < 0.001$) but not in the period July 2013–June 2015 (223). Consistent condom use and sexual partners greater than ten in the previous three months were associated in the earlier period but not in the later period.

Factors associated with HIV incidence reported by interventional trials (both data from PrEP trials) were not using PrEP (39) and undetectable tenofovir concentrations (216).

Table 2.4 Summary of observational studies on trends in HIV incidence and other STIs, PrEP use, and sexual behaviour post HIV diagnosis and associated factors, 1998 – 2020

Name of the study; study settings	First author (year); data collection period; sample size	Temporal trends				Factors associated			
		HIV incidence*	STIs	PrEP use	CLS post diagnosis	HIV incidence	STIs	PrEP use	CLS post diagnosis
Longitudinal cohorts from high-income countries									
ACS; Amsterdam	1) Dukers (2001); 1984 – 2000; 877 men	1985 – 1988: decrease 1989 – 1999: fluctuate in 1999: 2.0/100 PYs	increase (after 1996)						
	2) Van der Bij (2005); 1984 – 2002; 863 men	no change	increase			CLS	CLS		
	3) Jansen (2011); 1984 – 2009; 1,642 men	1992 – 1996: no change 1996 – 2009: increase				CLS, multiple sex partners, gonorrhoea, education			
	4) Heijman (2012); 1984 – 2008; 206 men				1 year: decrease after 1 year: increase				
	5) Van den Boom (2014); 2007 – 2011; 445 men	overall incidence 2.8/100 PYs*				CLS, serosorting			
	6) Coyer (2018); 2015 – 2017; 687 men			increase					
	7) Ward van Bilsen** (2020); 2009 – 2017; 905 men	decrease	increase						
AmPrEP; Amsterdam	Hornenborg (2018); 2015 – 2016; 328 men		no change						
HIM; Sydney	1) Jin (2009); 2001 – 2007; 1,427 men	overall incidence 0.8/100 PYs*				serosorting			
	2) Jin (2012); 2001 – 2007; 1,427 men						serosorting		

Name of the study; study settings	First author (year); data collection period; sample size	Temporal trends				Factors associated			
		HIV incidence*	STIs	PrEP use	CLS post diagnosis	HIV incidence	STIs	PrEP use	CLS post diagnosis
MSHC study; Melbourne	Medland** (2018); 2013 – 2017; 12,180 men	decrease				newly-arrived Asian-born, CLS, >10 sex partners			
FLUX study; Australia	Hammoud** (2019); 2014 – 2017; 1,257 men			increase				CLS, age, living in an state with PrEP trial, social engagement, illicit drugs, group sex.	
GUMCAD; England	1) Desai** (2017); 26,600 men	overall incidence 2.0/100 PYs*				bacterial STI, Black ethnicity, syphilis			
	2) Brown** (2017); 2014 – 2016; 3,067 new diagnoses	decrease							
Vanguard Project; Vancouver	Strathdee (2000); 1995 – 1998; 681 men	overall incidence 1.7/100 PYs*				CLS, injection drugs, age			
Omega Cohort Study; Montreal	Lavoie (2008); 1996 –2003; 1,587 men	overall incidence 0.6/100 PYs*				CLS			
Momentum Health Study; Vancouver	Mosley (2018); 2012 – 2018; 528 men			increase (awareness)				sexual behaviours, age, income, education	
St Louis Hospital Study; Paris	Noret (2018); 2015 –2017; 1,049 men	overall incidence 0.8/100 PYs*	Increase						
RADAR; Chicago	Newcomb (2018); 2015 – 2017; 953 men							CLS, sero-discordant partnerships	

Name of the study; study settings	First author (year); data collection period; sample size	Temporal trends				Factors associated			
		HIV incidence*	STIs	PrEP use	CLS post diagnosis	HIV incidence	STIs	PrEP use	CLS post diagnosis
PHSKC Cohort Study; Seattle	Montano (2018); 2014 – 2017; 183 men		increase (after PrEP)						
MACS; Baltimore, Pittsburgh, Chicago, Los Angeles	1) Swartz (2017); 1985 – 2008; 1044 men					CLS, nitrite drugs			
	2) Zhu (2018); 1985 – 2008; 558 men				decrease	sex with ≥2 partners, heavy drinking			
Metromates Cohort Study; Los Angeles	Gorbach (2018); 2009 – 2013; 328 men				no change				
Seroconversion Cohort Study; Seattle	Khosropur (2016); 2001 – 2013; 186 men				HIV- partners: decrease HIV+partners: increase serosorting: no change				
Generations study; US (50 states)	Holloway** (2020); 2016 – 2018; 470 men			increase					
Longitudinal cohorts from non-high-income countries									
Beijing VCT study; Beijing	Lau (2015); 2009 – 2012; 228 men	increase							
BMCS; Bangkok	Van Griensven (2015); 2006 –2013; 1,259 men	increase				age			

* Data were also extracted for studies that reported overall estimates of incidence within certain period instead of trends over time

**Articles identified from scoping reviews

Table 2.5 Summary of interventional studies on trends in HIV incidence, PrEP use, and sexual behaviour post HIV diagnosis, 1998 – 2020

Name of the study; study settings	First author (year); data collection period; sample size	Temporal trends				Factors associated			
		HIV* incidence	STIs	PrEP use	CLS post diagnosis	HIV incidence	STIs	PrEP use	CLS post diagnosis
Trials or interventional studies from high-income countries									
PROUD Trial; England	McCormack (2015); 2012 – 2014; 544 men	86% reduction	no change						
IPERGAY Trial; France and Canada;	Molina (2015); 2012 – 2014; 400 men	86% reduction	no change						
IPERGAY OLE; France and Canada	Molina (2017); 2014 – 2016; 361 men	97% reduction	no change			not using PrEP			
PRELUDE study; Sydney	Zablotska (2018); 2014 – 2016; 320 men	no incidence	no change						
San Francisco PEP study; San Francisco	Martin (2004); 1997 – 2000; 397 men	overall incidence 1.2/100 PYs*	no change						
EXPLORE study; Boston, Chicago, Denver, New York, San Francisco, Seattle	1) Koblin (2004); 1999 – 2003; 4,295 men	18% reduction							
	2) Donnel (2010); 1999 – 2003; 4,295 men	no change							
	3) Bedoya (2011) 1999 – 2003; 4,295 men	overall incidence 2.1/100 PYs*				CLS, popper use			
Project MIX; Chicago, Los Angeles; New York, San Francisco	Koblin (2011); 2004 – 2008; 645 men			low PrEP use					
Keep It Up; Atlanta, Chicago, New York	Mustanski (2018); 2013 – 2017; 901 men	no change	decrease						
Trials or interventional studies from non-high-income countries									
PrEP Brasil; Rio de Janeiro, Sao Paulo	Grinszteijn (2018); 2014 – 2017; 450 men	overall incidence 0.5/100 PYs*				undetected tenofovir			

Name of the study; study settings	First author (year); data collection period; sample size	Temporal trends				Factors associated			
		HIV* incidence	STIs	PrEP use	CLS post diagnosis	HIV incidence	STIs	PrEP use	CLS post diagnosis
Nanjing HIV Counselling; Nanjing	Huan (2013); 2008 – 2010; 430 men	decrease							
Pilot RCT Chennai; Chennai	Safren (2014); 2013; 96 men	no incidence	decrease						
CNRIST/TAR; Bangui	Marcel (2018); 2010 – 2012; 99 men	decrease	decrease						
Russia–Hungary Intervention Trial; St. Petersburg and Budapest	Amirkhanian (2015); 2007 – 2012; 586 men	decrease	decrease						

* Data were also extracted for studies that reported overall estimates of incidence within certain period instead of trends over time

2.3.5 Studies that have investigated trends in PrEP use and associated factors

Data regarding trends in PrEP use over time or associated factors were all from observational studies in high-income countries. I identified four cohort studies through the systematic review process and two other studies from an additional scoping review. Of all these six studies, one was conducted in the Netherlands, one in Canada, one in Australia, and three in the US (Table 2.4).

In the Netherlands, ACS reported that PrEP use increased between 2015 and 2017 among 687 GBMSM but remained under 10% (230). Among the participants, 32% met the eligibility criteria to use PrEP, and 51% had a high intention to use PrEP. Around the same period (2012-2016), in Canada, the Momentum Health Study reported that among 528 GBMSM in Vancouver, PrEP awareness increased over time, while the overall PrEP use prevalence during the study was only 2.3% (231). In Australia, data from 1,257 men enrolled during 2014-2015 in the Following Lives Undergoing Change (Flux) Study, a national, online, prospective observational study, reported that the proportion of men who reported current use of PrEP increased from 0% to 18.0% at 24 months (232). In the US, Project MIX reported a low prevalence of PrEP use among 645 men recruited for a behavioural intervention trial between 2004 and 2008 in four US cities, 2.4% (233). According to data from a nationwide probability sample of GBMSM from three age cohorts of men in the US, while PrEP use increased by 90%, from 4.1% in 2016 to 7.8% in 2018, this only represented a small percentage of overall uptake among eligible participants across time (6.6%) (234).

The Momentum Health study reported that PrEP use awareness was associated with higher annual income, education level greater than high school, practising viral load sorting as an HIV prevention strategy, being between 29 and 40 years, having used ecstasy in the previous six months, and reporting higher sexual sensation seeking scale scores (231). In the US, the RADAR study reported that among 953 young GBMSM between 2015 and 2017, PrEP use was associated with higher rates of receptive CLS (235). The Flux study reported that factors independently associated with non-uptake of PrEP were younger age, living in an Australian state without a PrEP trial, lower social engagement with other gay men, and being less likely to have engaged in HIV sexual risk behaviours such as group sex or any condomless anal sex (232). The incidence of PrEP initiation in the Flux study was higher among men who reported using any illicit party drugs in the previous six months (but not for sex) and among those who used any illicit party drugs specifically for sex, as compared to men who did not use any illicit party drugs in the previous three months (232).

At the time of the systematic review, no data had been published from longitudinal cohort studies in England on trends in PrEP use over time, apart from the PROUD trial itself (40). In

2018, data from the AURAH cross-sectional study were compared with baseline data from GBMSM in the AURAH2 prospective study and reported that self-reported PrEP use was relatively low in both AURAH (3.8%) and AURAH2 (5.5%) (155) (this is not included in Table 2.4 as this was not a longitudinal comparison).

2.3.6 Studies that have investigated changes in sexual behaviour post-HIV diagnosis

Four longitudinal cohorts (five publications) reported changes in sexual behaviour post-HIV diagnosis, all in high-income countries (Table 2.4), all were identified through the systematic review process.

In the Netherlands, ACS reported that the risk of having CLS one year after HIV diagnosis decreased compared with one year before diagnosis in both the pre-cART era and cART era in 206 MSM between 1984 and 2008 (236). In contrast to a continuing decrease of CLS in the pre-cART era (1984 – 1995), the probability of CLS in the cART era (1996 – 2008) increased again to pre-seroconversion levels four years after diagnosis. MACS in the US reported sharp reductions in CLS after diagnosis (seroconversion) in the early 1990s that rebounded considerably within the first decade of the 2000s among 1044 participants (composed of 348 seroconverting, 348 seronegative, and 348 seroprevalent participants matched on demographics, recruitment cohort, and study visits) (227). Another report from MACS of analyses of data from 4,616 GBMSM between 1984 and 2008 indicated that HIV seroconversion was associated with reduced odds of insertive anal sex with two or more partners, reduced odds of subsequent engagement in sex with two or more partners, and reduced odds of heavy drinking, and that seroconversion after 1996 was associated with further reduced odds of insertive anal sex with two or more partners (237). Among a retrospective seroconversion cohort of 186 GBMSM attending an STI clinic in Seattle who tested HIV positive between 2001 and 2013, the proportion reporting CLS with HIV negative partners declined at 12 months after diagnosis and remained stable for up to four years after diagnosis (238). From 2009 to 2012, the Metromates Study enrolled and followed for one year 328 GBMSM seeking testing for HIV in Los Angeles. This study reported little indication of behaviour change following HIV diagnosis and continued CLS (239).

2.4 Discussion

2.4.1 Summary of literature review

2.4.1.1 Within-person changes in sexual behaviour

Of the studies identified in the systematic review, in the last 20 years, globally, only a quarter (27%) provided data on individual-level changes in sexual behaviour among HIV-negative GBMSM. Direct comparisons between studies are challenging, as these studies differed in terms of types of outcome measures, definitions of the outcomes and approaches in analysing the data.

Several studies defined specific longitudinal trajectories of sexual behaviour over time to identify typical patterns of sexual risk behaviour at the population level. The main findings that broadly concur in many of these studies are that while GBMSM vary in their risk level, there remains a predominance of low-risk behaviour. For example, VPCNSS found that a majority of participants were identified as either 'monogamous' (26%) or 'risk minimisers' (31%) (169), MACS found that 63% of the participants rarely engaged in high-risk behaviours in their eight-year trajectory (171), and 78% were rarely users of stimulant drugs over time (172). ACS also identified that 90% of the sample followed a 'low risk' trajectory (164).

Some studies focused on the extent to which individuals transitioned in or out of a specific sexual behaviour group over time. Most evidence suggests that adult HIV-negative GBMSM in the era of cART have relatively consistent patterns of sexual risk behaviour across time and have limited movement between risk classes over time (164, 169, 171). For example, the probability of engaging in subsequent high-risk behaviour among the group initially defined as 'high risk' group in MACS was 71% over the eight-year study period (104), and 70% among the 'risk taker' group in VPCNSS (102). However, among younger GBMSM, there appears to be a higher level of movement in behavioural risk-taking over time (173). Findings also suggest that before cART was available, transitions between sexual roles were high among GBMSM (132).

There also appeared to be a within-person and between-person heterogeneity in CLS episodes, number of partners, and type of sexual contacts over time, with the construct of CLS activity among young GBMSM to be less stable than older GBMSM. A consistent increase in CLS acts within-individual since cART was available was also found among HIV-negative GBMSM.

Most studies identified younger age and drug use as the main predictors of membership in high-risk sexual behaviour groups. Drug use prior to sex may vary within-person over time

depending on various characteristics associated with sexual partners (casual/regular/main partners) or sexual roles (insertive or receptive). Findings also suggest that White ethnicity and positive/romantic relationship cognitions were associated with a higher number of CLS acts. The fact that sexual risk levels parallel stimulant drug use over time suggests that finding ways to lower rates of stimulant drug use among GBMSM could be a tool in HIV prevention (172).

2.4.1.2 Temporal trends in sexual behaviour (over calendar year or cohort follow-up)

The majority of the studies identified in the systematic review examined the overall temporal trends in sexual behaviour. Data from longitudinal observational studies indicated increasing sexual risk behaviours over time among GBMSM in high-income countries in the era of cART. Upward trends were seen in CLS, CLS with main and casual partners, CLS with HIV-negative partners (serosorting), and stable for CLS with partners of unknown or discordant HIV status. Most of these studies collected data in the early 2000s when the increase in HIV infections was also seen among GBMSM in high-income countries, despite increasing treatment coverage during the same time frame. GBMSM could be engaging in more serosorting, or they, or their partners, could be on ART and virally suppressed, with a reduced risk of transmission, or on PrEP to lower the risk of HIV acquisition. At the same time, in a non-high-income country (Thailand), the frequency of high-risk behaviours between 2006 and 2016 declined (192). Despite the decrease, a significant proportion of GBMSM reported consistently engaging in CLS, which could explain the persistently high level of HIV incidence observed (191, 192).

In both high-income and non-high-income countries, data from PrEP trials and demonstration studies in this review observed an increase in condomless sex over time, which might reflect participants' increasing confidence in the effectiveness of PrEP. Data from behavioural interventional studies, in contrast, showed reductions or no changes in CLS over time or between groups (intervention versus control). As the behavioural interventional studies were designed to reduce high-risk sexual behaviours and HIV acquisition through HIV prevention intervention, no increase in risky sex was to be expected from them. However, findings suggest that reduction in sexual risk behaviour achieved through brief behavioural interventions are often not sustained.

There appeared to be a stable or downward trend in the number of partners among GBMSM in the Netherlands (in 2002, 2015 – 2016) and Thailand (2006 – 2012) (187, 191, 206). The cause of this tendency is unknown. One Australian study found that GBMSM shifted away from open relationships, explaining the decrease in the number of partners (240). When discussing temporal trends in a cohort study, there are complicating factors such as the

ageing of the cohort that could also cause a stable or downward trend. Further investigation is required to determine the extent to which the declining trend is occurring and why.

2.4.1.3 Trends in HIV and STIs incidence over time (calendar year or cohort follow-up)

Data from observational cohort studies indicated that HIV incidence rates rose among GBMSM between 1984 and 2011 in high-income countries with available data (the US, the Netherlands and Australia). In non-high-income countries with available data (China and Thailand), the incidence rates among GBMSM were higher (above 5.0 per 100 PYs) than in high-income countries between 2006 and 2013. CLS and drugs or substance use remained the major predictors of incident HIV among GBMSM populations reported in this review.

Since 2012, a decline in HIV incidence was described in England, the Netherlands, and Australian cohorts. The lower transmission rates due to the increase in early diagnosis, early initiation of treatment and uptake of PrEP in the community would be the most plausible explanation for the overall decrease in HIV incidence found in these studies (109, 220, 223).

Findings also showed a rise in other STIs among GBMSM populations after 1996 in high-income countries. Given the gradual decline in condom use found in these studies, changes in sexual behaviour were likely driving this trend. Decreasing condom use might result from a lower perceived threat of HIV; HIV is seen as a less frequently occurring, chronic and manageable disease and because of risk compensation due to biomedical HIV prevention strategies. Future studies should focus on the effect of these and other HIV prevention strategies on sexual behaviour and their eventual influence on STI and HIV incidence in the GBMSM population.

PrEP trials and demonstration studies showed the efficacy of PrEP, both daily and on-demand, in reducing HIV incidence. HIV incidence in the intervention arm of these studies was low, with the highest reduction in HIV incidence due to the use of PrEP shown by the IPERGAY trial – OLE phase in 2014 – 2016 (42). For a median duration of follow-up of 18.4 months, the overall HIV incidence in the OLE phase was 0.19 per 100 PYs, 95% CI 0.01–1.08, 97% relative reduction when compared with that of the placebo group during the randomised phase of the study (6.60 per 100 PYs, 95% CI 3.60–11.05) (42). The incidence of other STIs was high and stable throughout the follow-up period; however, most studies reported no change in incidence. The high STI rates could be related to decreased condom use among PrEP users (41, 42). Selection bias might also be a factor, as these PrEP studies were more likely to include early adopters with high-risk behaviours, for example, those who are not always using condoms before starting PrEP. Counselling to prevent GBMSM from STIs other than HIV among PrEP users should be a critical component of a comprehensive approach to HIV prevention and protection against STIs among GBMSM.

While behavioural interventions seem to lower the rates of high-risk sexual behaviours, they did not lower HIV incidence to as great an extent as that seen in PrEP trials. In addition, these reductions in risk are usually in the short term. Studies that investigated long-term effects (>18 months, for example EXPLORE project), found more favourable estimates of effect in the first 12 – 18 months, with only an 18.2% difference of HIV acquisition between intervention and standard group (214). The evidence seems to suggest that the engagement of individuals at high risk in intensive interventions over a short period may not be effective in reducing HIV incidence.

2.4.1.4 Trends in PrEP use over time (calendar year or cohort follow-up)

Findings from the reviews point to the steep increases in PrEP use in the high-income countries that reported data on this, but also reinforce that PrEP use remained comparatively low until 2017 (<10% of GBMSM). This was primarily due to lack of approval of PrEP during the study period (231), the high costs associated with acquiring the medication, the relative difficulty in getting coverage through private insurance providers (234), or the unequal access to PrEP at the time of data collection (232). Data from ACS also showed that most of the eligible GBMSM were currently not using PrEP during the study period, suggesting that a large proportion of GBMSM at risk for HIV could benefit from it once accessibility improves (230).

Low PrEP use in these studies indicates room for improvement in strategies designed to make PrEP more accessible. PrEP is an essential advance in HIV prevention, and now in many high-income countries has become part of the HIV prevention package; there should be a focus on improving the implementation of PrEP programs. More research is also needed to improve the intention to use PrEP among eligible GBMSM.

2.4.1.5 Sexual behaviour changes post-HIV diagnosis

Findings from a few studies in this review suggest a pattern of evolving sexual behaviour following diagnosis. Observational cohorts reported that men rapidly and profoundly decreased behaviours associated with HIV transmission in the period immediately following diagnosis (2001 – 2008). However, data also showed that the decreases tended to be temporary, with high-risk behaviours tending to increase again, roughly within 12 months after diagnosis.

There was also substantial variation at the individual level, with the factors underlying this variation not well understood. Changes in sexual behaviour among GBMSM recently diagnosed with HIV have the potential to reduce HIV transmission to HIV-negative men. The reductions appeared more temporary following cART availability and awareness that people

on ART with suppressed viral load could not transmit the virus to others, highlighting the usefulness of early detection of HIV infection. For example, the Metromates study that collected data from 2009 to 2012, enrolled and followed for one year 328 GBMSM seeking testing for HIV in Los Angeles reported little indication of behaviour change following HIV diagnosis and a pattern of continued CLS (239).

2.4.2 Limitations

My findings should be interpreted in light of limitations. The varied samples included in the review may not represent all GBMSM as most were convenience samples or venue-based recruitment samples rather than population-based samples. Some important findings of significant change in risky sex behaviours were from cohorts of young or emerging adulthood GBMSM that are likely not representative of the older GBMSM population. Also, some analyses were based on early data (collected in the early 1990s but published later), limiting their relevance to the present time transmission dynamics.

In this review, rather than comparing the prevalence of each sexual behaviour between studies, I focused on whether there were trends (increases or declines) in sexual behaviour over time, with or without interventions. Prevalence comparison was challenging and was not the main goal of the review due to the studies' differences in several factors, such as study designs, recruitment settings or inclusion criteria. For example, some studies recruited only high-risk men or sexually active men, impacting the prevalence of condomless anal sex in the study. There may be errors or bias in reporting sexual behaviour due to several factors that should be taken into account, such as the ageing of the cohort. Furthermore, as I limited the literature review to longitudinal studies only, important findings from cross-sectional data might have been missed. However, in the results chapters (Chapters 4 to 8), I also included some crucial findings from other studies that were not identified in this review (modelling, cross-sectional, or data from surveillance).

A conventional double-screening process is generally recommended when conducting a systematic review (at least two reviewers conduct the review independently of each other) to ensure the reliability of the results. Therefore, I may have missed some studies. Lastly, only studies written in English were included in the review; therefore, some studies from non-English speaking countries could have been excluded.

Despite the limitations, the results have provided some framework for quantifying variation in sexual behaviour to help understand the HIV epidemic among GBMSM.

2.4.3 Conclusion, literature gaps and rationale for this thesis

In this chapter, I have summarised the findings from the literature showing that there were limited studies conducted among HIV-negative GBMSM investigating within-person changes in sexual behaviours. The majority of the findings on this topic were from the US, where the HIV epidemic among GBMSM is quite different from that in the UK or Europe; therefore, it may not be generalizable to the GBMSM in the UK. There was limited research conducted in the European setting and no data from the UK at the time of the systematic review. The effect of individual-level variation in sexual behaviour rates is very complex and deserves further study to understand better the dynamics in HIV transmission among GBMSM in the UK.

Declines in HIV incidence among GBMSM have been reported in some high-income countries. There remained, however, limited data from UK prospective studies assessing HIV acquisition risk, associated factors, and temporal trends for incident HIV. Such data is needed to provide insight regarding the risk factors driving the HIV epidemic among GBMSM in England.

A combination of PrEP scale-up, a large increase in ever and repeat HIV testing, and rapid ART initiation at diagnosis were likely responsible for the steep declines in HIV incidence seen in most recent years. However, there was no data on longitudinal trends in PrEP uptake and predictors of PrEP initiation from UK prospective studies. At the time of conducting this review, a fully commissioned programme for PrEP in England had been agreed upon; however, there had been some delays with the implementation. Such data would be helpful to inform the unrestricted PrEP implementation program in England about who can benefit most from PrEP and how much people are already aware of it.

International findings from some longitudinal cohorts reported that GBMSM reduced levels of CLS at the point of learning they were HIV positive. In the UK, the extent to which sexual behaviour that contributes to the risk for HIV infection increases, decreases, or is maintained post-diagnosis has not been determined. A thorough understanding of the pattern of risk behaviours among HIV-positive GBMSM shortly after diagnosis would be crucial to assess the potential risk of HIV spread in the community and give insight into the risk of transmission of other STIs.

Therefore, this thesis attempts to bridge the knowledge and understanding of:

(i) Individual changes in sexual behaviour among GBMSM in England in the era of cART, particularly in individual transitions between different classes of sexual behaviour and the factors that affect the transitions. This is the aim of Chapter 5.

(ii) Trends in PrEP use and the predictors of PrEP initiation among GBMSM in England. This is the aim of Chapter 6.

(iii) Trends in HIV incidence and the predictors of HIV acquisition among GBMSM in England. This is the aim of Chapter 7.

(iv) Longitudinal changes in sexual behaviour following HIV diagnosis and associated factors. This is the aim of Chapter 8.

Chapter 3: Methods: Attitudes to and Understanding Risk of Acquisition of HIV over time (AURAH2) study

3.1 Introduction

3.1.1 Chapter aims

The objectives of this chapter are:

(i) to explain the PhD work streams and data sources used to address research questions in this thesis
(ii) to outline the design and methodology of the prospective cohort study 'Attitudes to and Understanding Risk of Acquisition of HIV over time' (AURAH2)
(iii) to describe the linkage process between the AURAH2 and the UK Health Security Agency (UKHSA) data
(iv) to detail the data management of the AURAH2 study
(v) to describe the variable definitions used for analysis in the AURAH2 study

3.2 PhD work streams and data sources

Data from two prospective studies were used in this thesis to answer the underlying research questions (Chapter 2, Section 2.4.3). As an overview, work stream 1 involved analysis of data from the AURAH2 study: a cohort study of initially HIV-negative gay, bisexual, and other men who have sex with men (GBMSM) attending sexual health clinics (Chapters 4 to 7), while work stream 2 involved analysis of data from Guys' and St. Thomas' study of people newly diagnosed with HIV attending an HIV clinic (Chapter 8). These two studies ran concurrently (AURAH2 between 2013 and 2018, Guys' and St. Thomas' between 2015 and 2018), and both were quantitative in nature.

3.2.1 PhD work stream 1: Analysis of data from the AURAH2 study

This part of the PhD comprised four primary analyses, detailed in Chapters 4 to 7, and focused on the GBMSM who were HIV-negative or undiagnosed at study recruitment. The specific research questions this work stream sought to answer were:

(i) What are the baseline characteristics of GBMSM attending sexual health clinics and predictors of loss to follow-up amongst these men? (addressed in Chapter 4)
(ii) What are the within-individual patterns in sexual behaviour and the predictors of transition in sexual behaviour? (addressed in Chapter 5)

(iii) What have been the trends in pre-exposure prophylaxis (PrEP) use over time, and what are the predictors of PrEP initiation? (addressed in Chapter 6)
(iv) What have been the trends in HIV incidence over time, and what are the predictors of HIV incidence? (addressed in Chapter 7)

3.2.2 PhD work stream 2: Analysis of data from the Guy's and St. Thomas' study

This part of the PhD was concerned with changes in sexual behaviour after being diagnosed with HIV; analysis was conducted among a recently-diagnosed HIV-positive population. This second work stream involved data management and analysis of newly diagnosed GBMSM attending a central London HIV clinic. This work stream aimed to examine the changes in sexual behaviour among men newly diagnosed with HIV and factors associated with sexual behaviour in the initial period after diagnosis and is detailed in Chapter 8. The reason for selecting the Guys' and St. Thomas' data instead of the AURAH2 data for analysing changes in sexual behaviour after HIV diagnosis was because AURAH2 had a relatively low incidence (although 33 men were diagnosed with HIV during the AURAH2 study follow-up, data on sexual behaviour after HIV diagnosis were only available for 15 of these men, see Chapter 7).

In this chapter, methods and data management are only described for analysis using the AURAH2 data, while the complete methods and management of data using the Guy's and St. Thomas study are detailed in Chapter 8, together with the results. I separate the methods for these two studies to bring the methods section closer to the respective results chapters. Statistical analyses are described in each relevant results chapter (Chapters 4 to 7).

3.3 Attitudes to and Understanding of Risk of Acquisition of HIV over time (AURAH2) study

3.3.1 Aims and rationale for the AURAH2 study

The AURAH2 study aimed to determine incidence and predictors of new HIV infections and provide longitudinal data on changes in sexual behaviour, recreational drug use, HIV testing practices, and PrEP and PEP use over time and associated factors, among initially HIV-negative GBMSM (154).

The AURAH2 study's specific objectives were to determine:

(i) the prevalence and correlates of specific sexual behaviours, such as condomless sex, number of condomless sex partners, condomless sex with casual partners and

partners of unknown HIV status, insertive/receptive condomless sex, and other specific higher-risk sexual activities such as group sex and chemsex

(ii) the number of condomless sex partners before, during, and after the estimated period of primary HIV infection and time of HIV diagnosis in men who become infected during the study, as well as correlates of within-person changes in sexual behaviour

(iii) the frequency and type of HIV testing accessed over time (sexual health clinic, self-testing, general practitioner, surgery, hospital, other)

(iv) the extent to which baseline demographic, socioeconomic, and health and lifestyle factors (including recreational drug use and chemsex) are predictive of subsequent levels of condomless sex, incident HIV infection, and HIV-testing behaviours

(v) the association of attitudes to HIV transmission, disclosure, treatment, and prognosis, with high-risk sexual behaviours, HIV-testing behaviours, and subsequent HIV acquisition

(vi) the associations of participant characteristics, sexual behaviour, and attitudes with reported use of, and willingness to consider the use of, post-exposure prophylaxis (PEP) and PrEP

The AURAH2 study was an element of the PANTHEON programme grant, a five-year research programme funded by the National Institute for Health Research (NIHR) into the cost-effectiveness of HIV testing among men who have sex with men in the UK to reduce HIV transmission. The core group of researchers at UCL's Institute for Global Health responsible for the PANTHEON project were Professor Alison Rodger (Chief Investigator), Professor Andrew Phillips, and Dr Fiona Lampe.

The AURAH2 study was prompted by an increase in the annual number of new HIV infections among GBMSM in the United Kingdom in 2014, with a significant proportion of undiagnosed individuals (154). As a result, the AURAH2 was created to provide the first detailed longitudinal data on the incidence and predictors of new infections among HIV negative GBMSM at risk of HIV infection in the UK. As indicated by the original study objectives listed above, the AURAH2 study's findings were also intended to provide crucial insight into established and emerging risk behaviours that may be linked to HIV acquisition in GBMSM in the UK, changes in sexual behaviour over time within people, and information on HIV testing practices and to inform the development of future HIV prevention strategies. The AURAH2 study's wide range of themes was intended to allow for several focused health promotion measures tailored to the GBMSM that would be very relevant to HIV prevention efforts. The intention was that information gathered in the AURAH2 study would also be used to parameterise a mathematical model to assess the epidemiological impact and cost-

effectiveness of various GBMSM preventive efforts (1-3). The study's findings would also inform national policy targeted at reducing HIV incidence and increasing HIV testing in this population in the UK.

My PhD thesis contributes to addressing objectives (i), (ii), (iv), and (vi) of the AURAH2 objectives.

3.3.2 AURAH2 study design

The AURAH2 study was a prospective observational cohort study that recruited GBMSM who were HIV-negative or undiagnosed from three large sexual health clinics in London and Brighton: 56 Dean Street Clinic, London; Mortimer Market Clinic, London; and Claude Nicol Clinic, Brighton. These clinics had contributed the most significant number of GBMSM to the AURAH study, a cross-sectional self-administered questionnaire study among HIV-negative or undiagnosed GBMSM attending 20 sexual health clinics across the UK between 2013 and 2014 (153).

Methodological details of the AURAH2 study have been previously published (154). Participants were eligible for inclusion into the study if they:

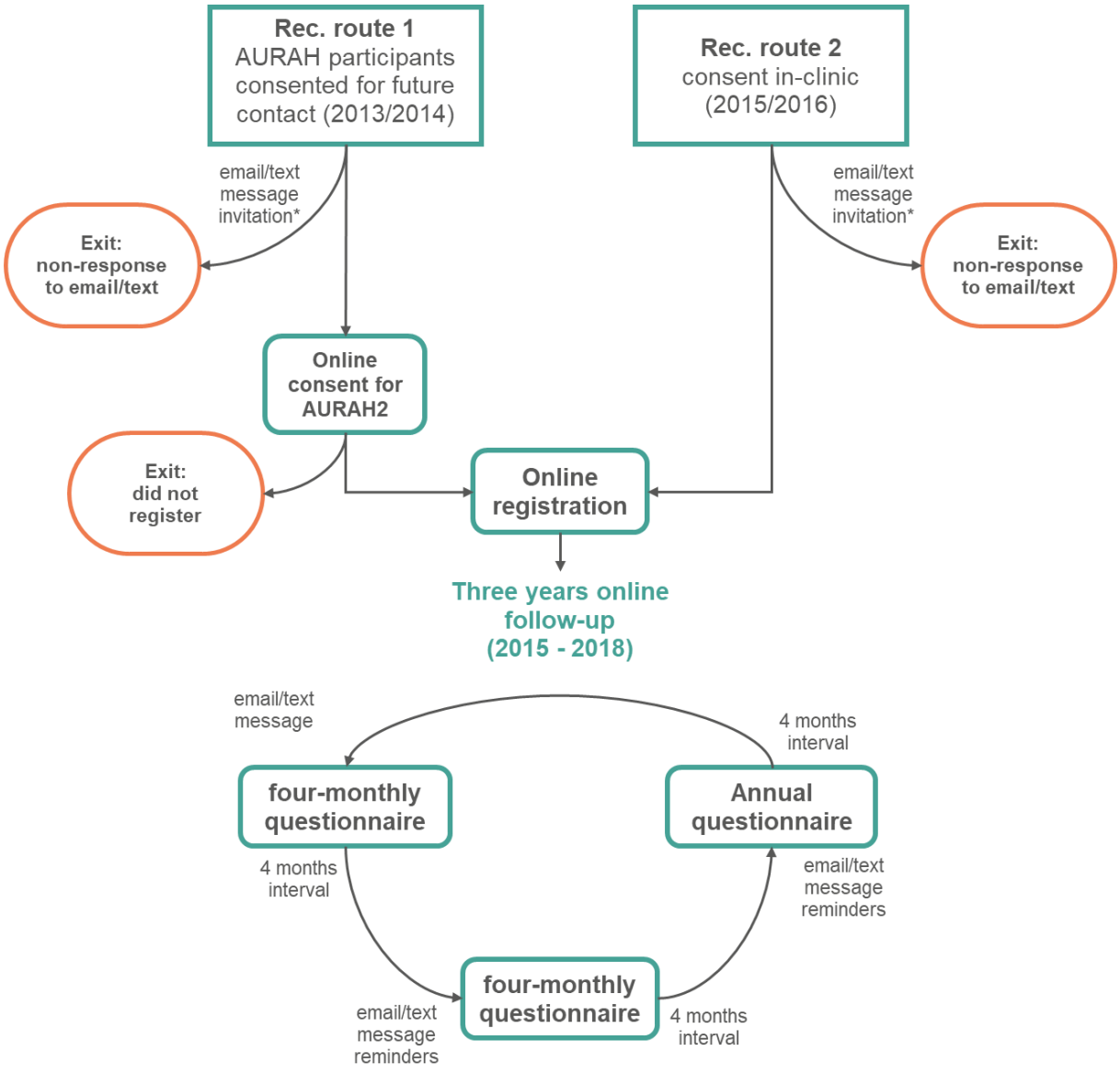
(i) were GBMSM (reported at least one of the following criteria: being gay or bisexual, having had anal sex with a man in the past three months, or having disclosed to their family, friends or workmates as gay, bisexual or attracted to men)
(ii) aged 18 years or older
(iii) had attended the study clinics for sexually transmitted infections (STIs) or HIV routine testing
(iv) were not diagnosed with HIV at the time of recruitment
(v) consented to be followed up over three years
(vi) were able to complete the questionnaires in English

3.3.3 AURAH2 participant recruitment

The AURAH2 study expanded on the design of the ‘Attitudes to and Understanding Risk of Acquisition of HIV (AURAH)’ questionnaire study, conducted between 2013 and 2014, by providing longitudinal data on HIV transmission risk and incidence in a cohort of initially HIV-negative GBMSM (see the AURAH2 study protocol, Appendix 3). The AURAH study design was cross-sectional and recruited 1,954 male participants (1,484 (75.9%) were GBMSM) from 20 sexual health clinics in England. Data were collected using a self-completed paper questionnaire (153). Due to the transition process from the AURAH study to the AURAH2 prospective study, participants were recruited into the AURAH2 study through two different

routes, route 1 (from the AURAH study) and route 2 (direct recruitment) (see Figure 3.1 and Sections *3.3.3.1* and *3.3.3.2* below).

Figure 3.1 AURAH2 participant recruitment routes and completion of questionnaires
reproduced from Sewell et al., 2016, p.6 (154)



3.3.3.1 Recruitment route 1 (March – April 2015)

Recruitment route 1 consisted of HIV-negative or undiagnosed GBMSM participants from the AURAH study who consented to contact for future follow up from any of the three AURAH sites that participated in the AURAH2 study. The final sites of AURAH were closed in September 2014; however, the three sites that had recruited the largest number of GBMSM to the study had been invited and accepted to participate in the AURAH2 study. GBMSM who attended these three clinics between September 2014 (when the other 17 AURAH study sites closed for recruitment) and March 2015 (the commencement of the AURAH2 study) who specifically consented to provide contact details with a view to joining the proposed prospective study, were emailed by the research group through the secure AURAH2 study website and invited to register and join the study in March – April 2015. As per ethics approval, participants were contacted a maximum of three times with an invitation via email (twice, a week apart) and or via text a week after the second email if they had provided a mobile number on the consent form; if not, they were emailed for a third and final time.

Participants who joined the AURAH2 study through this route were assigned the same study number in their online follow-up as their original AURAH study number so that online follow-up could be linked to responses in the original cross-sectional study.

3.3.3.2 Recruitment route 2 (March 2015 – December 2016)

This route consisted of HIV negative or undiagnosed GBMSM prospectively recruited at a routine clinic visit through the three AURAH2 clinic sites. Participant contact details were obtained during consent (see Section *3.3.3.4* below). Then they were invited to complete a baseline paper questionnaire in-clinic, and an email was sent inviting them to join the study and complete their first online questionnaire within four months (see Section 3.3.4).

3.3.3.3 Participant consent and ethics approval

All participants provided written, informed consent before taking part. For those participants who joined AURAH2 from AURAH, an individual invitation email was sent from the study website, from which they could click on a secure link to register with the study website online. They were directed to an online AURAH2 Patient Information Sheet (PIS) and consent form (see Appendix 4), which was automatically loaded onto the screen once they had clicked the AURAH2 link in the email. At the end of the online form, participants were required to select (click) on the consent boxes to indicate their consent. They also had the option of leaving the study website without consenting and joining the study. Participants

recruited directly into the AURAH2 study completed a PIS and consent form within the clinic setting (see Appendix 5) and did not need to complete a further one online.

Consent to participate in the AURAH2 study ensured that participants were aware of:

(i) participation in the AURAH2 study meant that participants would be asked to complete brief online questionnaires about sexual behaviour and HIV testing on a regular (four monthly) basis over a maximum of three years
(ii) provision of email addresses and mobile phone numbers was necessary, and participants needed to consent to receive reminders to complete the online questionnaires via email and/or text message (maximum two reminders by email followed by one text message), following which no further contact attempts would be made
(iii) provision of full name and date of birth was necessary as this information could be used to link with UK national clinical databases, including the national HIV and AIDS reporting system (HARS) database held by the UKHSA
(iv) results of any HIV test results from the day they joined the AURAH2 study or that were self-reported during the online phase of the study would be recorded and stored securely
(v) withdrawal from the online phase of the study was acceptable at any point via an email to the AURAH2 study coordinator (Dr Janey Sewell), and upon withdrawal, any personal data would be deleted without affecting care at their sexual health clinic

The AURAH2 study was approved by the designated research ethics committee, The National Research Ethics Service (NRES) committee London-Hampstead, ref: 14/LO/1881 in November 2014 (154). Based on the research protocol and all versions of study documents, the AURAH2 study subsequently received permission for clinical research at the three participating National Health Service (NHS) sites: Chelsea and Westminster NHS Foundation Trust, Central and Northwest London NHS Foundation Trust, and the Brighton and Sussex University Hospitals NHS Trust. The AURAH2 study was registered on the NIHR clinical research network portfolio.

3.3.3.4 Sample size calculations

The calculations of the AURAH2 sample size were completed by statistician and AURAH2 core group member Dr Fiona Lampe and were used to plan recruitment targets and submitted to the Research Ethics Committee. The sample size calculation was based on objective (ii) of the AURAH2 study, which was, “assess within-person changes in sexual behaviour after receiving an HIV diagnosis”. This outcome was more constrained by power than others because it relied on comparisons within the group who were diagnosed with HIV

during follow-up. Considering sexual behaviour classified as to whether or not a man reported more than three condomless sex partners in the past three months, 85 new HIV diagnoses would be needed to detect, with 80% power and 5% significance level, the following changes: 17 (20%) of men newly diagnosed switching from >3 to ≤3 condomless sex partners pre- to post-diagnosis, and 4 (5%) of men newly diagnosed switching from ≤3 to >3 condomless sex partners pre- to post-diagnosis. A sample size of 1000 would provide adequate power for these objectives.

3.3.4 Completion of AURAH2 questionnaires

The AURAH2 study collected longitudinal data. In total, there was one baseline paper-based questionnaire and up to nine online follow-up questionnaires. Participants self-completed all these questionnaires.

3.3.4.1 Completion of baseline questionnaire

Participants who consented to the AURAH2 study self-completed a confidential baseline paper questionnaire in the clinic (17 November 2014 – 29 April 2016). This questionnaire was the same as in the AURAH cross-sectional study. The baseline questionnaire gathered information on demographic, socio-economic, lifestyle, health and wellbeing-related factors, knowledge and understanding of HIV, sexual behaviours, STI diagnoses, and PrEP and post-exposure prophylaxis (PEP) use (see Appendix 6). Participants who joined the study from the AURAH cross-sectional study had already completed the baseline paper questionnaire since 2013 (30 July 2013 – 11 November 2014), and they were not asked to fill in a new baseline questionnaire but invited to complete the first four monthly questionnaires online (Section *3.3.4.2* below).

3.3.4.2 Completion of online follow-up questionnaires

During the follow-up period, participants self-completed subsequent four monthly and annual questionnaires available online from March 2015 until March 2018. Given the three-year follow-up period, if a participant recruited in March 2015 completed every questionnaire that they were prompted to, they would complete a total of ten questionnaires over three years; one baseline paper-based in the clinic, nine online follow-up questionnaires, of which at least three were annual, and six were four-monthly questionnaires. If a participant recruited from route 1 and had completed the baseline questionnaire in 2013, then completed every follow-up questionnaire, they would complete ten questionnaires over five years.

Participants were contacted via email within four months of completing the baseline paper questionnaire in the clinic for participants recruited directly into the AURAH2 study, and between March and April 2015 for participants who joined the study from the AURAH study.

When participants were due to complete a questionnaire, they were sent an email inviting them to fill in the questionnaire, followed by two reminder emails after two and four weeks (if they had not completed it) followed by a text message a week if a participant still had not logged in to the study website. If participants missed a questionnaire at any time during follow-up, they were still invited to complete subsequent questionnaires unless they specifically opted out of the study.

During the online follow-up period, participants' HIV status could change at any time, from negative to positive. To allow effective capture of information that was sensitive to a change in individual HIV status, five different types of online questionnaires were available for completion; two were designed for HIV-negative participants and three for HIV-positive participants:

(i) Four-monthly questionnaire for HIV-negative or undiagnosed participants
Participants were invited to complete this brief five-minute questionnaire twice a year. The questions in this questionnaire covered: recent HIV testing history and the result, sexual behaviour (condomless anal sex [CLS], number of CLS partners, CLS role [insertive, receptive, versatile], CLS with an HIV positive partner and group sex), STI (diagnoses of any STIs and the name of the STI) and chemsex (drugs used specifically before or during sex, including the name of the drugs and frequency of use). Unless stated otherwise, a three-month recall period was used for this questionnaire (see Appendix 7**)**.

(ii) Annual questionnaire for HIV-negative or undiagnosed participants
Participants were invited to complete this more extensive questionnaire that was designed to take approximately 20 minutes annually (see Appendix 8). All of the questions asked in the four monthly questionnaires were included in the annual online questionnaire, with additional questions on PEP use in the past year (including frequency of use and whether taken following chemsex), PrEP use in the past year (including the source of PrEP and frequency of use), recreational drug use, injection drug use, alcohol use (using the CAGE questionnaire (241) and the first two questions of the WHO AUDIT-C questionnaire (242)), physical symptoms (using a modified version of Memorial Symptom Assessment Scale Short-Form) (243), mental health (using the Patient Health Questionnaire for depression (PHQ-90) (244) and the General Anxiety Disorder scale for anxiety (GAD-7) (245). Unless stated otherwise, the annual questionnaires also used a three-month recall period.

(iii) 1st HIV positive questionnaire for participants who reported an HIV diagnosis since the last completion of an online follow-up questionnaire

The newly HIV diagnosed questionnaire asked specific questions related to an HIV diagnosis, including engagement in HIV care, sexual behaviour before HIV diagnosis (including CLS, number of CLS partners, new CLS partners), STI diagnoses (including which STIs), and chemsex use (including whether chemsex has increased or decreased since HIV diagnosis). This questionnaire also used a three-month recall period (see Appendix 9**)**.

(iv) Four-monthly questionnaire for HIV-diagnosed participants

In terms of questions and time of completion, the four monthly HIV-diagnosed questionnaire was comparable to the four monthly HIV-negative questionnaire. The only difference was that it additionally asked about participant engagement in HIV care, whether the participant had seen a healthcare practitioner since being diagnosed, if the patient was taking ART and when it started, and if the patient knew what the viral load was (detectable or undetectable) (see Appendix 10).

(v) Annual questionnaire for HIV-diagnosed participants

In terms of content and time for completion, the annual questionnaire for HIV-positive individuals was fairly comparable to the annual questionnaire for HIV-negative participants. It included questions on engagement in care, similar to the four-monthly questionnaire for HIV-positive patients. It did not include questions about PEP or PrEP use, unlike the annual questionnaire, and so took slightly less time to complete than the annual HIV negative questionnaire (see Appendix 11).

Participants enrolled in the AURAH2 study via route 1 completed the annual online questionnaire four months following their first online questionnaire (i.e., their baseline questionnaire was followed by an online four-monthly questionnaire, then the annual online questionnaire, then two online four-monthly questionnaires). This was to ensure that a complete set of data, including the annual questionnaire, was obtained in the study's first year, as the gap between baseline and the first online questionnaire could be up to one and a half years for participants recruited via route 1. Participants who were recruited via route 2 followed a specified questionnaire timeline to guarantee that relevant data was obtained annually (i.e. their baseline questionnaire was followed by two four monthly questionnaires, then the annual questionnaire, during the online phase of the study) (246).

3.3.5 AURAH2 participants

136 HIV-negative men joined the AURAH2 prospective study from the AURAH cross-sectional study (recruitment route 1). During the direct recruitment (route 2),1,866 eligible GBMSM were invited to participate in the three clinics from March 2015 to December 2016, with 982 men agreeing to do so (response rate 52%) (246). However, only 887 of those 982 who agreed to participate in the study completed baseline paper questionnaires between March 2015 and April 2016 (48%, 887/1,866). Between October 2014 and March 2015 (after the recruitment extension in three clinics had been granted to continue recruiting until the AURAH2 opened for direct recruitment), 144 men had previously agreed to join the study. In total, from recruitment route 2, 1,031 HIV-negative men joined the AURAH2 study.

There were 1,167(136 men from route 1 and 1031 from route 2) men in total, with 854 (73.2%) recruited from the 56 Dean Street clinic in London, 176 (15.1%) recruited from the Mortimer Market clinic in London, and 137 (11.7%) recruited from the Claude Nicol Centre in Brighton. Details about the characteristics of participants enrolled in the AURAH2 study and loss to follow-up among the participants are detailed in Chapter 4.

3.4 Data linkage with the UK Health Security Agency (UKHSA)

Consent to participate in the AURAH2 study included consent for limited participant identifiers to be used to link the data to the UKHSA's datasets at the end of the study (see Section *3.3.3.3*). The linkage allowed confirmation of the self-reported HIV status of participants, the identification of any new HIV diagnoses that have not been self-reported through the questionnaires, or any death during the three-year follow-up period (detailed in Chapter 7).

3.4.1 National HIV surveillance data

The national HIV surveillance collects information on new HIV diagnoses from laboratories, genito-urinary medicine (GUM) clinics, general practitioners (GPs), and other services where HIV testing takes place in England (247, 248). HIV clinics must report any new HIV diagnoses to the UKHSA. The HIV and AIDS Reporting Section at the UKHSA undertake timely and comprehensive data collection from a range of UK settings on:

- People receiving HIV care (collected quarterly)
- First HIV and AIDS diagnoses (collected annually)
- Deaths among HIV positive individuals (collected annually)
- Late HIV diagnoses (collected annually)

Data items collected include geography of residence, a pseudonymised name (Soundex code), date of birth, gender, probable route of exposure and other demographic factors. UKHSA uses the Soundex algorithm as an indexing system for encoding surnames because all data collected as part of the national HIV surveillance programme in the UK is pseudo-anonymised; no names are collected. Soundex provides an anonymised representation of a surname, consisting of the initial letter of the surname and three digits. No soundex is unique to a single name, and a name cannot be recreated from a Soundex code.

3.4.2 AURAH2 items collected

The following data items were collected at various time points in the AURAH2 study and were necessary for matching to the national HIV surveillance data:

- date or year of birth (DoB or YoB, where available)
- surname
- first name (initial)
- alternative surname and first name (if any)
- ethnicity
- country of birth (CoB)
- years in the UK (if born outside the UK)
- gender identity (male or transgender)
- originating clinic

3.4.3 Matching process

AURAH2 data was submitted to the UKHSA via the secure HIV & STI Web Portal and was then password protected and stored on a secure network drive. Based on the data items mentioned above items in Section 3.4.2, a deterministic and hierarchical algorithm using Stata software was used to link the data, which is also routinely used by the UKHSA for cross-system linkages and de-duplication (see Appendix 12).

The following matching criteria were used:

(i) Soundex (or alternate Soundex), Initial (or alternate initial), Gender, DoB (or YoB), Clinic, Ethnicity, CoB
(ii) Soundex, Initial, Gender, DoB, Ethnicity, CoB
(iii) Soundex, Initial, Gender, DoB, Ethnicity
(iv) Soundex, Gender, DoB, Ethnicity
(v) Soundex, Initial, Gender, DoB, Clinic

(vi) Soundex, Initial, Gender, DoB

(vii) Soundex, DoB, Clinic, additional manual review

For each matching criteria, a Stata algorithm compared records in the AURAH2 dataset to the national HIV surveillance databases. For each record matched, a two-stage eyeballing process was used to verify that the linkage was correct, with data being reviewed by a data analyst and scientist at the UKHSA.

For each study participant that matched to the HIV surveillance dataset, the UKHSA data were provided on the following data items:

- Date of diagnosis (data source: HIV and AIDS New Diagnosis and Deaths; HANDD)
- Region of diagnosis (data source: HANDD)
- CD4 at HIV diagnosis (data source: HANDD)
- Viral load at HIV diagnosis (data source: HANDD)
- Time from diagnosis to linkage to care (data source: HIV and AIDS Reporting System; HARS)
- Time from diagnosis to treatment initiation (data source: HARS)
- Death indicator (data source: HARS / HANDD)

The UKHSA also provided additional information on the number of STI diagnoses 12 months prior to and following HIV diagnosis, only where data available. The data source for this information was the Genito-Urinary Medicine Clinic Activity Dataset (GUMCAD), the primary surveillance system for STIs in England (249). GUMCAD STI surveillance system includes mandatory reporting from more than 600 sexual health services in England. GUMCAD only includes STI testing services provided free by the government and is an electronic, pseudo-anonymised patient-level dataset. Given the limited identifiers reported through GUMCAD, there were a number of people UKHSA was not able to link and provide STI history for. As GUMCAD does not collect Soundex, initials or date of birth, UKHSA relies heavily on the reported Clinic ID to match the HIV datasets, which can vary for the same patient between systems. Data on STIs that I received from the UKHSA were only provided for some HIV-positive individuals, and no data were available for HIV-negative individuals. Therefore, for the analyses of STI, only data from AURAH2 questionnaires were used.

3.5 Data management of the AURAH2 study

At the time of starting this PhD in May 2018, the data collection for the AURAH2 study had just been completed (data were available for use in April 2018). I was provided with the AURAH2 baseline and online datasets by Dr Janey Sewell, the AURAH2 study coordinator, in May 2018. The final and complete de-identified datasets for AURAH2 were stored on an encrypted memory stick, with a backup on the UCL Data Safe Haven, a secure service owned by UCL that allows for the secure storage and exchange of sensitive personal data (250).

When receiving the datasets, the majority of checks and data cleaning processes, including data validation (running checks on the answer options that contained numerical values, to check answers were within an appropriate range), dealing with missing data, and dealing with data discrepancies, had been done by Dr Janey Sewell for the questionnaire data. All of the data management procedures that I have carried out and are relevant to this thesis have centred on variable derivation, creating new datasets for analyses, and managing linked data from the UKHSA.

3.5.1 Baseline data

The baseline data for AURAH2 were received in Stata and Excel formats. There were 1,167 data entries in the final AURAH2 baseline dataset. The proportion of missing data in the AURAH2 baseline questionnaire data was minimal, with ≤5% of all variables in the analyses having missing data. For specific binary variables, a non-response to a question was interpreted that a measure or event had not occurred. A missing response for CLS, for example, was interpreted as no acts were performed. This was because there appeared to be a pattern in the responses to questions where only behaviours or symptoms experienced were ticked. As a result, unless otherwise noted in an individual table or figure, missing was included with ‘no’ for all analyses in the AURAH2 study's subsequent results chapters (Chapters 4–7), except for age, ethnicity, country of birth, sexual identity, financial status, and housing status, for which missing responses were excluded from analyses. Initial analyses that were undertaken to investigate whether excluding missing values (when defining each variable) impacted findings, demonstrated that this was not the case.

3.5.2 Online data

I received five separate Excel spreadsheets of AURAH2 online data from Dr Janey Sewell and one Stata dataset, which fully merged the five spreadsheets. Those five were datasets containing:

(i) four-monthly questionnaires completed by HIV-negative participants

(ii) annual questionnaires completed by HIV-negative participants
(iii) first HIV positive questionnaire completed by HIV-diagnosed participants
(iv) four-monthly questionnaires completed by HIV-diagnosed participants
(v) annual questionnaires completed by HIV-diagnosed

These online datasets contained data from 622 participants; 136 were recruited from route 1 and 486 from route 2. These 622 men provided a total of 3277 online data observations, including 2283 (69.7%) four monthly HIV negative questionnaires, 918 (28.0%) annual HIV negative questionnaires, 37 (1.1%) four monthly HIV positive questionnaires, 24 (0.7%) annual HIV positive questionnaires, and 15 (0.5%) first HIV positive questionnaires.

There was very minimal missing data in the AURAH2 study's online questionnaires (from the 622 participants); only 1% of the data for online questions utilised in the analysis was missing. Unless otherwise mentioned in a specific table or figure, missing data for specific binary variables were also treated as ‘no' in all analyses.

3.5.3 Linked data from the UK Health Security Agency

The data matching process was completed in November 2019. Dr Andrew Speakman, the AURAH2 study data manager and Dr Valerie Delpech and Dr Sara Croxford from the UKHSA, oversaw the data linking process. The data received from the UKHSA were in the form of multiple Locked-Excel spreadsheets. The UKHSA identified two duplicates among AURAH2 participants found in the UKHSA databases as HIV-positive, based on their date of birth, originating clinic, and initials. Dr Andrew Speakman stored the linked data in UCL Data Safe Haven (250) and identified that there were further three duplicates among HIV-negative participants in the AURAH2 datasets, based on their name and date of birth, I confirmed this.

In compliance with data governance protocols, I only extracted the study identifier and date of diagnosis of the HIV positive cases in AURAH2 from the UKHSA datasets and stored this information on the encrypted memory stick for the purposes of analysis. The date of diagnosis from the UKHSA was used for the ascertainment of HIV incidence (Chapter 7). Data on STI diagnoses from the UKHSA were incomplete and only available for HIV-positive participants; therefore, in this thesis, only self-reported STI diagnoses data from participants’ questionnaires were used in the analysis.

3.5.4 Merging and creating new datasets

I used various datasets in each chapter due to each chapter's different analysis purposes. Baseline datasets (containing data from baseline (paper, in clinic) questionnaires completed by 1167 participants) were used to investigate factors linked to non-participation in the online follow-up phase (Chapter 4), assess trends in PrEP and PEP awareness over calendar time

of recruitment (Chapter 6), and assess baseline factors associated with subsequent HIV incidence (Chapter 7). Online datasets (datasets containing data from online questionnaires completed by 622 participants) were used to assess transitions in sexual behaviour and the predictors, and to assess trends over the calendar year in some measures of sexual behaviour: chemsex and bacterial STI diagnosis (Chapter 5). For analysis of trends in HIV incidence (Chapter 7), a matched UKHSA dataset (containing dates of HIV diagnosis from the UKHSA and other variables from baseline and online questionnaires) was used.

In other analyses using data from the AURAH2 study, pooled data from baseline and online questionnaires were required. In Chapter 5, to assess trends over the calendar year in condomless anal sex, condomless anal sex and group sex, a merged dataset containing data from all baseline and online (four monthly and annual) questionnaires from all participants was used. To assess the loss to follow-up and the predictors (Chapter 4) and predictors of HIV incidence (Chapter 7), merged data of baseline and online (four monthly and annual) questionnaires among a subgroup of men who completed at least an online follow-up questionnaire were used. Finally, in Chapter 6, to assess trends over calendar year in PrEP use (among all participants) and predictors of PrEP initiation (among those who reported no PrEP use at baseline), merged datasets of baseline and annual follow-up data were used. Therefore, I merged the baseline and online follow-up data to produce new, separate datasets for these objectives.

To bring together these datasets, I explored datasets separately before merging. Merging these datasets requires that both have at least one identifier in common. I used the study identification number, assigned to each participant at the time of enrolment, as the unique identifier to link the online and baseline datasets. I also made sure I selected all possible common variables to perform 1:1 merge in Stata, such as the participant's originating clinic, date of baseline questionnaire completion, and socio-demographic variables. If using categorical data, I made sure that categories on both datasets refer to the same thing (i.e., 1 "Yes", 2 "No", 3 "missing" on both). As Stata is case sensitive (i.e., "Year" is not the same as "year") and for variables that do not match, Stata will add missing values. I also made sure that the variables that referred to the same query in both datasets had the same variable names. Where necessary, the data were reshaped from a wide to long format, whereby Stata was informed which variables were time-updated and time constant in preparation for analysis. Once I had merged these datasets in Stata and identified and deleted data inconsistencies, the final datasets were then used in analyses.

3.6 Variable definitions in the AURAH2 study

Variable definitions detailed in this chapter are limited to demographic, socio-economic and partnership status, sexual and other HIV-related behaviour, and health and lifestyle variables. While the definitions and constructions of the following outcomes measures: (i) non-participation and loss to follow-up (LTFU), (ii) 'higher-risk' and 'lower-risk' sexual behaviour, (iii) PrEP and PEP use, and (iv) incident of HIV diagnosis, are detailed in each relevant results chapter (Chapters 4 to 7).

Table 3.1 summarizes the categories and recall period of each of the covariates used in this thesis, classified as: demographic, socio-economic and partnership status, sexual and other HIV-related behaviour, and health and lifestyle characteristics. The definitions of these variables are detailed in Sections 3.6.1 until 3.6.3.

Table 3.1 Socio-demographic, sexual and other HIV related behaviours, and health and lifestyle variables in the AURAH2 study

Characteristics	Variables	Collected at			Categories	Recall period
		Baseline	Four-monthly	annual		
Demographic	Age group	√	–	–	<25; 25 – 29; 30 – 34; 35 – 39; 40 – 44; and ≥45 years	Current
	Country of birth and ethnicity	√	–	–	Born in the UK, White; Born in the UK, Other ethnicitiy; Non-UK born, White; Non-UK born, Other ethnicitiy	
	Sexual identity	√	–	–	Gay; Bisexual / other	
Socio-economic and partnership status	University education status	√	–	–	Yes; No	Current
	Employment status	√	–	–	Employed; Unemployed / other	Current
	Financial status*	√	–	–	All of the time; Most of the time**;** Sometimes or no	Current
	Housing status	√	–	–	Renting; Home owner; Unstable or other	Current

Characteristics	Variables	Collected at			Categories	Recall period
		Baseline	Four-monthly	annual		
	Ongoing relationship status	√	–	√	***Baseline***: Yes – living with partner; Yes – not living with partner; No ***Annual***: Yes; No	Current
Sexual and other HIV related behaviour	Recent HIV test	√	√	√	Yes; no	***Baseline***: past 6 months ***Four-monthly & annual***: past 3 months
	Condomless anal sex	√	√	√	Yes; No	past 3 months
	Number of CLS partners	√	√	√	***Baseline***: none; one; 2 – 4; 5 – 10; >10 partners ***Four-monthly and annual***: none or one; ≥2 partners	past 3 months
	CLS with HIV positive partners	√	√	√	Yes; No	past 3 months
	Sexual CLS role	√	√	√	Only insertive (top); Only receptive (bottom); Sometimes insertive / receptive	past 3 months
	Group sex	√	√	√	Yes; No	past 3 months
	Number of new sexual partners	√	–	–	0 – 10; 11 – 49; 50 – 99; >100 partners	past 12 months
	Fisting or sex toys	√	–	–	Yes; No	past 3 months

Characteristics	Variables	Collected at			Categories	Recall period
		Baseline	Four-monthly	annual		
	Sex for drugs or money	√	–	–	Yes; No	past 3 months
	Bacterial STI diagnoses**	√	√	√	Yes; No	***Baseline***: past 12 months ***Four-monthly and annual***: past 3 months
	PrEP use	√		√	Yes; No	past 12 months
	PEP use	√		√	Yes; No	past 12 months
Health and lifestyle	Recreational drug use	√	–	√	No**;** Non-injection drug and non-chemsex use; Chemsex-related drug use (no-injection); Injection drug use	past 3 months
	Chemsex	–	√	√	Yes; No	past 3 months
	Injection drug use	√	–	√	Yes; No	past 3 months
	Smoking status	√	–	–	Never smoked; Ex-smoker; Regular smoker	current
	Depressive symptoms	√	–	√	Yes; No	past two weeks
	Anxiety symptoms	√	–	√	Yes; No	past two weeks
	Higher alcohol consumption	√	–	√	Yes; No	current

* having enough money to cover basic needs, e.g. for food and heating
**only data from participants' questionnaires were used

3.6.1 Socio-demographic measures

Three demographic variables included and investigated in this thesis were:

(i) Age group: constructed from variable date of birth, sometimes also used as a continuous variable
(ii) Country of birth and ethnicity: constructed from questions: '*Which ethnic group best describes you?*' and '*Were you born in the UK*?'
(iii) Sexual identity ('bisexual or other' category included other plurisexual identities that are not explicitly based on attractions to one sex/gender) (251)

Socio-economic and partnership-status variables were:

(i) University education status
(ii) Employment status (being employed included full-time, part-time or self-employment; not being employed or other included unemployed, student, permanently/temporarily sick, looking after a home, retired, other, or a missing response)
(iii) Financial status (having enough money to cover basic needs, e.g. for food and heating)
(iv) Housing status (renting included private or council; unstable or other including homeless, temporary accommodation, staying with partner, friends, family, or other)
(v) Ongoing relationship status

Socio-demographic measures were only asked at baseline, ongoing relationship status was asked at baseline and annual follow-up questionnaires (Table 3.1).

3.6.2 Sexual and other HIV-related behaviour measures

Twelve sexual and HIV-related behaviour measures were considered for analyses in this thesis (unless stated otherwise, all in the previous three months):

(i) CLS
(ii) CLS with two or more partners
(iii) CLS with partners known to be HIV positive
(iv) Sexual CLS role (which position / partner were you during anal sex without condom)
(v) Group sex (sex with more than one other person on the same occasion)
(vi) Sex for drugs or money (ever received money or drugs for having sex)
(vii) Fisting sex or sex toys use
(viii) Recent HIV test (in the past six months at baseline questionnaire, and the past three months at four-monthly and annual follow-up questionnaires)
(ix) Bacterial STI diagnoses: defined as a self-report of one of four bacterial infections: Gonorrhoea, Chlamydia, Syphilis, and/or Lymphogranuloma

Venereum (LGV), constructed from questions: '*Have you been diagnosed with STI*?' and '*Do you know what STI it was*?'

(x) Number of new sexual partners (in the past 12 months)

(xi) PrEP use (in the past 12 months)

(xii) PEP use (in the past 12 months)

Sex for drugs or money, fisting sex or sex toys use, and the number of new sexual partners were sexual behaviour measures that were only asked at baseline, PrEP and PEP use were asked at baseline and annual questionnaires, all other sexual behaviour questions were asked at baseline and follow-up (four-monthly and annual). For an STI diagnosis, participants were asked whether they had been diagnosed with an STI in the past year at baseline questionnaire and the previous three months at four-monthly and annual follow-up questionnaires. Data from STI diagnoses from the UKHSA were not used.

3.6.3 Health and lifestyle measures

There were seven health and lifestyle characteristics variables included and investigated in this thesis (Table 3.1):

(i) Recreational drug use:

Participants were asked to report whether they had used recreational drugs in the past three months at baseline and annual questionnaires, and, if so, to select which drug or drugs from the following list of 18 options; acid, lysergic acid diethylamide (LSD), or magic mushrooms (all grouped as psychedelics); anabolic steroids; cannabis (marijuana, grass); cocaine (coke); crack; codeine; crystal meth (methamphetamine); ecstasy (MDMA or E); GHB (GBL or liquid ecstasy); heroin, ketamine (k); khat (chat); mephedrone; morphine; opium; poppers (amyl nitrites); speed (amphetamine); erectile dysfunction drugs (Viagra); and other (whereby participants were asked to specify the drug). Where applicable, other drugs were coded to the above groups (in most cases participants specified one of the drug options under a different or street name).

For analysis involving baseline and annual data (for example analysis in Chapter 6, trends in PrEP use), I recreated a new variable of recreational drug use, that was classified into four categories: no drug use; non-injection drug use and non-chemsex use; non-injection chemsex related drug use; and injection drug use. This variable was used in analyses using baseline and annual data, and it was constructed from three variables: recreational drug use, name of recreational drug used, and injection drug use, please see Table 3.2 below.

Table 3.2 Hierarchy classification of 'recreational drug use' variable

Forming variables	Construction	Classified as
• recreational drug use • name of recreational drugs • injection drug use	answer 'No' to all the three forming variables	None
	answer 'Yes' to recreational drug use, answer 'No' to injection drug use, and the name of recreational drugs being used do not include one of the three chemsex-associated drugs (crystal methamphetamine, mephedrone or GBH/GBL)	Non-injection and non-chemsex related drug use
	answer 'Yes' to recreational drug use, answer 'No' to injection drug use, and mention one of the three chemsex-associated drugs (crystal methamphetamine, mephedrone or GBH/GBL)	Use of ≥1 non-injection chemsex-related drug
	answer 'Yes' to recreational drug use and answer 'Yes' to injection drug use	Injection drug use

(ii) Chemsex:

Chemsex was only asked directly in the online questionnaire (four-monthly and annual). The question in the online questionnaire asked specifically about the use of specific drug use in the context of sex: "*have you used drugs before or during sex (chemsex) in the last three months*?", classified as 'yes' or 'no'). A question asking specifically about chemsex use was not available in the baseline questionnaire; therefore, a proxy measure was created in which a participant was classified as positive for 'use of chemsex-related drugs' in the past three months if they reported use of one of three chemsex associated drugs (crystal methamphetamine, mephedrone or GBH/GBL).

(iii) Injection drug use:

Information about injection recreational drug use were asked at baseline and annual questionnaires: 'in the past three months have you slammed/injected recreational drugs?'. This variable was used to construct a hierarchical recreational drug use (into four categories, see point (i) above).

(iv) Depressive symptoms:

The validated Patient Health Questionnaire-9 (PHQ-9) (244) was used to measure the prevalence of clinically significant depressive symptoms in the AURAH2 study. The PHQ-9 is a nine-item screening tool based on the Diagnostic

and Statistical Manual of Mental Disorders version four. In the PHQ-9, participants are asked to rate how often over the past two weeks they have been bothered by nine specific problems:

1) little interest or pleasure in doing things
2) feeling down, depressed, or hopeless
3) trouble falling or staying asleep, or sleeping too much
4) feeling tired or having little energy
5) poor appetite or overeating
6) feeling bad about yourself, or that you are a failure or have let yourself or your family down
7) trouble concentrating on things such as reading the newspaper or watching television
8) moving or speaking so slowly that other people have noticed
9) thoughts that you would be better off dead, or of hurting yourself in some way

A depressive symptom score was calculated by adding responses for each question, for which the options are: 'not at all' (0), 'several days' (1), 'more than half the days' (2), and 'nearly every day' (3), resulting in a total score with a possible range from 0 to 27. On the PHQ-9, a cut-off point of 10 or higher was regarded as the presence of a clinically severe depressive illness, in line with standard scoring. Depressive symptoms were assessed at both the baseline and annual questionnaires.

(v) Anxiety symptoms:

The validated Generalised Anxiety Disorder-7 (GAD-7) scale was used to measure anxiety symptoms (245). Anxiety symptoms were assessed at both the baseline and annual questionnaires. It is a standard seven-item questionnaire, with response options for each symptom: 'not at all' (0), 'several days' (1), 'more than half the days' (2), and 'nearly every day' (3). An anxiety symptom score was generated by adding responses for each of the seven questions. The standard definition of a total score of ≥10 (from potential range 0 to 21) was used to define anxiety symptoms. The seven items are (in the past two weeks):

1) feeling nervous, anxious or on edge
2) not being able to stop or control worrying
3) worrying too much about different things
4) becoming easily annoyed or irritable

5) trouble relaxing
6) being so restless that it is hard to sit still
7) feeling afraid as if something awful might happen

(vi) Higher alcohol consumption:
Participants were asked the first two questions of the WHO AUDIT-C questionnaire in the baseline and annual questionnaires: *'How often do you have a drink that contains alcohol?*' and *'How many units of alcohol do you drink on a typical day when you are drinking?'.* An alcohol use score was generated by adding responses for each question. Question 1 was coded as follows: 'never' (0), 'monthly or less' (1), '2-4 times per month' (2), '2-3 times per week' (3), and '4+ times per week' (4). Question 2 was coded as follows: '1-2' (0), '3-4' (1), '5-6' (2), '7-9' (3), and '10+' (4). The total score had a possible range from 0 to 8 (242). The AUDIT-C questionnaire includes a third question (how often you have had eight or more units if male on a single occasion in the last year), and a total score of eight or more is considered higher-risk drinking. As the third question was not included in AURAH2, a total score of six or more was considered to indicate higher risk drinking in this thesis.

(vii) Smoking status:
Participants were asked whether they smoked regularly at least one cigarette, only at baseline questionnaire.

3.6.4 Additional time-to-event variables from baseline and online questionnaires

I created time-to-event variables that are relevant for analyses. The variables were tailored to the needs of analyses in each different chapter and were necessary as estimates of the actual time-at-risk (in years). How these person-time variables were calculated and constructed are described in each relevant results chapter (Chapters 4,6, and 7). Briefly, there were three main person-time variables created in different datasets:

(i) the number of person-years it took for an HIV diagnosis to occur (Chapter 7)
(ii) the number of person-years it takes for a person to start PrEP (Chapter 6)
(iii) the number of person-years it takes for a person to drop out of the study (Chapter 4)

Chapter 4: Baseline characteristics and risk factors for loss to follow-up among participants in the AURAH2 study

4.1 Introduction

4.1.1 Background

One of the challenges of prospective cohort studies is to minimize the loss to follow-up (LTFU) or attrition rate. Potential analytical bias can occur because of possible differences between the participants being followed or retained in the study and the lost participants concerning the outcome variables or exposure of interest (252-254). Significant and systematic attrition can also reduce the generalisability of outcomes and the statistical power to detect effects of interest (255).

Previous studies have reported that specific socio-demographic characteristics, such as lower education or low socioeconomic status; and some lifestyle and sexual behaviour variables, such as drug use, alcohol intake, inconsistent condom use or smoking, are factors associated with loss to follow-up or non-participation in cohort studies among gay, bisexual, and other men who have sex with men (GBMSM) (256-261). However, these studies were conducted in North and South America, where predictors for LTFU could be different from those among GBMSM in the UK or Europe.

To the best of my knowledge, no data are available from longitudinal cohort studies in the UK on risk factors of LTFU among HIV-negative GBMSM. Such a study is needed to improve the knowledge of barriers to retention in studies among GBMSM, but is also needed for this thesis, to help interpret subsequent results of the AURAH2 study and consider the impact of any possible biases due to LTFU. This is particularly relevant to Chapters 5 and 6 and not to the incidence analysis (Chapter 7), for which data linkage was carried out for all participants enrolled in the study.

4.1.2 Chapter aims

The objectives of this chapter are:

(i) to describe the baseline characteristics of GBMSM participating in the AURAH2 study and the differences among men who did participate and did not participate in the online follow-up phase of the study

(ii) to identify baseline factors associated with non-participation in the online follow-up phase among all men enrolled in AURAH2

(iii) to describe the rates of loss to follow-up among men who continued on the online follow-up phase

(iv) to evaluate predictors of loss to follow-up among men who completed at least one online follow-up questionnaire

4.2 Methods

4.2.1 Non-participation in the online follow-up phase

Non-participation in the follow-up (NPFU) was defined as being enrolled in the AURAH2 study by completing a baseline paper questionnaire but having dropped out before completing the first online follow-up questionnaire.

4.2.2 Loss to follow-up during online follow-up phase

Participants who completed at least one online questionnaire were defined as LTFU if they were late by ten months for their subsequent scheduled follow-up questionnaire or did not complete two subsequent consecutive follow-up questionnaires, or they did not engage in the follow-up within the final six months of the study. Participants who engaged in the online follow-up of the study within the final six months and never missed two consecutive questionnaires were classified as retain in the study. The date of loss to follow-up was defined as the date when a participant filled out his last online questionnaire (see statistical analysis, Section 4.2.4 below for details).

4.2.3 Socio-demographic, health and lifestyle, and sexual / HIV-related behaviour measures

For a detailed description of the categories, definitions, and recall period of each of the socio-demographic, health and lifestyle, and sexual/HIV-related behaviour variables used in this chapter, please see Chapter 3 (thesis methods, Sections 3.6.1 – 3.6.3).

Baseline measures included:

- socio-demographic and partnership status variables: age, country of birth and ethnicity, sexual identity, university education status, ongoing relationship status, employment status, financial status, and housing status
- sexual / HIV-related behaviour variables: condomless anal sex (CLS), number of CLS partners, CLS with partners known to be HIV positive, sexual CLS role, group sex, sex for drugs or money, fisting or sex toys use, recent HIV test, bacterial sexually transmitted infection (STI) diagnosis, number of new sexual partners, pre-exposure prophylaxis (PrEP) use, and post-exposure (PEP) use

- health and lifestyle variables: recreational drug use, smoking status, depressive symptoms, anxiety symptoms, and higher alcohol consumption

Time-updated measures included:

- variables derived from four-monthly and annual questionnaires: age, recent HIV test, CLS, CLS with two or more partners, sexual CLS role, group sex, chemsex (a different variable from recreational drug use variable at baseline questionnaire, see Section 3.6.3), and bacterial STI diagnosis
- variables derived from only annual questionnaire during follow-up: ongoing relationship status, PrEP use, PEP use, recreational drug use, injection drug use, depressive symptoms, anxiety symptoms, and higher alcohol consumption

4.2.4 Statistical analysis

First, descriptive analyses were done to compare baseline socio-demographic and health and lifestyle characteristics of all AURAH2 study participants who completed the baseline questionnaire and the subset of participants who subsequently participated in the online follow-up by completing at least one online questionnaire. Unadjusted analysis using a chi-square test was done to compare characteristics of men who only completed the baseline questionnaire versus men who participated in the online follow-up phase.

To assess the association between baseline characteristics and non-participation in the online follow-up phase, logistic regression models were used, unadjusted and adjusted for age at baseline (as a continuous variable). Adjustment for age was modelled considering that almost all health outcomes, including non-participation or loss to follow-up, occur at different rates in different age groups. Data from all men enrolled in AURAH2 were used for this analysis. Odds ratios (ORs) and age-adjusted odds ratios (aOR) with 95% confidence intervals (CIs) are presented.

Next, the loss to follow-up (LTFU) rate per 100 person-years (PYs) was calculated among a sub-group of men who enrolled in the online follow-up phase (men who completed at least an online questionnaire). Person-years of follow-up were calculated from the date of completing the first online questionnaire (2015) until:

(i) for men who became lost to follow-up: the date of the last questionnaire completion before lost to follow-up definition as fulfilled. For men who re-engaged in the follow-up after dropping out, the first date of the last completion of the questionnaire, whether they later returned or not, was used (considering the first event only)

(ii) for men who were retained in the study: the date of last questionnaire completion within the final six months of the follow-up

Finally, Cox proportional hazard models were used to assess the association between time-updated factors and subsequent incidence of LTFU. Hazard ratios (HRs) with 95% CIs are presented unadjusted and adjusted for age.

4.3 Results

4.3.1 Baseline characteristics of the AURAH2 study participants

There were 1,167 men in the final AURAH2 baseline dataset (see Chapter 3, Section 3.5.1). After linking the AURAH2 datasets to national HIV surveillance data by the UK Health Security Agency (UKHSA), five duplicates were found among 1,167 men recorded in the baseline dataset. There were, therefore, 1,162 HIV-negative or undiagnosed men enrolled in the study between July 2013 and April 2016, of whom 136 joined the study from the AURAH cross-sectional study (recruitment route 1, detailed in Chapter 3 Section *3.3.3.1*). Among these 1,162 men, 849 (73.1%) were recruited from 56 Dean Street Clinic, London, 176 (15.1%) were recruited from Mortimer Market Clinic, London, and 137 (11.8%) were recruited from the Claude Nicol Centre, Brighton.

Table 4.1 (second column) shows the baseline socio-demographic and health and lifestyle characteristics of the 1,162 men. At baseline, the mean age of participants was 34 years (standard deviation [SD]: 10·4; interquartile range [IQR]: 26 – 39), 81.9% were of White ethnicity, 93.6% self-reported being gay, 74.4% had a university degree, 82.9% reported being employed, and 77.4% always had money to cover basic needs. Approximately 12.2% of men reported clinically significant depressive symptoms, 9.3% reported clinically significant anxiety symptoms, and 13.0% reported higher alcohol consumption. The proportion of missing responses was low (<5% for all variables, see Chapter 3, Section 3.5.1 and Table 4.1).

Of the 1,162 men enrolled, 622 (53.5%) men completed at least one online follow-up questionnaire. Among the 622 men, three individuals did not complete the baseline questionnaire (socio-demographic data for these three men were not available, except for age). As shown in Table 4.1 (third and last columns), men who continued on the study were older (mean age 34 versus 32 years, *p-value* from chi-square test comparing 622 men in the 'online cohort' versus 540 men who completed only the baseline questionnaire <0.001), had greater financial security (had money all of the time 82.4% versus 71.1%, p<0.001), had more stable housing (homeowner 33.0% versus 21.0%, p<0.001), were more likely to have

university-level education (76.8% versus 70.5%, *p*=0.017) and less likely to be employed (88.8% versus 93.1%, *p*=0.010).

Table 4.1 Baseline socio-demographic and health and lifestyle characteristics among participants who completed the baseline and online follow-up questionnaire in the AURAH2 study, 2013 – 2018

Socio-demographic and health and lifestyle characteristics	All men enrolled in the study (N=1162)		Completing only baseline questionnaire (n=540)		Completing at least an online questionnaire (n=622)		p-value*
	N	n (%)	N	n (%)	N	n (%)	
Age category							
<25	1153	275 (23·9%)	538	142 (26.4%)	615	133 (21·6%)	**<0.001**
25 – 29		207 (17·9%)		120 (22.3%)		87 (14·1%)	
30 – 34		227 (19·6%)		104 (19.3%)		123 (20·0%)	
35 – 39		156 (13·6%)		68 (12.6%)		88 (14·3%)	
40 – 44		121 (10·5%)		52 (9.7%)		69 (11·2%)	
≥45		167 (14·5%)		52 (9.7%)		115 (18·7%)	
Mean age, years (SD)		**34 (10·4)**		**32 (9.5)**		**34 (11·3)**	
Median age, years (IQR)		**31 (26 – 39)**		**30 (25 – 37)**		**33 (26 – 41)**	
Country of birth & ethnicity							
Born in the UK, White	1150	568 (49·4%)	538	250 (46.5%)	612	318 (51·9%)	0.205
Born in the UK, Other ethnicity[§]		60 (5·2%)		31 (5.8%)		29 (4·7%)	
Non-UK born, White		374 (32·5%)		179 (33.3%)		195 (31·9%)	
Non-UK born, Other ethnicity		148 (12·9%)		78 (14.5%)		70 (11·4%)	
Sexual identity							
Gay	1150	1076 (93·6%)	535	495 (92.5%)	615	581 (94·6%)	0.179
Bisexual / other		74 (6·4%)		40 (7.5%)		33 (5·4%)	
University education status							
Yes	1146	853 (74·4%)	540	381 (70.5%)	617	474 (76·8%)	**0.017**
No		293 (25·6%)		159 (29.5%)		143 (23·2%)	
Employment status[†]							
Employed	1149	952 (82·9%)	540	503 (93.1%)	617	548 (88·8%)	**0.010**
Unemployed / other		197 (17·1%)		37 (6.9%)		69 (11·2%)	
Financial status**							
All of the time	1158	896 (77·4%)	540	384 (71.1%)	618	509 (82·4%)	**<0.001**
Most of the time		194 (16·8%)		114 (21.1%)		81 (13·1%)	
Sometimes / No		68 (5·8%)		42 (7.8%)		28 (4·5%)	
Housing status[≗]							
Homeowner	1147	314 (27·4%)	539	113 (21.0%)	608	201 (33·0%)	**<0.001**
Renting		680 (59·3%)		351 (65.1%)		328 (54·0%)	
Unstable / other		153 (13·3%)		75 (13.9%)		79 (13·0%)	
Ongoing relationship status							
Yes	1159	465 (40·2%)	540	204 (37.8%)	619	257 (41·5%)	0.169
No		693 (59·8%)		336 (62.2%)		362 (58·5%)	
Higher risk alcohol consumption (WHO AUDIT-C ≥6)							
No	1159	1008 (87·0%)	540	469 (86.8%)	619	537 (86·8%)	0.941
Yes		151 (13·0%)		71 (13.2%)		82 (13·2%)	
Depressive symptoms (PHQ-9 score ≥10)							
No	1159	1018 (87·8%)	540	474 (87.8%)	619	544 (87·9%)	0.991

Yes		141 (12·2%)		66 (12.2%)		75 (12·1%)	
Anxiety symptoms (GAD7 score ≥10)							
No	1159	1033 (89·1%)	540	471 (87.2%)	619	562 (90·8%)	0.057
Yes		126 (10·9%)		69 (12.8%)		57 (9·2%)	

* p-value from $\chi 2$ test for differences between men who completed only baseline questionnaire (n= 540) and men who continued on the study by completing at least an online questionnaire (n=622)
** Having enough money to cover basic needs e.g. for food and heating
§ Other ethnicity includes Black, Asian, Mixed, and other ethnic group
ɇ Renting housing includes private renting and renting from council or housing association; unstable or other housing includes temporary accommodation, staying with friends or family, other accommodation, and homeless.
† Employed group includes full-time (n=845) and part-time (n=107) employment / self-employment; Unemployed / other group includes unemployed registered or not registered for benefits (n=60), sick or disabled (n=6), retired (n=24), and other (student or training or looking after home or dependents or other) (n=107)

SD standard deviation, IQR interquartile range, AUDIT-C alcohol use disorders identification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

4.3.2 Association of baseline factors with non-participation in the online follow-up phase

Adjustment for age at baseline had minimal effects on associations between factors and NPFU. In the age-adjusted analysis shown in Table 4.2 (including the factors shown in Table 4.1 and additional sexual / HIV-related behaviour and other health and lifestyle factors), socio-demographic characteristics associated with non-participation were age younger than 45 years old, with men younger than 25 years old having the highest odds of non-participation (aOR 2.36, 95% CI 1.58 – 3.58, p<0.001), not having a university degree (aOR for no study qualification 3.03, 95% CI 1.19 – 7.66, global p=0.004), less stable financial status (aOR for had no money or only sometimes for basic needs 1.21, 95% CI 1.21 – 3.41, global p=0.001), and less stable housing status (aOR for renting housing versus homeowner 1.53, 95% CI 1.12 – 2.09, global p=0.013). I have also discussed the differences in these factors in the previous section (Section 4.3.1).

Regarding sexual / HIV-related behaviour factors, men who reported higher-risk sexual behaviours were more likely to join the online follow-up phase. Having had a recent HIV test (aOR for non-participation in the online follow-up 0.73, 95% CI 0.56 – 0.95, p=0.018), having had more than ten new sexual partners (aOR 0.75, 95% CI 0.58 – 0.97, global p=0.038), having had group sex (aOR 0.68, 95% CI 0.53 – 0.86, p=0.002), and having used sex toys or fisting (aOR 0.61, 95% CI 0.48 – 0.78, p<0.001) were associated with reduced odds of NPFU in the age-adjused models.

Table 4.2 Associations of baseline characteristics with non-participation in the online follow-up phase among 1162 GBMSM enrolled in the AURAH2 study, 2013 – 2018

Baseline characteristics	Unadjusted OR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value
Demographic characteristics				
Age as continuous variables	1153 obs **0.97 (0.96 – 0.98)**	**<0.001**	1153 obs **0.97 (0.96 – 0.98)**	**<0.001**
Age at baseline category, years	1153 obs	**<0.001**	1153 obs	**<0.001**
<25	**2.36 (1.58 – 3.53)**		**2.36 (1.58 – 3.53)**	
25-29	**3.05 (1.98 – 4.68)**		**3.05 (1.98 – 4.68)**	
30-34	**1.87 (1.22 – 2.84)**		**1.87 (1.22 – 2.84)**	
35-39	**1.71 (1.08 – 2.69)**		**1.71 (1.08 – 2.69)**	
40-44	**1.67 (1.02 – 2.71)**		**1.67 (1.02 – 2.71)**	
≥45	1 (Ref)		1 (Ref)	
Country of birth and ethnicity	1150 obs	0.056	1149 obs	0.095
Born in the UK, White	1 (Ref)		1 (Ref)	
Born in the UK, Other ethnicity	1.36 (0.80 – 2.32)		1.23 (0.72 – 2.11)	
Non-UK born, White	1.17 (0.90 – 1.52)		1.15 (0.89 – 1.50)	
Non-UK born, Other ethnicity	1.42 (0.99 – 2.04)		1.35 (0.93 – 1.94)	
Sexual Identity	1150 obs	0.181	1141 obs	0.242
Gay	1 (Ref)		1 (Ref)	
Bisexual / other	1.38 (0.86 – 2.21)		1.33 (0.82 – 2.14)	
Socio-economic characteristics and partnership status				
University education status*	1159 obs	**0.006**	1150 obs	**0.004**
University degree	1 (Ref)		1 (Ref)	
Other qualification	1.30 (0.99 – 1.70)		**1.33 (1.01 – 1.75)**	
No qualification	**2.83 (1.15 – 6.95)**		**3.03 (1.19 – 7.66)**	
Employment status	1159 obs	**0.011**	1150 obs	0.161
Employed	1 (Ref)		1 (Ref)	
Unemployed / other	**0.58 (0.38 – 0.88)**		0.72 (0.46 – 1.14)	
Financial status**	1158 obs	**<0.001**	1150 obs	**<0.001**
All of the time	1 (Ref)		1 (Ref)	
Most of the time	**1.89 (1.38 – 2.59)**		**1.77 (1.28 – 2.44)**	
Sometimes / No	**2.14 (1.29 – 3.56)**		**2.03 (1.21 – 3.41)**	
Housing status	1142 obs	**<0.001**	1146 obs	**0.013**
Homeowner	1 (Ref)		1 (Ref)	
Renting	**1.89 (1.44 – 2.49)**		**1.53 (1.12 – 2.09)**	
Unstable or other	**1.71 (1.55 – 2.53)**		1.29 (0.84 – 1.99)	
Ongoing relationship status	1159 obs	0.128	1150 obs	0.512
Yes, living with partner	1 (Ref)		1 (Ref)	
Yes, not living with partner	1.13 (0.78 – 1.64)		0.95 (0.65 – 1.39)	
No	1.24 (0.94 – 1.65)		1.08 (0.81 – 1.45)	
Sexual / HIV-related behaviour characteristics				
HIV test in the past 6 months	1159 obs	**0.043**	1150 obs	**0.018**
No	1 (Ref)		1 (Ref)	
Yes	**0.77 (0.59 – 0.99)**		**0.73 (0.56 – 0.95)**	
CLS in the past 3 months	1154 obs	0.949	1150 obs	0.808
No	1 (Ref)		1 (Ref)	
Yes	0.99 (0.78 – 1.26)		0.97 (0.76 – 1.24)	

Baseline characteristics	Unadjusted OR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value
Number of CLS partners in the past 3 months	1159 obs		1150 obs	
No CLS partners	1 (Ref)	0.083	1 (Ref)	0.107
One CLS partner	1.13 (0.85 – 1.51)		1.06 (0.80 – 1.43)	
2 – 4 CLS partners	0.95 (0.70 – 1.28)		0.96 (0.71 – 1.30)	
5 – 10 CLS partners	0.47 (0.26 – 0.85)		0.46 (0.25 – 0.83)	
More than 10 CLS partners	0.80 (0.46 – 1.41)		0.83 (0.47 – 1.46)	
CLS with partners known to be HIV positive in the past 3 months	1159 obs		1150 obs	
No	1 (Ref)	0.310	1 (Ref)	0.385
Yes	0.83 (0.59 – 1.18)		0.85 (0.60 – 1.22)	
Sexual role CLS in the past 3 months	1159 obs		1150 obs	
No CLS / didn't state	1 (Ref)	0.993	1 (Ref)	0.844
Always insertive	0.82 (0.59 – 1.14)		0.83 (0.59 – 1.16)	
Always receptive	1.35 (0.93 – 1.95)		1.24 (0.85 – 1.80)	
Versatile (Sometimes insertive, sometimes receptive)	0.92 (0.70 – 1.22)		0.91 (0.69 – 1.21)	
Number of new sexual partners in the past 12 months	1154 obs		1150 obs	
0 – 10 new partners	1 (Ref)	**0.027**	1 (Ref)	**0.038**
11 – 49 new partners	**0.73 (0.57 – 0.95)**		**0.75 (0.58 – 0.97)**	
50 – 99 new partners	0.91 (0.56 – 1.48)		0.89 (0.55 – 1.46)	
100 or more new partners	0.69 (0.34 – 1.43)		0.70 (0.34 – 1.46)	
Group sex in the past 3 months	1159 obs		1150 obs	
No	1 (Ref)	**0.001**	1 (Ref)	**0.002**
Yes	**0.66 (0.52 – 0.84)**		**0.68 (0.53 – 0.86)**	
Fisting or sex toys use in the past 3 months	1159 obs		1150 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**0.59 (0.46 – 0.75)**		**0.61 (0.48 – 0.78)**	
Sex for drugs or money in the past 3 months	1159 obs		1150 obs	
No	1 (Ref)	0.723	1 (Ref)	0.879
Yes	1.10 (0.64 – 1.89)		0.96 (0.55 – 1.66)	
PEP use in the past 12 months	1159 obs		1150 obs	
No	1 (Ref)	0.585	1 (Ref)	0.685
Yes	1.08 (0.81 – 1.44)		1.06 (0.79 – 1.41)	
PrEP use in the past 12 months	1159 obs		1150 obs	
No	1 (Ref)	0.813	1 (Ref)	0.609
Yes	1.06 (0.63 – 1.81)		1.15 (0.67 – 1.96)	
Bacterial STI diagnoses in the past 12 months	1159 obs		1150 obs	
No	1 (Ref)	0.786	1 (Ref)	0.896
Yes	1.03 (0.81 – 1.31)		0.98 (0.77 – 1.25)	

Baseline characteristics	Unadjusted OR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value
Health and lifestyle characteristics				
Smoking status	1152 obs		1145 obs	
Never smoked	1 (Ref)	0.459	1 (Ref)	0.460
Ex-smoker	0.84 (0.64 – 1.12)		0.93 (0.70 – 1.25)	
Regular smoker	1.18 (0.88 – 1.59)		1.15 (0.86 – 1.55)	
Recreational drug use in the past 3 months	1159 obs		1150 obs	
No	1 (Ref)	0.338	1 (Ref)	0.327
Non-injection drug and non-chemsex use	0.76 (0.58 – 1.01)		0.78 (0.59 – 1.04)	
Chemsex-related drug use (no-injection)	0.85 (0.64 – 1.13)		0.82 (0.61 – 1.09)	
Injection drug use	1.01 (0.52 – 1.95)		1.15 (0.59 – 2.25)	
Higher risk alcohol consumption (modified WHO AUDIT-C score ≥6)	1159 obs		1150 obs	
No	1 (Ref)	0.315	1 (Ref)	0.387
Yes	0.86 (0.64 – 1.15)		0.88 (0.65 – 1.18)	
Depressive symptoms (PHQ-9 score ≥10)	1159 obs		1150 obs	
No	1 (Ref)	0.991	1 (Ref)	0.951
Yes	1.00 (0.70 – 1.42)		0.99 (0.69 – 1.41)	
Anxiety symptoms (GAD7 score ≥10)	1154 obs		1150 obs	
No	1 (Ref)	0.058	1 (Ref)	0.095
Yes	1.43 (0.99 – 2.08)		1.38 (0.94 – 2.01)	

* Classified into three categories instead of only two (yes / no)
** Having enough money to cover basic needs e.g. for food and heating

OR odds ratio, CI confidence interval, CLS condomless anal sex, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis, STI sexually transmitted infection, AUDIT-C alcohol use disorders identification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

4.3.3 AURAH2 attrition rates during online follow-up phase

The number of follow-up questionnaires (four monthly and annual) completed by the 622 men who completed at least one online questionnaire by the end of the study period was 3277. Participants completed a median of 6 (Interquartile range (IQR): 3 – 7) online questionnaires. The median follow-up time among these 622 men was 2.12 years (IQR 1.22 – 2.77 years) (for participants who re-engaged in the study after they fulfilled the criteria of LTFU, this included the time they spent in the study after re-started doing questionnaires), a mean of 2.06 years (SD: 1.10).

Of the 622 who completed at least one online questionnaire, 487 (78.3%) completed at least two, 458 (73.6%) completed at least three, 417 completed at least four (67.0%), 395 (63.5%) completed at least five, 376 (60.5%) completed at least six, 282 (45.3%) completed at least seven, 168 (27.0%) completed at least eight and 72 (11.6%) completed nine. However, not all participants had the opportunity to complete the ninth questionnaire as the online phase of the study closed at the end of March 2018, and therefore some participants (who joined the study after March 2015) would not have been scheduled to receive a final questionnaire (if their previous questionnaire was less than four months preceding the end of follow-up). The pattern of missingness is also detailed in Chapter 5 using the lasagna plot framework (Section 5.3.2).

According to the definitions of LTFU described in the methods section of this chapter, 211 (33.9%) men dropped out at different times during the follow-up period, while 66.1% of men were retained in the study at the end of the follow-up period. Over a total of 1275 person-years, the overall rate of LTFU was high, 16.5 per 100 PYs. The highest rate was concentrated in 2016, with a total of 101 participants were classified as LTFU and rate of LTFU 21.5 per 100 PYs (Table 4.3).

Table 4.3 Loss to follow-up among 622 men who completed at least one online follow-up questionnaire in the AURAH2 study, 2015 – 2018

Calendar year	PYs	No. of LTFU	Attrition rates (per 100 PYs)	95% CI
2015	498.25	70	14.05	10.93 – 17.72
2016	469.69	101	21.50	17.50 – 26.11
2017 / 2018	306.95	40	13.03	9.31 – 17.74
Overall	**1274.89**	**211**	**16.54**	**14.39 – 18.93**

PYs person-years, LTFU loss to follow-up, CI confidence interval

4.3.4 Predictors of LTFU among men who participated in the online follow-up phase

Predictors of LTFU among the 622 men are shown in Table 4.4. In the age-adjusted Cox proportional hazard models, men who were aged younger than 25 years (aHR 1.64, 95% CI 1.08 – 2.50, global p=0.009, versus ≥45 years) and 30 – 34 years (aHR 1.73, 95% CI 1.13 – 2.64, versus ≥45 years), self-reported being bisexual (aHR 1.41, 95% CI 1.05 – 2.15, p=0.027, versus gay), without university education (aHR 2.51, 95% CI 1.88 – 3.35, p<0.001), with unstable housing status (aHR 1.58, 95% CI 1.04 – 2.41, global p=0.040), reported the use of chemsex in the past three months (aHR 1.39, 95% CI 1.14 – 1.70, p=0.001), reported higher alcohol consumption (aHR 1.47, 95% CI 1.09 – 1.98, p=0.012), and reported anxiety symptoms (aHR 1.95, 95% CI 1.04 – 3.67, p=0.037) were more likely to

drop-out during follow-up. Group sex was predictive of retention in the study (aHR 0.70, 95% CI 0.53 – 0.92, *p*=0.010).

Less stable financial status (HR 1.52, 95% CI 1.15 – 2.02, global *p*=0.018), anxiety symptoms (HR 2.07, 95% CI 1.12 – 3.82, *p*=0.020), and non-UK born from other ethnicity (HR 1.45, 95% CI 1.04 – 2.02, global *p*=0.050, versus UK-born White ethnicity) were predictive of LTFU only in the unadjusted models. Calendar year was not associated with LTFU.

Table 4.4 Associations of time-updated factors with subsequent incidence of loss to follow-up among 622 GBMSM in the AURAH2 study who completed at least an online follow-up questionnaire, 2015 – 2018

Time-updated characteristics*	Unadjusted HR (95% CI)	p-value	Age-adjusted HR (95% CI)	p-value
Demographic characteristics				
Age as continuous variable, per year	615 obs **0.98 (0.97 – 0.99)**	**0.005**	615 obs **0.98 (0.97 – 0.99)**	**0.005**
Age category, years	615 obs		615 obs	
<25	**1.64 (1.08 – 2.50)**	**0.009**	**1.64 (1.08 – 2.50)**	**0.009**
25-29	1.46 (0.91 – 2.34)		1.46 (0.91 – 2.34)	
30-34	**1.73 (1.13 – 2.64)**		**1.73 (1.13 – 2.64)**	
35-39	1.22 (0.75 – 2.00)		1.22 (0.75 – 2.00)	
40-44	1.27 (0.75 – 2.13)		1.27 (0.75 – 2.13)	
≥45	1 (Ref)		1 (Ref)	
Country of birth and ethnicity	615 obs		615 obs	
Born in the UK, White	1 (Ref)	**0.050**	1 (Ref)	0.074
Born in the UK, Other ethnicity	0.85 (0.43 – 1.65)		0.79 (0.40 – 1.56)	
Non-UK born, White	1.14 (0.87 – 1.49)		1.12 (0.86 – 1.47)	
Non-UK born, Other ethnicity	**1.45 (1.04 – 2.02)**		1.40 (1.01 – 1.94)	
Sexual identity	618 obs		613 obs	
Gay	1 (Ref)	**0.047**	1 (Ref)	**0.027**
Bisexual / other	**1.49 (1.00 – 2.21)**		**1.41 (1.05 – 2.15)**	
Socio-economic characteristics and partnership status				
University education	620 obs		615 obs	
Yes	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
No	**2.49 (1.87 – 3.32)**		**2.51 (1.88 – 3.35)**	
Employment status	613 obs		613 obs	
Employed	1 (Ref)	0.503	1 (Ref)	0.484
Unemployed / other	1.10 (0.82 – 1.48)		1.11 (0.83 – 1.47)	
Financial status^	620 obs		615 obs	
All of the time	1 (Ref)	**0.018**	1 (Ref)	0.061
Most of the time	**1.52 (1.15 – 2.02)**		1.39 (1.03 – 1.86)	
Sometimes / No	1.24 (0.72 – 2.13)		1.23 (0.71 – 2.12)	
Housing status	611 obs		611 obs	
Homeowner	1 (Ref)	**0.002**	1 (Ref)	**0.040**
Renting	**1.53 (1.13 – 2.07)**		1.37 (0.97 – 1.94)	
Unstable / other	**1.79 (1.23 – 2.61)**		**1.58 (1.04 – 2.41)**	
Ongoing relationship **	620 obs		615 obs	

Time-updated characteristics*	Unadjusted HR (95% CI)	p-value	Age-adjusted HR (95% CI)	p-value
Yes	1 (Ref)	0.130	1 (Ref)	0.330
No	1.21 (0.95 – 1.55)		1.13 (0.88 – 1.45)	
Sexual / other HIV-related behaviour characteristics				
HIV test in the past 3 months	622 obs		615 obs	
No	1 (Ref)	0.242	1 (Ref)	0.154
Yes	0.87 (0.68 – 1.10)		0.83 (0.65 – 1.07)	
CLS in the past 3 months	622 obs		615 obs	
No	1 (Ref)	0.308	1 (Ref)	0.205
Yes	0.88 (0.69 – 1.12)		0.85 (0.67 – 1.09)	
CLS with two or more partners in the past 3 months	622 obs		615 obs	
One / none	1 (Ref)	0.875	1 (Ref)	0.828
2 or more	1.02 (0.80 – 1.29)		1.03 (0.80 – 1.31)	
Sexual role CLS in the past 3 months	622 obs		613 obs	
No CLS / didn't state	1 (Ref)	0.269	1 (Ref)	0.521
Always insertive	0.93 (0.66 – 1.29)		0.96 (0.69 – 1.33)	
Always receptive	0.96 (0.66 – 1.38)		0.91 (0.63 – 1.31)	
Versatile (sometimes insertive, sometimes receptive)	0.84 (0.63 – 1.12)		0.92 (0.69 – 1.21)	
Group sex in the past 3 months	622 obs		615 obs	
No	1 (Ref)	**0.005**	1 (Ref)	**0.010**
Yes	**0.67 (0.51 – 0.88)**		**0.70 (0.53 – 0.92)**	
PEP use in the past 12 months**	483 obs		479 obs	
No	1 (Ref)	0.587	1 (Ref)	0.640
Yes	1.17 (0.66 – 2.08)		1.14 (0.65 – 2.01)	
PrEP use in the past 12 months**	483 obs		479 obs	
No	1 (Ref)	0.214	1 (Ref)	0.086
Yes	1.52 (0.79 – 2.93)		1.79 (0.92 – 3.48)	
Bacterial STI diagnoses in the past 3 months	622 obs		615 obs	
No	1 (Ref)	0.215	1 (Ref)	0.085
Yes	0.83 (0.62 – 1.11)		0.77 (0.57 – 1.04)	
Health and lifestyle characteristics				
Recreational drug use in the past 3 months**	484 obs		479 obs	
No	1 (Ref)	0.225	1 (Ref)	0.199
Yes	0.73 (0.45 – 1.21)		0.72 (0.44 – 1.18)	
Chemsex in the past 3 months	622 obs		613 obs	
No	1 (Ref)	**0.003**	1 (Ref)	**0.001**
Yes	**1.36 (1.11 – 1.67)**		**1.39 (1.14 – 1.70)**	
Injection drug use in the past 3 months**	484 obs		479 obs	
No	1 (Ref)	0.765	1 (Ref)	0.583
Yes	1.21 (0.34 – 4.37)		1.42 (0.40 – 5.05)	
Higher risk alcohol consumption (modified WHO AUDIT-C equals ≥6)**	482 obs		478 obs	
No	1 (Ref)	**0.028**	1 (Ref)	**0.012**
Yes	**1.39 (1.03 – 1.87)**		**1.47 (1.09 – 1.98)**	

Time-updated characteristics*	Unadjusted HR (95% CI)	p-value	Age-adjusted HR (95% CI)	p-value
Depressive symptoms (PHQ-9 score ≥10)**	482 obs		480 obs	
No	1 (Ref)	0.050	1 (Ref)	0.076
Yes	1.82 (0.99 – 3.32)		1.72 (0.95 – 3.13)	
Anxiety symptoms (GAD7 score ≥10)**	482 obs		480 obs	
No	1 (Ref)	**0.020**	1 (Ref)	**0.037**
Yes	**2.07 (1.12 – 3.82)**		**1.95 (1.04 – 3.67)**	
Calendar year	624 obs		615 obs	
2015	1 (Ref)	0.279	1 (Ref)	0.286
2016	1.28 (0.99 – 1.65)		1.23 (0.95 – 1.59)	
2017/2018	0.73 (0.50 – 1.07)		0.74 (0.51- 1.08)	

* sexual/HIV related behaviour and health and lifestyle data were based on the last time man asked; number of new sexual partners, fisting or sex toys, sex for drugs or money, and smoking status were not included in the analysis because they were only asked at the baseline questionnaire.
** data were not collected at the four-monthly questionnaire (only baseline and annual questionnaires)
^ having enough money to cover basic needs e.g. for food and heating

HR hazard ratio, CI confidence interval, CLS condomless anal sex, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis, STI sexually transmitted infection, AUDIT-C alcohol use disorders identification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

4.4 Discussion

4.4.1 Summary of results

Although a large number of men enrolled in the AURAH2, only just over half (53.5%) continued on the study by completing at least an online follow-up questionnaire. The proportion of participants who were retained until the end of follow-up among the online follow-up enrollers was 66.1% (411 of 622). Among all men enrolled in the study, those younger than 45 years old and those with socio-economic disadvantage (without a university degree, with less stable financial and housing status) were more likely to not participate in the online follow-up phase. In contrast, men who reported high-risk sexual behaviours such as group sex, sex toys use or fisting, had more than ten new sexual partners, and having had a recent HIV test were more likely to join the online follow-up period. Among the online follow-up enrollers, those younger than 25 years and between 30 and 34 years, who were bisexual, without a university degree, reported the use of chemsex in the past three months, reported higher risk of alcohol consumption and reported anxiety symptoms were more likely to drop-out during follow-up. Reporting group sex was predictive of retention during follow-up.

4.4.2 Non-participation or loss to follow-up in cohort studies among GBMSM

In AURAH2, the retention rate from completing the baseline questionnaire in the clinics to registering online and completing an online questionnaire was not optimal. Participants were approached and asked to participate in the study in the clinic and offered the opportunity to fill in the baseline questionnaire on paper. It is possible that some may not be willing to participate in an online study but find the paper-based questionnaire in-clinic acceptable, or they may lack time to register and complete online questionnaires.

There was also a relatively long gap between recruitment and the beginning of the online follow-up, for those recruited through route 2 during the recruitment extension before the AURAH2 opened for direct recruitment (October 2014 until March 2015, see Chapter 3, Section 3.3.5). This might have caused those interested in the study to drop out before starting. This was not the case for those recruited through route 1 (from AURAH cross-sectional study), as all 136 of them continued on the follow-up phase. Among the follow-up enrollers, those who were lost to follow-up over time possibly because they found the study burden increased over time; therefore, they may be more likely to stop answering the questionnaires.

To the best of my knowledge, there are no other longitudinal observational studies in recent years that have recruited HIV-negative GBMSM from sexual health clinics in the UK or Europe to compare retention rates from the AURAH2 study. A few studies in North and South America have assessed attrition and retention rates in the GBMSM population (256, 257, 261, 262). These studies generally reported the proportion of retention, and in some studies, data were collected before the introduction of combined antiretroviral therapy (cART) in 1998. These cohorts observed relatively high retention rates, with retention rates being higher during the initial period of the study then remaining stable over time.

In the United States, data from Multicenter AIDS Cohort Study (MACS) among 4,954 GBMSM at risk for HIV between 1984 and 1993 reported a high retention rate, 88.5%, in nine and a half years of follow-up (256). Another US cohort of 643 Latino population of GBMSM in Chicago and San Francisco reported retention rates of 83% and 80% in three and six months of follow-up in 2004 (257). In Brazil, the Brazilian Praça Onze cohort study monitored 750 seronegative high-risk GBMSM in Rio de Janeiro between 1995 and 1998 and reported high retention rates of 97%, 91%, and 88% at six, 12, and 18 months of follow-up respectively (262). The Project Horizonte, an open cohort with a long duration of follow-up (17 years) among 1,197 GBMSM in Brazil, also reported an overall attrition rate of 11.8 per 100 PYs, with slight decreases in the loss to follow-up over time between 1994 and 2011 (261). It is difficult to compare the results from the AURAH2 study with the cohorts

mentioned above due to the methodological differences (including different definitions of retention, data collection method and how often participants were asked to complete questionnaires or interviews), study settings, participants' characteristics, and period of data collection. It seems that men who participated in HIV research during the period when cART was still not available were more likely to be retained in the cohort, possibly due to the perception of risk.

4.4.3 Factors associated with non-participation or LTFU among GBMSM

4.4.3.1 Younger age

In AURAH2, men younger than 25 years and between 30 and 34 years were more likely to be lost to follow-up. Younger age has been widely reported as a predictor of non-participation, pre-treatment drop-out, attrition, and other measurements of non-participation in HIV prevention research (258-260, 263, 264). MACS reported that age under 30 years was associated with loss to follow-up (256). A study funded by the US National Institute of Mental Health that examined factors associated with non-participation in an HIV prevention-controlled trial in four US cities among 539 GBMSM between 2002 and 2004 reported that men between the ages 20 to 39 were two to three times more likely to not enrol in an HIV prevention programs compared with men who were 40 years and older (260). Project Horizonte in Brazil also showed a greater loss of men aged 21 – 30 years during the study's follow-up (261).

Younger participants may lack the available time or interest to contribute to the study; therefore, they tend to drop-out. Also, men younger than 25 years may have more changing circumstances than older ones. It is possible that given in AURAH2 sexual risk measures were predictive of joining the follow-up or retention during follow-up, and some younger men have a period of risk which they then move on from; the study seems less relevant to them. Some have theorized that younger men may feel less vulnerable to HIV; thus, their commitment to changing risky behaviours may be less strong (264). A younger generation that did not live through the first couple of decades of the AIDS epidemic may become complacent with risky behaviours in light of available antiretroviral treatment (265).

4.4.3.2 Lower education level

Not having a university degree was also associated both with NPFU and LTFU among GBMSM in AURAH2. Compared with those with university degrees, those with no qualification were three times more likely to not enrol in the online follow-up phase, and those with no or other qualifications were two and half times more likely to drop out.

It has been previously reported that lower education is a predictor of loss to follow-up and not participating in HIV and drug abuse research (260, 266, 267). A three-month online prospective study of 2,607 GBMSM in the US in 2011 that determined the association of race and incentive level with two retention outcomes: (i) agreeing to participate in a follow-up survey and providing an email address and (ii) linking into the follow-up survey at the follow-up time point, observed that having a college education or some college education were associated with increased odds of linking into the follow-up survey compared with a high school level of education (262).

4.4.3.3 Less stable financial status

Men with less stable financial status were also less likely to participate in the online follow-up in AURAH2 than those who had enough money to cover necessities all of the time, which is in line with results from other longitudinal studies (258, 261). People with socio-economic hardships likely have more pressures or difficult circumstances in their lives, which means they need to prioritise other things; therefore, they may be more likely to drop out (268). Data from 340 gay and bisexual men who enrolled in a 14-session HIV prevention program between 1992 and December 1993 in Washington reported that those men who did not complete counselling tended to have lower levels of income and experience logistical barriers to participation (258).

4.4.3.4 Minority groups

In AURAH2, bisexual identity compared with gay identity was associated with LTFU. Some bisexual men may feel stigmatised and not wish to disclose their sexuality or sexual relationships with other men; therefore, they may be more likely to not participate in programs and research specifically recruiting and targeting homosexuals.

In Brazil, Project Horizonte reported that bisexual men were twice as likely to drop-out of the study than those who reported being exclusively gay (261). Bisexuals were also nearly twice as likely as those who classified themselves as homosexual to be among the non-responders in a US study financed by the National Institute of Mental Health investigating correlates of non-participation in an HIV prevention programme (2002 – 2004, N=539) (260). One study among Black men who have sex with men in New York City reported that bisexual men felt obligated to maintain a private sexual identity because they see bisexuality as a stigmatised identity (269). Many men in this qualitative study reported feelings of shame regarding their same-sex behaviours and conflict regarding the meaning of these behaviours for their sexual identity (269).

Anxiety and depression could be related to higher loss to follow-up among bisexual people, as the association between anxiety symptoms and LTFU was also observed in AURAH2. One systematic review and meta-analysis investigating the prevalence of depression and anxiety among bisexual people compared to gay, lesbian and heterosexual individuals between 1995 and 2016 also reported that bisexual people exhibited higher rates of anxiety and depression in comparison to gay, lesbian and heterosexual people (270).

Men of non-White ethnicity who were not born in the UK were linked to LTFU during follow-up in the unadjusted analysis in this chapter. Those of minority ethnicity have already been identified as a subset of GBMSM with the highest rate of HIV study dropout (266). In the US, Khosropour and colleagues (2011) found that minority ethnic (Hispanic and Black) study participants in a three-month online prospective study were less likely to be retained in the study compared with White participants, despite bearing a tremendous burden of HIV incidence among men who have sex with men in the United States (266). Other data from a 2021 prospective study in New York City among 633 men also found that minority men (Hispanic) were more likely to be non-participant in a mental health and HIV prevention trial than the non-Latin White homosexual men (271).

4.4.3.5 Sexual behaviour and lifestyle

Condomless anal sex was not a predictor of LTFU or NPFU in the analysis in this chapter. However, interesting findings were found in terms of other sexual behaviour characteristics. Individuals with higher baseline levels of higher-risk sexual behaviours (group sex, more than ten new sexual partners, and sex toy use) were more likely to join the online follow-up phase, probably because they felt the AURAH2 study was relevant to them. In contrast, among those who enrolled in the online phase, men who reported the use of drugs before or during sex (chemsex) were more likely to drop out before the study completion.

Conflicting results were also reported in terms of risky behaviour in the literature, particularly condomless sex. Khosropour and colleagues in the US identified condomless anal sex as one of the predictors of retention in a three-month online prospective study in 2009 (266), while Roffman and colleagues (1992 – 1993 in the US) (258) and Silva and colleagues in the Project Horizonte in Brazil (261) reported that individuals who prematurely dropped out of the study reported being more likely to have condomless anal sex compared with those who either dropped out of the study later or completed the follow-up (258, 261).

In regards to drugs and alcohol use, Orellana and colleagues reported that those who reported using drugs before or during sex one to four times in the previous 90 days were more likely not to attend any counselling session, and those who reported injection drug use were more than six times more likely not to receive any treatment (260). Similar findings

were found in the literature concerning injection drug use and participation rates in alcohol or other drug or mental health studies (259, 260).

4.4.4 Limitations

In AURAH2, exact reasons for non-participation or loss to follow-up were not collected and were not the purpose of the AURAH2 study; therefore, these cannot be explored extensively. Because sexual and other HIV-related and lifestyle characteristics were self-reported in this study, findings may be sensitive to specific recall bias and social desirability bias in men's responses in the questionnaires. Finally, due to the sample of men being solely from sexual health clinics in London and Brighton with large gay communities, the results from this chapter may not be directly generalizable to the broader GBMSM in the UK. They may also not reflect the behaviour and lifestyle choices of clinic attendees in other regions of England or outside metropolitan centres.

4.4.5 Conclusion

In conclusion, the number of AURAH2 participants who dropped out before follow-up was considerable, although, of those who enrolled in online follow-up, the proportion of men who remained in the study within the final six months of the study was more than 60%.

Findings from this chapter contribute to a better understanding of factors associated with the loss to follow-up among GBMSM attending sexual health clinics in London and Brighton, at the same time exposing some limitations that could affect how the AURAH2 study results are interpreted. Differences were observed among men who dropped out, either early or later dropped out, and those who completed the study. The individuals who dropped out were more vulnerable and socio-economically disadvantaged (younger, less educated, had less stable financial status, had less stable housing status, minor group, bisexual) than those who remained until the end of the follow-up, suggesting differential bias. Therefore, the results I present in the subsequent Chapters (5 and 6) will need to be interpreted in this light of limitation. Despite using an online approach in data collection to try to retain participants, the AURAH2 study was not as effective in retaining young and less educated individuals, those who used chemsex and alcohol or those who reported anxiety symptoms until the end of the follow-up.

The implications of findings from this chapter and recommendations for future research are discussed in the final conclusion chapter of this thesis (Chapter 9).

Chapter 5: Trends over time and within-person changes in sexual behaviour among GBMSM in the AURAH2 study

5.1 Introduction

5.1.1 Background

The effect of individual-level variation in sexual behaviour over time deserves further study due to its complexity, and there has been evidence that individual heterogeneity plays an important role in driving the HIV epidemic (132, 133). Modelling studies have also shown that behavioural heterogeneity in terms of number of sexual partners (272) and short-term increases in risk behaviour (sometimes referred to as episodic risk) (273) have a significant impact on the chances of HIV elimination by test-and-treat strategies, confirming that individual-level sexual behaviour is a major determinant of population-level intervention efficacy. Understanding of how long people stay in periods of high risk will be helpful to inform the clinical perspective and HIV models.

Based on the systematic review of longitudinal studies that I conducted until December 2020 (see Chapter 2, Section 2.3.2), the majority of available findings regarding within-person changes in sexual behaviour among HIV-negative GBMSM globally are from studies based in the United States. Data originating from Europe are minimal (164, 167, 168), and no studies have been conducted in the UK. Several series of cross-sectional studies in the UK have examined population trends in sexual behaviour (see Chapter 1, Section *1.3.4.2*, Table 1.1) (146, 150, 152, 274); however, given their study design, they were unable to investigate patterns of sexual risk behaviour within individuals specifically.

There are several approaches in identifying individual-level changes using repeated observations of the same variable over time (275). In most cases, mixed-effects models are used to estimate an average population trajectory and the variation of individual trajectories around this average (276, 277). More recently, the focus of modelling such data has moved towards investigating whether there are multiple typical trajectories, leading to the characterisation of latent subgroups of individuals who share a typical profile over time. Aiming to classify individuals into subgroups based on their longitudinal data has been described as being a person-centred approach instead of the variable-centred approach typical of many regression analyses (278). European data that described typical trajectories of changing sexual behaviour across the life course in GBMSM is available from the Amsterdam Cohort Study (ACS) (164).

Transition analyses, in which we estimate the probabilities of transitions among behaviour patterns over time, have also been applied to prospective cohort data to quantify changing behaviours over time and are useful to identify unobserved risk patterns in longitudinal data, characterise high-risk GBMSM and quantify individual transitions over time (169, 279). To my knowledge, there were no UK studies that have measured the probabilities of transitions between different groups of risk and the predictors that affect the transitions.

5.1.2 Chapter aims

The objectives of this chapter are:

(i) to describe the overall prevalence of, and trends in, sexual behaviour measures among all men enrolled in AURAH2 over calendar year (2013 – 2018)
(ii) to assess within-person changes in the frequency of condomless anal sex with two or more partners (CLS2+) among men in AURAH2 who completed at least one online questionnaire over three years of the online follow-up period, at four-month intervals (first online questionnaire – last online questionnaire)
(iii) to assess whether there are different patterns in reporting CLS2+ among men AURAH2 who completed at least one online questionnaire over three years of the online follow-up period, at four-month intervals
(iv) to estimate the transition probabilities from 'higher-risk' behaviour (reporting CLS2+) to 'lower-risk' behaviour (reporting none or CLS with one partner only) and vice versa from 'lower-risk' to 'higher-risk' behaviour among men in AURAH2 who completed at least two consecutive online questionnaires over three years of the online follow-up period, at four-month intervals
(v) to examine the extent to which current socio-demographic characteristics, HIV-related behaviour, and health and lifestyle factors might be associated with the transitions in sexual behaviour among men in AURAH2 who completed at least an online questionnaire over three years of the online follow-up period, at four-month intervals

5.2 Methods

5.2.1 Lasagna plot

In this thesis, the lasagna plot framework is used to visualize individual patterns in sexual behaviour. A *lasagna* plot is a graphical tool that can display longitudinal data and explore complex patterns within cohorts of participants throughout a study (280, 281). The plot presents the subject-specific trajectories by utilizing gradients of colour (heatmap) to depict

the outcome (282). Over time, each subject's trajectory is shown in a horizontal layer, with the simultaneous plotting of trajectories resulting in the stacking of layers, as in lasagna. Using this framework, cohort, group, and individual-level behaviour can be visualized and ascertained, intermittent missing data can be identified, data are preserved regardless of the number of participants or time points, and the distribution of onset and end times can also be displayed (280, 283). The lasagna plot is added to the traditional tables and graphs analyses by revealing trends over time, which are hard to present with numbers and point estimates and is useful when data is recorded for every individual subject or parameter at the same set of uniformly spaced time intervals, such as daily, monthly, or quarterly (as in AURAH2). The plots could also be of additional value for studies that report on multiple outcomes that are often interrelated and may occur at different times.

5.2.2 Markov transition probability model

Transition analysis is an analytical framework to address questions about state-switching processes occurring within a person, dyad, group, or system over time (284, 285). Transition analysis gives information on whether there is a change between events (for example, from high-risk to low-risk behaviour) or latent classes across time and the probability that the individual will change the class or be in the same class at the following observation.

A modelling technique that has been used to give useful information about the longitudinal transition is the Markov chain modelling technique (286). Markov models offer an intuitive approach for modelling individuals' transitions between a number of discrete states over time (287-290) and have been used in a variety of clinical settings, including estimating HIV incidence and detection rates (291) and modelling HIV progression (292). Markov models can be either discrete-time, where transitions can only occur at fixed time points, or continuous-time, where transitions can occur at any time. The Markov assumption is that the probability of a transition from one state to another does not depend on the previous states visited or the time spent in the current state (290) and that the transition rates are constant through time and are common for all individuals (293). The Markov transition probability approach is ideal for modelling the stability or volatility of risk behaviours over time and is particularly informative given the longitudinal structure of the AURAH2 data. Therefore, this chapter uses this technique to model the transitions between different sexual behaviour levels.

5.2.3 'Higher-risk' sexual behaviour definition

In this chapter, CLS with two or more partners (CLS2+) was defined as the main measure of 'higher-risk' sexual behaviour. While the literature has studied a variety of risky behaviours, there is a lack of consensus about the definition of high-risk sexual behaviour (294-296).

Researchers have defined *risky sexual behaviour* as sexual activities which expose the person to the risk of contracting sexually transmitted infections (STIs), including HIV, thus affecting their health (294-296). CLS with one partner was considered to be less likely to represent behaviour potentially linked to high-risk of acquisition of HIV because this may occur in the context of a long-term relationship where HIV status is known with more confidence. CLS with an HIV-positive partner when the HIV-positive partner is taking antiretroviral drugs with good adherence and has a fully suppressed viral load is also not a high-risk behaviour because the risk of HIV transmission through anal sex is zero in this context (32, 33). Therefore, considering the U=U period and the relatively low PrEP use in the UK during the data collection period of the AURAH2 study, CLS with multiple partners (at least two) was considered as 'higher-risk' sexual behaviour, and vice versa, CLS with only one partner or none was considered as 'lower-risk' behaviour.

5.2.4 Socio-demographic, health and lifestyle, and other sexual/HIV-related behaviours measures

For a detailed description of the categories, definitions, and recall period of each socio-demographic, health and lifestyle, and sexual behaviour variables used in this chapter, please see Chapter 3 (thesis methods, Sections 3.6.1 – 3.6.3).

Socio-demographic variables included age group, country of birth and ethnicity, sexual identity, university education status, ongoing relationship status, employment status, financial status, and housing status.

In addition to condomless anal sex with two or more partners, six other measures of sexual and other HIV-related behaviours were considered for this analysis: condomless anal sex (CLS), group sex, bacterial STI diagnoses, recent HIV test, pre-exposure prophylaxis (PrEP), and post-exposure prophylaxis (PEP) use.

Health and lifestyle factors included recreational drug use, chemsex use, injection drug use, depressive symptoms, anxiety symptoms, and higher alcohol consumption.

Country of birth and ethnicity, sexual identity, university education status, employment status, financial status, and housing status were fixed variables derived from the baseline questionnaire, whereas age, sexual / HIV-related behaviours, and health and lifestyle factors were time-varying variables (using either four-monthly or annual questionnaires). As explained in Chapter 3 (thesis methods, Sections 3.5.1 and 3.5.2), missing values for variables were treated as 'No', except for variables: age, country of birth and ethnicity, sexual identity, financial status, and housing status, for which missing values were excluded.

5.2.5 Statistical analysis

The prevalence of and trends in the sexual behaviour and lifestyle measures were calculated according to calendar period, using three-month periods from the first enrolment (July 2013) to the end of the AURAH2 study period (March 2018). Information from each participant's questionnaires was ascribed to the three-month period in which the questionnaire was completed. Data for the last two quarters of 2013 (July to December 2013) were combined as one calendar period because the number of men recruited between July and September 2013 was too small to be considered a separate period. Univariable generalised estimation equation (GEE) models with a logit link and robust standard errors (SEs) were used to assess trends over calendar time during the period of July 2013, to March 2018, in the proportion of questionnaires for which the different sexual behaviours were reported, accounting for multiple questionnaire responses from individual participants. The calendar year was fitted as a continuous variable to obtain a test for linear trends. To describe trends in the past three months in CLS, CLS2+, and group sex, data from 4,438 questionnaires (baseline, four-monthly and annual follow-up) from 1,162 participants were used. For trends on bacterial STI diagnosis and chemsex, data were not included from the baseline questionnaires, as it asked about diagnoses of STIs in the previous 12 months rather than in the last three months and did not ask specifically about chemsex (total questionnaires used 3,277 questionnaires). To describe trends in the past three months of recreational drug use and injection drug use, data from 2,103 questionnaires (baseline and annual follow-up) were used because these data were not collected at four-monthly questionnaires.

Analyses of within-person changes in this chapter are devoted and limited only to CLS2+, which was the measure chosen to capture 'higher-risk' sexual behaviour (see Section 5.2.3). Data from 622 men who completed at least an online questionnaire were used for this analysis. To graphically visualize longitudinal changes in CLS2+, first, a descriptive analysis was done to present changes in the frequency of men who reported CLS2+ and did not report on this behaviour among those men who reported CLS with two or more partners in the previous visit, and the proportion who reported on this behaviour and did not report CLS with two or more partners among those who did not report CLS with two or more partners in the previous visit. To assess patterns of change, only responses from men who completed at least two consecutive online questionnaires were included (total observations used 3,081 questionnaires).

In addition, the lasagna plotting framework is presented by plotting individual data as horizontal layers on top of each other. Each layer represents a participant, and each column represents a time point (visit or number of the questionnaire). This framework was also used to identify if a participant missed a questionnaire at any point. Unsorted and entire-row

sorted based on sexual behaviour (by placing lower-risk behaviour at the top and higher-risk behaviour at the bottom) plots are presented.

To estimate transition probabilities from ‘higher-risk’ to ‘lower-risk’ and vice versa, homogenous / one component discrete-state Markov chain models were fitted.
The *mixmcm* procedure in Stata (297), a community-contributed command that fits the general class of mixed Markov chain models, was used to investigate individuals' predictability over time. The *mixmcm* performs multiple multinomial logistic regressions to estimate parameters of transition probabilities (logits or log-odds for each cell of the transition table) (297). Multinomial regression values were modelled using longitudinal data, providing probabilities (probabilities being a function of logits). To account for the possibility of incomplete information within the data (that is, unobserved heterogeneity), the model is fit with maximum likelihood using the expectation-maximization algorithm. To observe at least one transition, for this analysis, data from 542 participants who completed at least an online questionnaire and had at least two time-points data of follow-up (total observations used 3,197 questionnaires) were used.

To assess the contributions of socio-demographic, health and lifestyle, and other HIV-related behaviours factors in explaining the odds of remaining in the initial state or switching to another state, Markov chain models were also fitted (297). Covariates were examined individually in univariable models. The resulting coefficients of the explanatory variables explain the degree to which covariates contribute to individual transitions, where remaining in the current behaviour is the reference scenario. The impacts of explanatory variables on log-odds ratios are difficult to interpret directly; however, in general, the exponentiated coefficients are odds ratios in multinomial logit models. Therefore, exponentiated coefficients are presented as the odds ratios in this chapter.

An additional cross-sectional analysis was also done using GEE logistic models to examine factors associated with reporting CLS2+ in the past three months, using all available baseline and follow-up questionnaires from 542 participants who had at least two-time points data of follow-up. This was done to compare results with those in the transition analysis using Markov chain models. Odds ratios (ORs) for factors, (i) unadjusted, (ii) adjusted for age, and (iii) adjusted for age, country of birth and ethnicity, sexual identity and university education status with their 95% CIs are presented. The adjustment for variables (ii) was determined a priori on factors that were considered not to be influenced by CLS2+. All analyses were done using Stata SE version 15.1. The lasagna plots were reproduced using Tableau 2018.3.

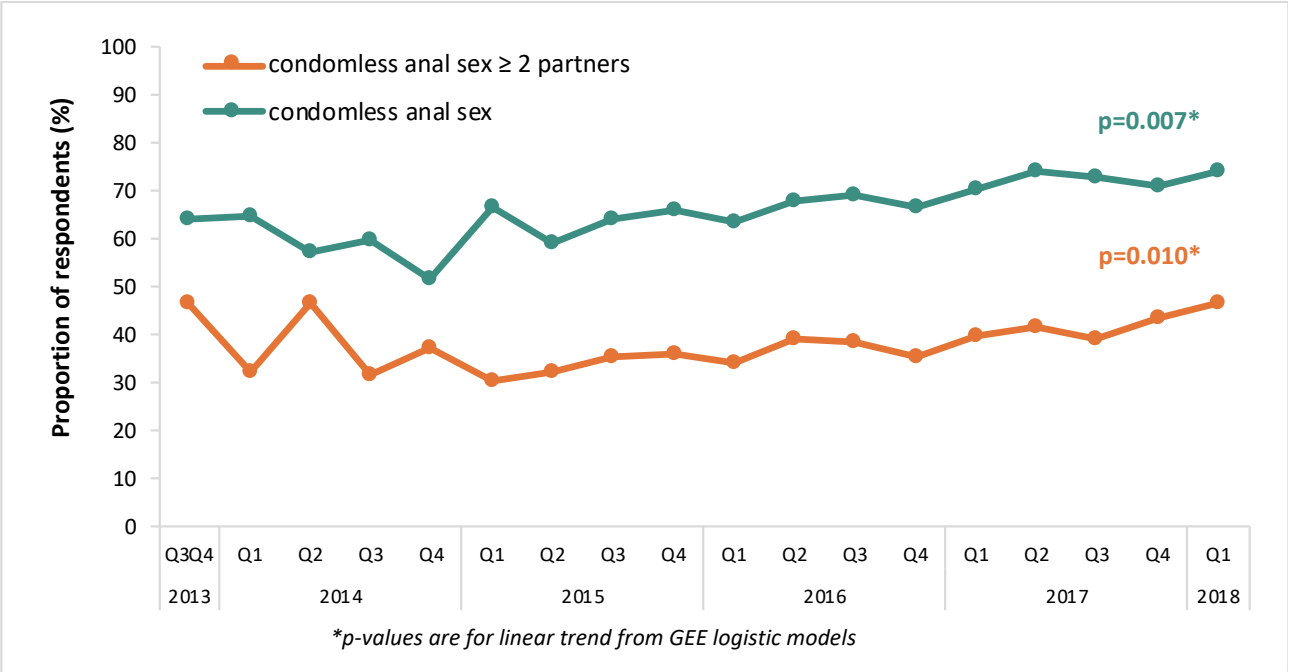
5.3 Results

5.3.1 Prevalence of, and trends in, sexual behaviour according to calendar year

Figure 5.1 shows trends in reporting CLS and CLS2+ in the past three months from 2013 to 2018. Overall, CLS and CLS with two or more partners were reported in 2,973 and 1,665 baseline and follow-up questionnaires (66.9% and 37.5%).

Prevalence of both sexual behaviours declined up to the end of 2014 and then increased until the end of the follow-up period (Figure 5.1); CLS rose from 64.3% in the last two quarters of 2013 to 74.4% by January to March 2018 (unadjusted OR 1.09 per year, 95% CI 1.03 – 1.17, *p-value for linear trend from GEE-logistic model*=0.007); CLS with two or more partners increased from 46.4% in the period of July to December 2013, to 46.9% in January to March 2018 (unadjusted OR 1.09 per year, 95% CI 1.02 – 1.16, *p-trend*=0.010). Both significant trends seem to be driven by data from 2015 onwards, as early data were relatively small numbers.

Figure 5.1 Prevalence of CLS and CLS with two or more partners in the past three months over time among GBMSM in the AURAH2 study, 2013 – 2018*

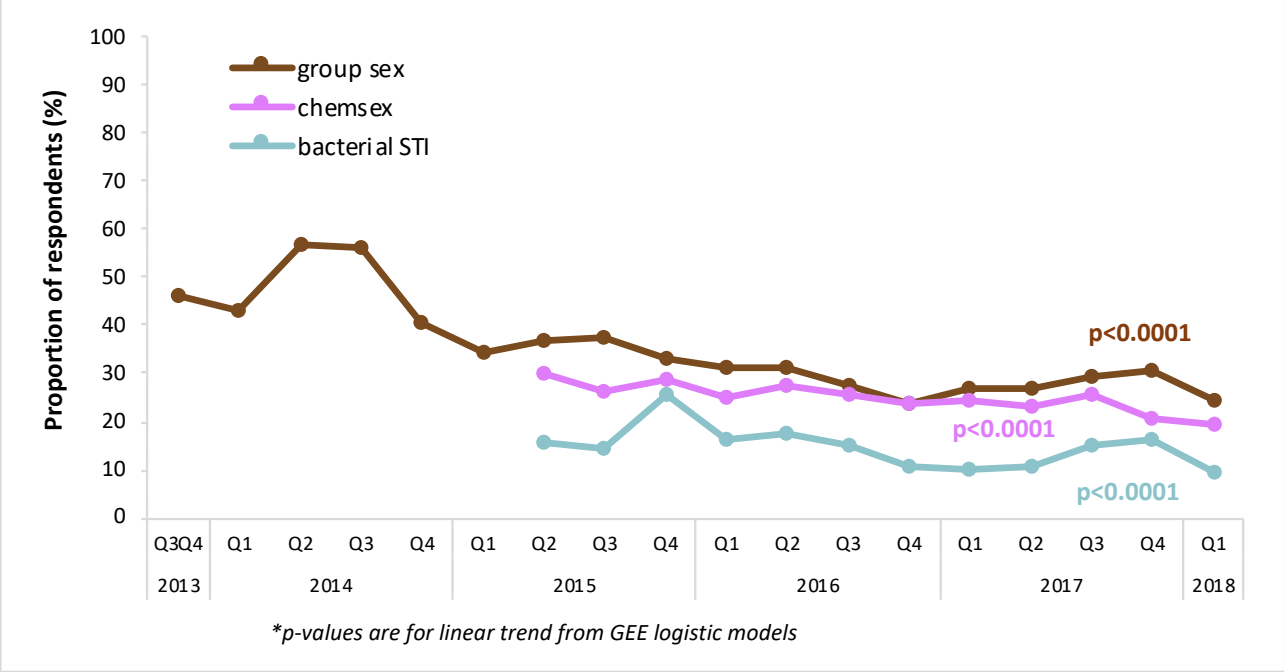


	2013	2014				2015				2016				2017				2018
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Number of questionnaire	28	37	28	25	62	192	444	376	466	449	387	331	312	298	282	260	254	207
CLS in the past three months	18	24	16	15	32	128	262	242	307	286	264	229	208	210	209	189	180	154
CLS ≥2 partners in the past 3 months	13	12	13	8	23	58	144	133	169	155	153	128	110	119	117	102	111	97

*Data from baseline, four-monthly, and annual questionnaires, missing values on CLS and CLS with two or more partners were treated as No (N = 1,162 participants provided 4,338 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment).

Figure 5.2 shows trends in reporting group sex, chemsex and bacterial STIs in the past three months from 2013 to 2018. Overall, 1,398 of 4,438 questionnaires (31.5%) reported group sex, 487 of 3,277 follow-up questionnaires (14.9%) reported a diagnosis of bacterial STIs, and 822 of 3,277 follow-up questionnaires (25.1%) reported chemsex. Prevalence of group sex declined substantially from 46.4% to 24.2% (*p-trend*<0.001), as did bacterial STI diagnoses from 15.7% in March to June 2015 to 9.2% by January to March 2018 (*p-trend*<0.001), and chemsex from 30.8% in March to June 2015 to 19.3% by January to March 2018 (*p-trend*<0.001).

Figure 5.2 Prevalence of group sex*, bacterial STIs and chemsex** in the past three months over time among GBMSM in the AURAH2 study, 2013 – 2018**

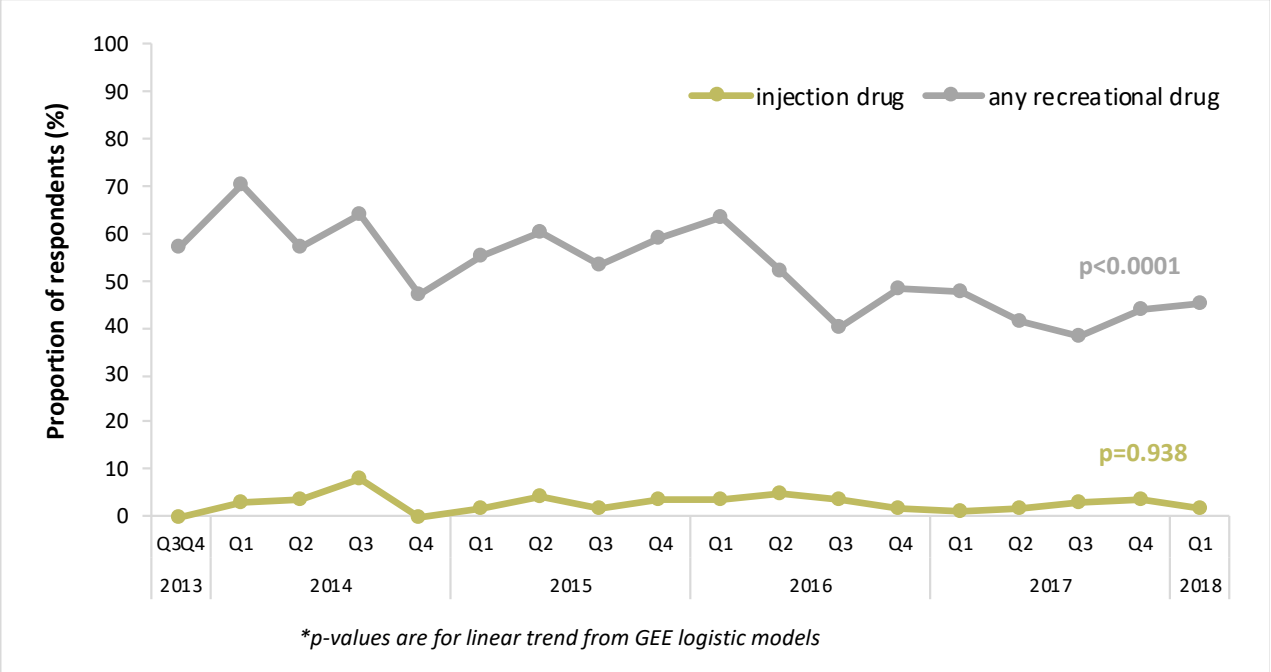


	2013	2014				2015				2016				2017				2018
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Group sex in the past 3 months / total number questionnaire	13/28	16/37	16/28	14/25	25/62	66/192	165/144	142/376	155/466	141/449	122/387	90/331	74/312	80/298	75/282	77/260	77/254	50/ 207
Bacterial STIs in the past 3 months / total number questionnaire						3 / 32	24 / 140	28 / 194	84 / 325	51 / 318	56 / 324	49/ 331	33 / 312	30/ 298	30/ 282	39 / 260	41/ 254	19/ 207
Chemsex in the past 3 months / total number questionnaire						7/ 32	46/ 140	51 / 194	94/ 325	80/ 318	89/ 324	84/ 331	74/312	73/298	65/282	67/ 260	52/ 254	40/ 207

*Data from baseline, four-monthly, and annual questionnaires, missing values on group sex were treated as No (N = 1,162 participants provided 4,338 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment);
**Data from four-monthly and annual questionnaires, missing values on bacterial STIs were treated as No (N = 1,162 participants provided 3,277 questionnaires.

The overall prevalence of any recreational drug use and injection drug use was 52.5% (1,104/2,103) and 2.9% (61/2,103), respectively. Any recreational drug use in the past three months decreased from 57.1% to 45.5% (*p-trend*<0.001), while injection drug use (prevalence around 2%, *p-trend*=0.938) was stable (Figure 5.3).

Figure 5.3 Prevalence of recreational drug use and injection drug use in the past three months over time among GBMSM in the AURAH2 study, 2013 – 2018*



	2013	2014				2015				2016				2017				2018
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Number of questionnaire	28	37	28	25	62	160	304	273	152	166	148	173	129	78	68	110	107	55
Any recreational drug use	16	26	16	16	29	88	184	147	90	105	77	69	62	37	28	42	47	25
Injection drug use	0	1	1	2	0	3	13	5	5	6	7	6	2	1	1	3	4	1
Chemsex-related drug use	3	7	6	3	17	45	82	81	34	48	36	30	35	19	14	22	23	13

*Data from baseline and annual questionnaires, missing values were treated as No (N = 1,161 participants provided 2,103 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment).

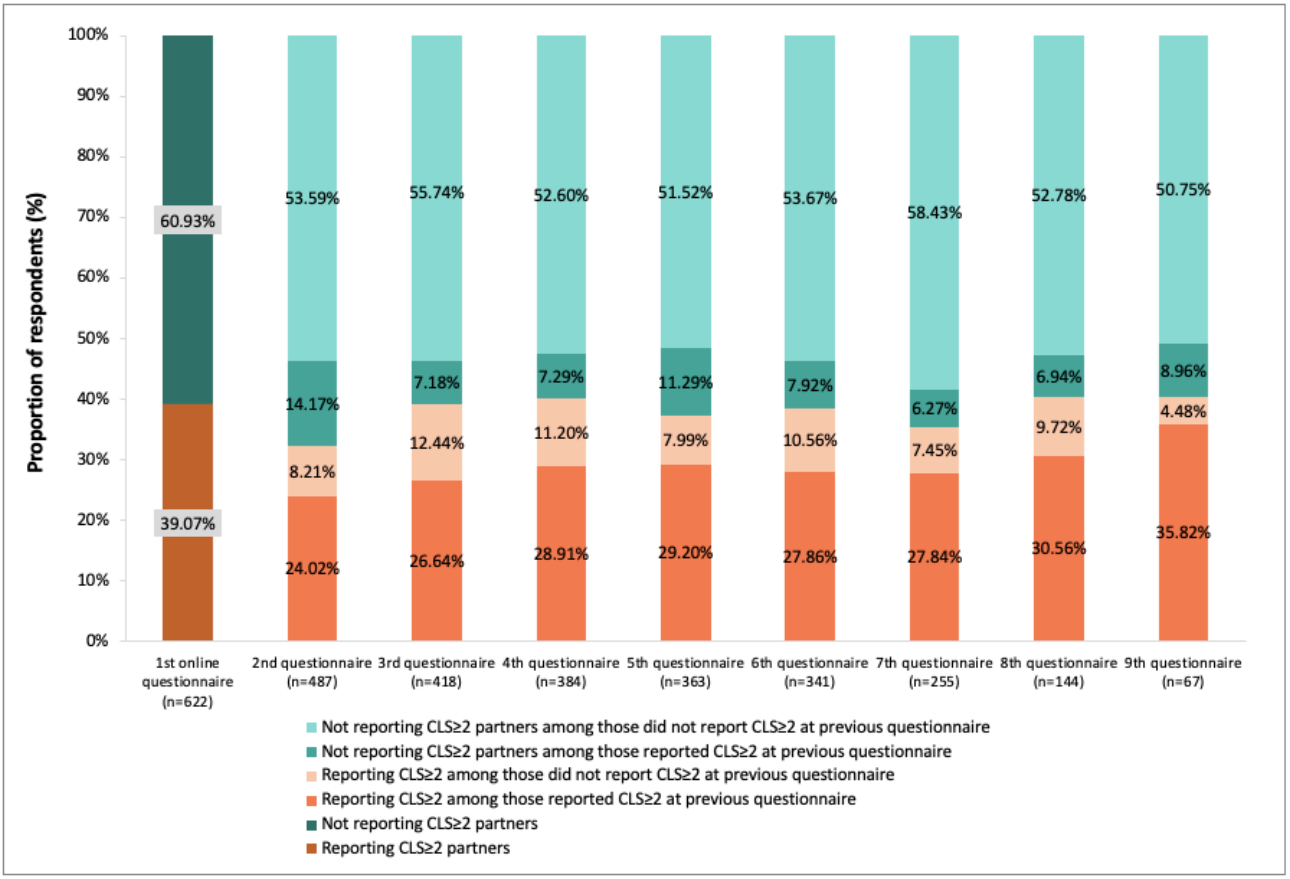
5.3.2 Within-person changes in the frequency of condomless anal sex with two or more partners

Figure 5.4 shows the change in the proportion reporting CLS with two or more partners, among 622 men, from the first online questionnaire to the last online questionnaire. In this analysis, only responses of behaviour changes (CLS2+ → no CLS2+ or vice versa) were included, while the responses that included missing (missing → CLS2+, missing → no CLS2+ and vice versa) were excluded. In Chapter 4 (Section 4.3.3), I have described the number of men who completed first, second, third, until the ninth questionnaire.

The observed proportions of CLS2+ among the 622 men in the online cohort remained relatively stable: 39.1% at the first online questionnaire (darkest orange) and 40.3% at the ninth online questionnaire (accumulation of medium orange and pale orange). The overall prevalence of CLS with two or more partners among these men across nine questionnaires was 37.9%, similar to those among the 1,162 men. The proportion of men who switched to report CLS with two or more partners, given that they did not report this behaviour at the

previous questionnaire, was between 5% and 12% of total respondents (shown in pale orange). While the proportion of men who transitioned out of the 'higher-risk' at each questionnaire was between 6% and 14% (shown in medium green).

Figure 5.4 Proportional changes in the frequency of condomless anal sex with two or more partners among 622 GBMSM in the AURAH2 study during follow-up



5.3.3 Lasagna plots

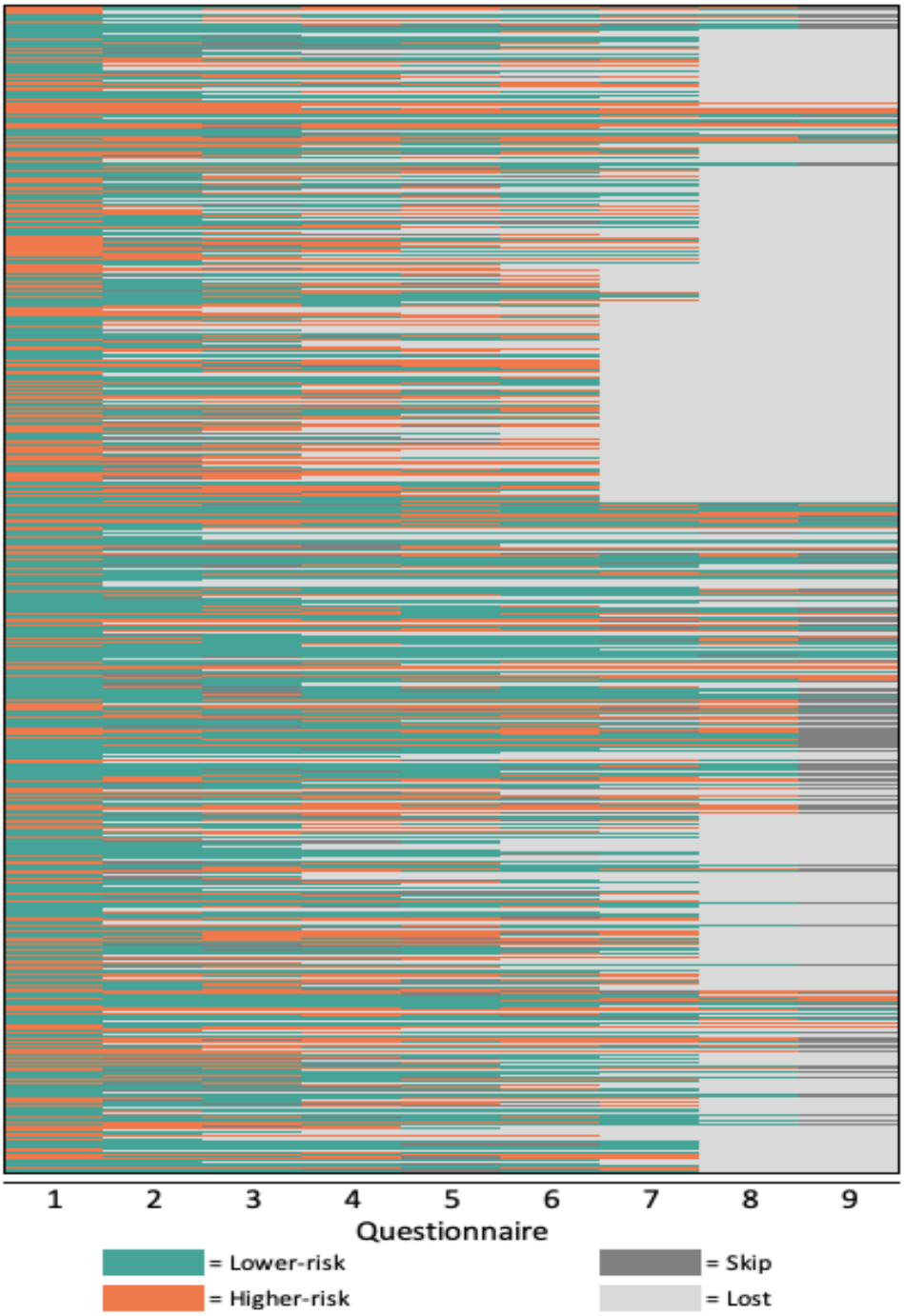
The lasagna plots of the AURAH2 study among 622 men are shown in Figure 5.5. For this analysis, I classified responses at each questionnaire into four groups so that I could also assess the patterns of missingness: higher-risk, lower-risk, skipping a questionnaire (did not complete a questionnaire at a specific time, but later came back), and lost (never came back to the study).

The first plot (A) shows an unsorted lasagna plot, where the horizontal axis of the plot represents the time (number of questionnaires being completed) and the vertical axis represents the participants. Thus, every horizontal layer represents the follow-up of an individual over time. The second plot (B) shows the entire-row sorted (based on sexual

behaviour reported) plot by plotting higher-risk behaviour at the bottom of the plot, and lower-risk behaviour at the top of the plot first (the first column), followed by skipping a questionnaire, and then lost (never came back to the study). In the plots, orange surfaces represent higher-risk behaviour, and green surfaces represent lower-risk behaviour, which covered the majority of the plots, in accordance with Figure 5.2. There appeared to be a relatively stable pattern in reporting sexual behaviours, a pattern of increasing frequency of loss to follow-up and a decreasing frequency of skipping a questionnaire over time.

Figure 5.5 Lasagna plots illustrating trajectories in reporting sexual behaviours among 622 GBMSM in the AURAH2 study (n=5598 observations)

(A) unsorted lasagna plot



(B) Entire row sorted plot (based on sexual behaviour)

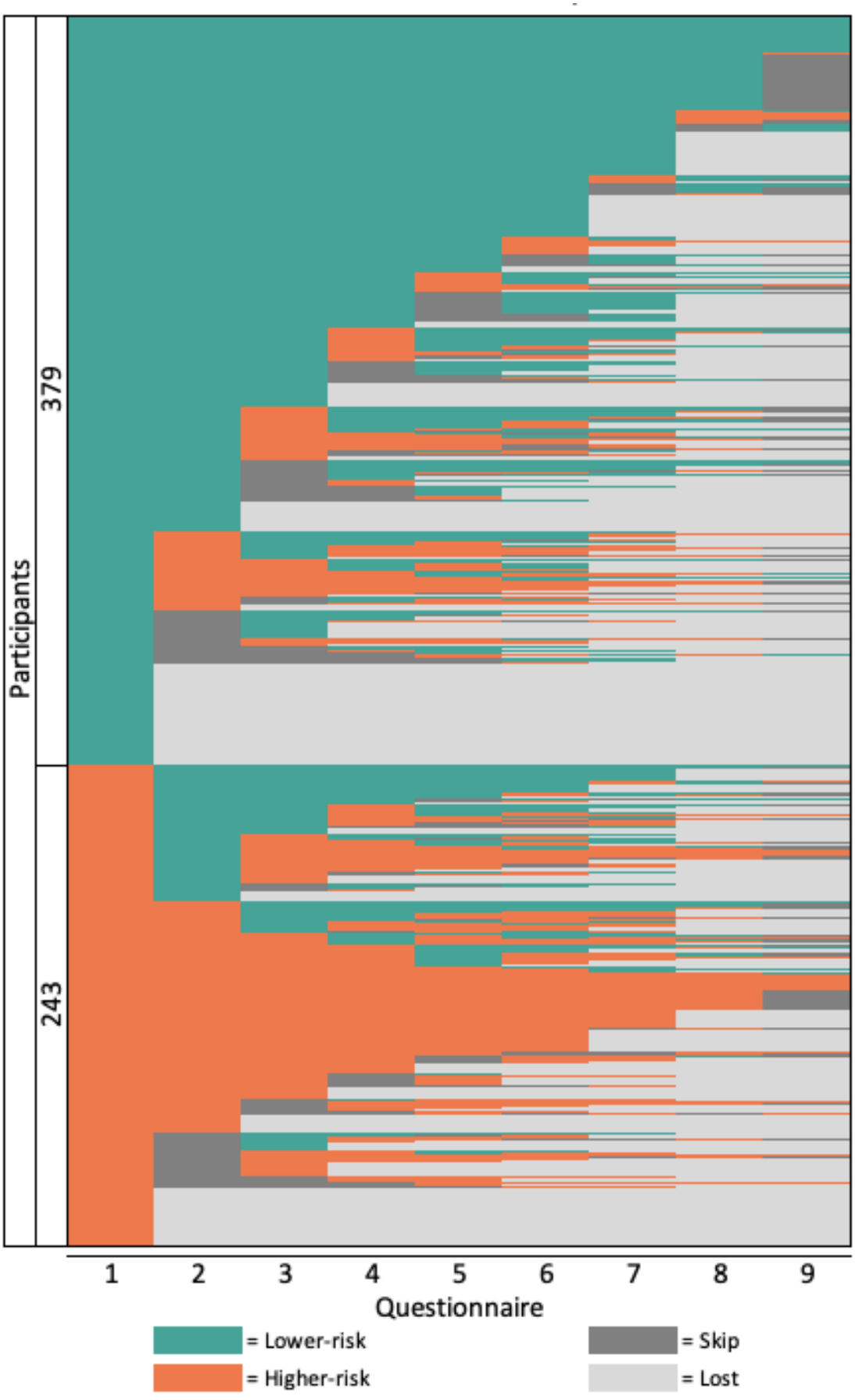


Table 5.1 illustrates the proportion of changes from a different initial state (*higher-risk; lower-risk; skipping questionnaire; loss to follow-up*) within an individual in each questionnaire, according to the previous questionnaire among these men, as shown in the sorted lasagna plot.

Table 5.1 Individual changes in reporting sexual behaviours among 622 GBMSM in the AURAH2 study over time (based on lasagna plot)

	proportion of changes from questionnaire to questionnaire*							
	1 – 2	**2 – 3**	**3 – 4**	**4 – 5**	**5 – 6**	**6 – 7**	**7 – 8**	**8 – 9**
No changes (regardless of initial state)	60.8%	69.3%	71.4%	74.9%	75.6%	70.6%	70.1%	81.5%
Transition out (regardless of initial state)	39.2%	30.7%	28.4%	25.1%	24.4%	29.4%	29.9%	18.5%
higher-risk – higher risk	18.8%	16.6%	17.8%	17%	15.3%	11.4%	7.1%	3.9%
higher-risk – lower-risk	11.1%	4.8%	4.5%	6.6%	4.3%	2.6%	1.6%	1.0%
higher-risk – skip	4.5%	1.9%	1.9%	1.4%	2.1%	1.3%	0.2%	6.4%
higher-risk – lost	4.7%	1.9%	3.4%	1.9%	2.6%	8.4%	8.0%	0.0%
lower-risk – lower-risk	42.0%	37.5%	32.5%	30.1%	29.4%	24.0%	12.2%	5.5%
lower-risk – higher-risk	6.4%	8.4%	6.9%	4.7%	5.8%	3.1%	2.3%	0.5%
lower-risk – skip	4.3%	4.0%	2.1%	3.9%	1.4%	1.8%	0.6%	9.8%
lower-risk – lost	8.2%	3.2%	4.5%	1.4%	2.6%	8.0%	13.3%	0.0%
skip – skip	0.0%	2.4%	3.1%	1.9%	1.6%	0.8%	0.0%	0.0%
skip – higher risk	0.0%	2.7%	2.3%	2.6%	2.6%	2.4%	1.9%	0.2%
skip – lower risk	0.0%	3.7%	3.1%	2.6%	3.1%	1.9%	1.9%	0.6%
lost – lost	0.0%	12.9%	18.0%	25.9%	29.3%	34.4%	50.8%	72.2%

*** Proportions from 622 questionnaires at each visit**

Regardless of their initial state, 61% - 82% of men in each questionnaire would maintain the same level of risk in the subsequent questionnaire (including skip and lost). The consistencies in reporting higher-risk and lower-risk behaviours tended to decrease over time (staying in higher-risk behaviour from 19% at the second questionnaire 4% at the last online questionnaire; staying in lower-risk behaviour from 42% to 6%); however, this was due to the increase in missing responses (changes from ‘lost’ to ‘lost’). As a result, Table 5.2 was produced, which excluded observations of changes from ‘lost’ to ‘lost’.

Table 5.2 Individual changes in reporting sexual behaviours among 622 GBMSM in the AURAH2 study over time (based on lasagna plot, excluding questionnaire from lost participants)

	proportion of changes from questionnaire to questionnaire							
	1 – 2	2 – 3	3 – 4	4 – 5	5 – 6	6 – 7	7 – 8	8 – 9
Higher risk to higher risk	18.8%	19.0%	21.8%	23.0%	21.6%	17.4%	14.4%	13.9%
Higher risk to lower risk	11.1%	5.5%	5.5%	8.9%	6.1%	3.9%	3.3%	3.5%
Higher risk to skip	4.5%	2.2%	2.4%	2.0%	3.0%	2.0%	0.3%	23.1%
Higher risk to lost	4.7%	2.2%	4.1%	2.6%	3.6%	12.7%	16.3%	0.0%
Lower risk to lower risk	42.0%	43.0%	39.6%	40.6%	41.6%	36.5%	24.8%	19.7%
Lower risk to higher risk	6.4%	9.6%	8.4%	6.3%	8.2%	4.7%	4.6%	1.7%
Lower risk to skip	4.3%	4.6%	2.5%	5.2%	2.0%	2.7%	1.3%	35.3%
Lower risk to lost	8.2%	3.7%	5.5%	2.0%	3.6%	12.3%	27.1%	0.0%
Skip to skip	0.0%	2.8%	3.7%	2.6%	2.3%	1.2%	0.0%	0.0%
Skip to higher risk	0.0%	3.1%	2.7%	3.5%	3.6%	3.7%	3.9%	0.6%
Skip tp lower risk	0.0%	4.2%	3.7%	3.5%	4.3%	2.9%	3.9%	2.3%
Number of questionnaire	622	542	510	461	440	408	306	173

After excluding 'lost' to 'lost' observations, there appeared to be reasonably high stability among the group of men who consistently reported lower-risk behaviour, up to the 7th online questionnaire. Men who reported higher-risk behaviour also tended to stay in this behaviour over time until the 9th questionnaire. There were high proportions of skipping questionnaires at the last online questionnaire, but this was because not all participants had the opportunity to fill in the last online questionnaire (see Chapter 4, Section 4.3.3). The proportion of men who reported an 'unstable' trajectory (a switch from lower-risk to higher-risk and vice versa from questionnaire to questionnaire) tended to decrease over time, and the proportions were relatively small.

5.3.4 Overall transition probabilities

The fitted models predicting overall transition probabilities among 542 men who had at least two consecutive questionnaires during follow-up agreed with the observed trajectories in the lasagna plots; those men were less likely to move across behaviours in the following subsequent questionnaire whatever their initial state.

Table 5.3 reports results for transition probabilities. **p12** is the estimated probability of transitioning to state 2 (not reporting CLS2+) from state 1 (reporting CLS2+) in the next period, given the process is in state 1 in the current period. The probability of staying in higher-risk behaviour is therefore **1 – 0.22 = 0.78**, which implies that state 1 is quite persistent. Similarly, the probability of staying in state 2 is **1 – 0.12 = 0.88**, which exhibits a high probability to remain in the same behaviour for two consecutive questionnaires.

Table 5.3 Transition probabilities for sexual risk behaviour among 542 GBMSM in the AURAH2 study

State	estimated log odds ratio	Z	p-value	95% CI
'higher-risk'	-1.11	-14.91	<0.001	-1.25 – -0.96
'lower-risk'	-1.68	-24.97	<0.001	-1.81 – -1.55
p12	**0.22**			0.19 – 0.24
p21	**0.12**			0.11 – 0.13

CI confidence interval

5.3.5 Predictors of transition probabilities

5.3.5.1 Explanatory variables of transition probabilities from 'higher-risk' to 'lower-risk' behaviour

Table 5.4 presents the exponentiated coefficients (odds ratios) of the explanatory variables of transition probabilities. The exponentiated coefficients from the Markov chain models showed that recent HIV test, PrEP use, PEP use, and calendar year significantly contributed to the reduced probability to transition from having two or more CLS partners to have one or none CLS partner. This can be interpreted that, men who reported an HIV test in the past three months (OR 0.38, 95% CI 0.27 – 0.54, p<0.001), the use of PrEP in the past 12 months (OR 0.13, 95% CI 0.05 – 0.35, p<0.001), and the use of PEP in the past 12 months (OR 0.31, 95% CI 0.10 – 0.91, p=0.033) were less likely to transition to safer behaviour and more likely to remain in higher-risk behaviour in subsequent questionnaires. The more recent calendar year (OR 0.78, 95% CI 0.63 – 0.96, p=0.018) also decreased the probability of men transitioning to safer risk behaviour. On the other hand, men with less stable housing tended to transition to safer risk behaviour than to remain in higher-risk behaviour in the subsequent questionnaire (OR 1.04, 95% CI 1.01 – 1.07, p=0.016).

5.3.5.2 Explanatory variables of transition probabilities from 'lower-risk' to 'higher-risk' behaviour

Similarly, less stable housing status decreased the probability of men to transition out from the lower-risk behaviour in a subsequent questionnaire (OR 0.97, 95%CI 0.94 – 0.99, p=0.035), while reporting recent HIV test (OR 1.80, 95% CI 1.33 – 2.43, p<0.001), PrEP use (OR 2.57, 95% CI 1.13 – 5.86, p=0.024), and PEP use (OR 2.54, 95% CI 1.23 – 5.25, p=0.012) predicted the transition from lower-risk to higher-risk behaviour. In addition, the probabilities of switching to CLS with two or more partners were predicted by a bacterial STIs diagnosis (OR 2.12, 95% CI 1.37 – 3.27, p=0.001), the use of recreational drugs (OR 2.02, 95% CI 2.01 – 3.39, p=0.009), injection drugs (OR 5.82, 95% CI 4.48 – 7.55, p<0.001),

and chemsex drugs (OR 2.27, 95% CI 1.60 – 3.21, *p*<0.001). The use of injection drugs had the highest effect in predicting a switch to higher-risk behaviour from lower-risk behaviour, up to almost six-fold higher.

Table 5.4 Explanatory variables of transition probabilities from univariable Markov transition probability models among 542 GBMSM in the AURAH2 study, 2015 – 2018

	Transition probabilities from *'higher-risk' to 'lower-risk'*		**Transition probabilities from *'lower-risk' to 'higher-risk'***	
Explanatory covariates	**exp. coef (OR) 95% CI**	**p-value**	**exp. coef (OR) 95% CI**	**p-value**
Demographics characteristics				
Age	0.98 **(**0.97 – 1.00)	0.056	1.00 **(**0.99 – 1.02)	0.492
Country of birth and ethnicity	1.05 **(**0.92 – 1.20)	0.482	1.05 **(**0.92 – 1.19)	0.481
Sexual identity	0.57 (0.27 – 1.22)	0.154	0.88 (0.49 – 1.59)	0.680
Socio-economic characteristics and partnership status				
University education status	1.24 (0.88 – 1.76)	0.216	0.87 (0.63 – 1.21)	0.421
Employed	1.17 (0.72 – 1.89)	0.526	1.24 (0.77 – 2.00)	0.380
Financial status	0.75 (0.53 – 1.05)	0.091	1.01 (0.76 – 1.33)	0.949
Housing status	**1.04 (1.01 – 1.07)**	**0.016**	**0.97 (0.94 – 0.99)**	**0.035**
Ongoing relationship	0.96 (0.71 – 1.30)	0.807	1.12 (0.84 – 1.48	0.432
Other HIV-related behaviour characteristics				
Recent HIV test	**0.38 (0.27 – 0.54)**	**<0.001**	**1.80 (1.33 – 2.43)**	**<0.001**
PrEP use	**0.13 (0.05 – 0.35)**	**<0.001**	**2.57 (1.13 – 5.86)**	**0.024**
PEP use	**0.31 (0.10 – 0.91)**	**0.033**	**2.54 (1.23 – 5.25)**	**0.012**
Bacterial STI diagnosis	0.80 (0.57 – 1.14)	0.225	**2.12 (1.37 – 3.27)**	**0.001**
Health and lifestyle characteristics				
Recreational drug use	0.68 **(**0.37 – 1.27)	0.229	**2.02 (2.01 – 3.39)**	**0.009**
Injection drug use	0.27 (0.03 – 2.12)	0.214	**5.82 (4.48 – 7.55)**	**<0.001**
Chemsex use	0.76 (0.56 – 1.04)	0.087	**2.27 (1.60 – 3.21)**	**<0.001**
Higher risk alcohol consumption	1.01 (0.65 – 1.54)	0.999	1.04 (0.69 – 1.58)	0.839
Depressive symptoms	0.57 (0.32 – 1.02)	0.061	0.81 (0.49 – 1.34)	0.414
Anxiety symptoms	0.68 (0.32 – 1.44)	0.315	0.68 **(**0.38 – 1.24)	0.210
Calendar year	**0.78 (0.63 – 0.96)**	**0.018**	1.12 **(**0.93 – 1.34)	0.231

CI confidence interval, exp.coef exponentiated coefficients, OR odds ratio, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis, STI sexually transmitted infection

5.3.6 Cross-sectional factors associated with condomless anal sex with two or more partners

Table 5.5 presents odds ratios of condomless anal sex with two or more partners for factors (unadjusted, adjusted for age (as a continuous variable), and adjusted for age, country of birth and ethnicity, sexual identity and university education status), with their 95% CIs. Adjustment for age, country of birth and ethnicity, sexual identity and university education status produced similar results as the age-adjusted models.

In age-adjusted models, compared to those with university education, CLS with two or more partners increased among men without university education (aOR 1.46, 95% CI 1.06 – 2.20, *p*<0.021). Behavioural factors associated with reporting CLS with two or more partners in the cross-sectional analysis were similar to those explanatory factors of transition probabilities from lower-risk to higher-risk among 542 men. In particular, a recent HIV test, recreational drug use, injection drug use, chemsex use, the use of PrEP and PEP in the previous 12 months, and bacterial STI diagnosis. Calendar year as a continuous variable was also strongly associated with an increased odds of reporting CLS with two or more partners (aOR 1.08, 95% CI 1.00 – 1.16, *p*<0.040). The strongest association was found between CLS with two or more partners and injection drug use (aOR 8.08, 95% CI 3.6 – 18.11, *p*<0.001).

Table 5.5 Factors associated with reporting condomless sex with two or more partners from GEE logistic models among 542 GBMSM in the AURAH2 study*

	Unadjusted OR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value	Adjusted OR** (95% CI)	p-value
Demographic characteristics						
Age category, years	3131 obs		3131 obs		3121 obs	
<25	1 (Ref)	0·174	1 (Ref)	0·174	1 (Ref)	0·118
25-29	0·91 (0·54 – 1·53)		0·91 (0·54 – 1·53)		0·94 (0·56 – 1·59)	
30-34	1·14 (0·74 – 1·75)		1·14 (0·74 – 1·75)		1·18 (0·74 – 1·78)	
35-39	1·40 (0·88 – 2·23)		1·40 (0·88 – 2·23)		1·34 (0·84 – 2·15)	
40-44	1·68 (1·01 – 2·80)		1·68 (1·01 – 2·80)		1·60 (0·95 – 2·70)	
≥45	1·46 (0·94 – 2·20)		1·46 (0·94 – 2·20)		1·39 (0·90 – 2·16)	
Country of birth & ethnicity	3131 obs		3131 obs		3121 obs	
Born in the UK, White	1 (Ref)	0·279	1 (Ref)	0·699	1 (Ref)	0·490
Born in the UK, Other ethnicity §	1·71 (0·97 – 3·02)		1·87 (1·06 – 3·33)		1·91 (1·07 – 3·39)	
Non-UK born, White	0·98 (0·71 – 1·34)		0·99 (0·72 – 1·37)		1·01 (0·73 – 1·39)	
Non-UK born, Other ethnicity	1·12 (0·72 – 1·74)		1·17 (0·75 – 1·82)		1·28 (0·82 – 2·00)	
Sexual identity	3137 obs		3121 obs		3121 obs	
Bisexual / other	1 (Ref)	0·219	1 (Ref)	0·290	1 (Ref)	0·288
Gay	1·51 (0·78 – 2·93)		1·42 (0·74 – 2·72)		1·46 (1·06 – 2·04)	
Socio-economic characteristics and partnership status						
University education status	3131 obs		3131 obs		3121 obs	
Yes	1 (Ref)	**0·012**	1 (Ref)	**0·021**	1 (Ref)	**0·021**
No	**1.50 (1·09 – 2·06)**		**1·46 (1·06 – 2·02)**		**1·17 (0·96 – 1·43)**	
Employment status	3147 obs		3131 obs		3121 obs	
Employed	1 (Ref)	0·639	1 (Ref)	0·465	1 (Ref)	0·457
Unemployed / other	1·12 (0·63 – 1·09)		0·82 (0·49 – 1·38)		0·82 (0·49 – 1·38)	
Financial status^	3147 obs		3131 obs		3121 obs	
All of the time	1 (Ref)	0·231	1 (Ref)	0·694	1 (Ref)	0·931
Most of the time	1·39 (0·92 – 2·12)		1·47 (0·96 – 2·23)		1·38 (0·90 – 2·11)	

	Unadjusted OR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value	Adjusted OR** (95% CI)	p-value
Sometimes / No	0·79 (0·37 – 1·71)		0·72 (0·32 – 1·62)		0·68 (0·30 – 1·53)	
Housing status	3103 obs		3103 obs		3093 obs	
Homeowner	1 (Ref)	0·049	1 (Ref)	0·121	1 (Ref)	0·055
Renting	**0·70 (0·52 – 0·96)**		0·77 (0·54 – 1·10)		0·70 (0·48 – 1·01)	
Unstable / other	0·65 (0·41 – 1·02)		0·72 (0·43 – 1·19)		0·72 (0·43 – 1·18)	
Ongoing relationship	3147 obs		3131 obs		3121 obs	
Yes	1 (Ref)	0·974	1 (Ref)	0·642	1 (Ref)	0·662
No	0·99 (0·75 – 1·32)		1·07 (0·80 – 1·43)		1·07 (0·80 – 1·42)	
Other HIV-related behaviour characteristics						
Recent HIV test in the past 3 months	2984 obs		2957 obs		2947 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**1·50 (1·31-1·72)**		**1·53 (1·33 – 1·76)**		**1·54 (1·33 – 1·77)**	
PEP use in the past 12 months	902 obs		893 obs		891 obs	
No	1 (Ref)	**0.038**	1 (Ref)	**0.026**	1 (Ref)	**0.036**
Yes	**1·42 (1·02 –1·97)**		**1·47 (1·05 – 2·06)**		**1·44 (1·02 – 2·02)**	
PrEP use in the past 12 months	902 obs		893 obs		891 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**6·83 (4·69 – 9·96)**		**7·10 (4·86 – 10·38)**		**6·96 (4·73 – 10·25)**	
Health and lifestyle characteristics						
Recreational drug use in the past 3 months	926 obs		915 obs		913 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**2·17 (1·59 – 2·98)**		**2·35 (1·70 – 3·24)**		**2·39 (1·72 – 3·33)**	
Injection drug use in the past 3 months	922 obs		911 obs		909 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**8·04 (3·62 – 17·83)**		**8·08 (3·60 – 18·11)**		**7·07 (3·39 – 14·70)**	
Chemsex use in the past 3 months	3164 obs		3131 obs		3121 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**3·38 (2·69 – 4·24)**		**3·39 (2·70 – 4·26)**		**3·35 (2·67 – 4·20)**	
Bacterial STI diagnoses in the past 3 months	3153 obs		3121 obs		3111 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**	1 (Ref)	**<0.001**
Yes	**1·56 (1·33 – 1·82)**		**1·59 (1·36 – 1·87)**		**1·59 (1·35 – 1·87)**	
Higher risk alcohol consumption (modified WHO AUDIT-C ≥6)	3147 obs		3131 obs		3121 obs	
No	1 (Ref)	0·825	1 (Ref)	0·673	1 (Ref)	0·705
Yes	0·95 (0·62 – 1·46)		0·91 (0·59 – 1·40)		0·92 (0·59 – 1·41)	
Depressive symptoms (PHQ-9 score ≥10)	3147 obs		3131 obs		3121 obs	
No	1 (Ref)	0·708	1 (Ref)	0·696	1 (Ref)	0·794
Yes	1·09 (0·70 – 1·68)		1·09 (0·69 – 1·71)		1·06 (0·68 – 1·64)	
Anxiety symptoms (GAD7 score ≥10)	3147 obs		3131 obs		3121 obs	
No	1 (Ref)	0·506	1 (Ref)	0·662	1 (Ref)	0·627
Yes	0·84 (0·49 – 1·41)		0·89 (0·52 – 1·50)		0·88 (0·52 – 1·48)	
Calendar year	3164 obs **1·08 (1·01 – 1·16)**	**0·031**	3131 obs **1·08 (1·00 – 1·16)**	**0·040**	3121 obs **1·07 (1·00 – 1·15)**	**0·046**

* Ethnicity, sexual identity, education, employment, money status, and housing status are fixed variables; Age, lifestyle characteristics, and HIV-risk behaviour are time-updated variables

** Adjusted for age, country of born and ethnicity, sexuality and education level

^ Having enough money to cover basic needs e.g. for food and heating

OR odds ratio, CI confidence interval, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis, STI sexually transmitted infection, AUDIT-C alcohol use disordersiIdentification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

5.4 Discussion

5.4.1 Summary of results

Among 1,162 HIV-negative GBMSM attending sexual health clinics in England and Brighton between 2013 and 2018, there was a slight increase in the overall prevalence of reported CLS with two or more partners. Among 622 men enrolled in AURAH2 who completed at least an online questionnaire, a similar trend was also observed between 2015 and 2018, from the first online questionnaire until the last online questionnaire. Lasagna plots depicted some variation in the patterns of sexual behaviour over time within an individual, with a tendency to remain stable throughout the follow-up period. Among a subset of 542 GBMSM with at least two consecutive data during follow-up, there was general stability across risk classes; men had an overall 78% probability of reporting CLS with two or more partners in the subsequent questionnaires and 88% probability of remaining in the lower-risk behaviour in the subsequent questionnaires.

The recent calendar year, a recent HIV test, the use of PrEP, and the use of PEP were the predictive characteristics of remaining to report CLS with two or more partners in the subsequent questionnaires. In comparison, less stable housing status predicted men to transition to lower-risk behaviour. Vice versa, these factors also affected the probabilities of men switching to higher-risk behaviour from lower-risk behaviour, with additions of a bacterial STI diagnosis, the use of any recreational drugs, the use of injection drugs, and the use of chemsex. In the cross-sectional analysis among these 542 men, behavioural factors associated with reporting CLS with two or more partners were similar to those explanatory factors of transition probabilities from lower-risk to higher-risk sexual behaviour.

5.4.2 Trends of condomless sex in the UK and other high-income countries among GBMSM

The increasing trends in CLS and CLS with two or more partners among men in AURAH2, although relatively modest, are consistent with findings from other UK studies (146, 150, 152, 274) (see also Chapter 1, Section *1.3.4.2*, Table 1.1, literature review of UK studies). For example, data from ten cross-sectional studies done between 2000 and 2013 (the Gay Men's Sexual Health Survey) among 11,876 men visiting gay venues reported that the proportion of GBMSM who reported CLS in the past year increased significantly from 42% in 2000 to 51% in 2013 (152). In another study of sexual behaviour of gay men, among those who used gyms in London between 1998 and 2008, Lattimore and colleagues also observed an increase in CLS among HIV-negative men with partners of the same status, from 12% in 1998 to 21% in 2008 (150). Compared to these previous studies that were done before the

U=U era, the annual prevalence of sexual risk behaviours among men in AURAH2 was much higher (CLS >60%, CLS with two or more partners >30%). This suggests that GBMSM attending sexual health clinics may be more likely to report not using condoms compared to GBMSM attending gay venues or those selected from the general population (298-302), and this could also suggest that men are more likely to practice riskier behaviours in the recent years (**U=U** era).

Internationally, a systematic review of studies conducted in the United States, Europe, and Australia between 1990 and 2013 had found increasing sexual risk behaviours (condomless anal sex and condomless anal sex with partners of unknown or discordant HIV status) over time among GBMSM (130), and my systematic review on temporal trends in sexual behaviour (Chapter 2, Sections *2.3.3.1* until *2.3.3.6*) suggests that this has continued. That review reported a steady increase in condomless sex from the 1990s through 2013, but the meta-analysis suggested the rate of increase may have been slightly lower in 2003 and later compared to the earlier years. This could be explained by a more rapid change in condom norms after the introduction of ART with a slowing of change over time. Data from the National HIV Behavioural Surveillance, a cross-sectional survey done in 21 cities in the United States, found that among 30,547 HIV-negative GBMSM, concordant (21% to 27%) and discordant (8% to 13%) condomless anal sex increased between 2005 and 2014 (303). In the European settings, recent data from large online cross-sectional surveys for GBMSM (EMIS) among 156,018 men in 2010 and 125,837 men in 2017 also reported an increase in condomless anal sex with the last non-steady partners by 62% between 2010 and 2017 (304).

The declining trends in group sex and diagnosis of bacterial STIs in AURAH2 have been reported previously among men in AURAH2 who completed at least an online follow-up (n=622) during the online follow-up period (2015 – 2018) (305). Notably, the decline in bacterial STIs contrasted with data from the UKHSA, which showed a resurgence in STIs with a disproportionate number of new infections found within GBMSM in 2017/18 (306). In 2018, 447,694 new diagnoses of STIs were made at SHSs in England, a 5% increase since 2017. Gonorrhoea and syphilis have re-emerged as major public health concerns, especially among GBMSM. In 2018, 47% of gonorrhoea and 75% of syphilis diagnoses were in GBMSM. Since 2009, gonorrhoea and syphilis diagnoses have risen by 249% and 165%, respectively, and by 643% and 236% among GBMSM. Higher risk behavioural changes, including more condomless sex with new or casual partners, likely contribute to these trends. In the UK, the number of STI tests performed at sexual health clinics increased by 17.5% between 2013 and 2017, with the most significant increase in gay men (44%) (307). Over the past decade, the incidence of syphilis among GBMSM has also increased markedly in

other countries. For example, primary or secondary syphilis among GBMSM in the United States increased from 11.7 cases per 100,000 populations in 2014 to 18.7 per 100,000 in 2018 (308). A recent meta-analysis reported that the global pooled prevalence among GBMSM from 2000 to 2020 was 7.5% (309). Among GBMSM who are receiving PrEP against HIV infection, the incidence of syphilis was exceptionally high, possibly due to the increase in condomless sex (310).

This opposite trend in STI incidence could reflect engagement with sexual health clinics by GBMSM in the AURAH2 study, as over half that completed a final follow-up questionnaire in AURAH2 reported having had a recent (within three months) HIV test. Repeat questionnaires were used in the study, which may have intervention-like effects on participants by causing them to reflect or change their behaviour due to repeated questioning. Evidence suggests that participating in questionnaires that encourage behaviour reflection may have contributed to study participants becoming more aware of the consequences of their choices, which could have resulted in behaviour change (311), and may help to explain the decline in bacterial STI diagnoses seen in this cohort. The results could also be a 'regression to the mean', whereby as a result of recruiting GBMSM from sexual health clinics, which is presumably a time of high risk, the risk would tend to fall subsequently. This could have contributed to trends, although it is unlikely to be the only factor as some measures of sexual activity did not fall and increased over time.

In contrast to these trends in STIs, the prevalence of injection drug use remained relatively stable between 2013 – 2018 (baseline – the end of follow-up). Suppose participants became engaged with chemsex support services or became more aware of issues relating to chemsex through exposure to information in clinics. In that case, the decline in chemsex among the AURAH2 participants could be explained in part by the recruitment of participants attending sexual health clinics known for their focus on integrating substance use services with sexual health services. The 56 Dean Street and Mortimer Market Clinic, two of the clinics that took part in the AURAH2 study, are speciality chemsex support centres in London, where chemsex awareness is high and psychosocial therapies are regularly offered to high-risk GBMSM. In Brighton, the Claude Nicol clinic also offers a GBMSM-specific programme that includes one-on-one counselling and advice on chemsex and drug use. The study clinics' increased awareness and community engagement around chemsex may have resulted in a higher proportion of those engaging in chemsex choosing to attend them, which could mean there was a higher level of chemsex in the clinic populations we focused on compared with those attending other UK clinics and, secondly, may not be a true reflection of chemsex trajectories among GBMSM attending sexual health clinics without integrated

specialist services, or indeed among GBMSM engaged in chemsex who do not do at all (246).

5.4.3 Trajectories of sexual risk behaviours among GBMSM

As stated in Chapter 2 (Section *2.3.2.1*), studies among GBMSM investigating variation in trajectories used different approaches and modelling techniques. In this chapter, the lasagna plot was used to identify typical and straightforward trajectories of sexual behaviour of each individual during the follow-up period after participants completed the first online questionnaire. Lasagna plots showed that while the overall proportions of each sexual risk group were generally stable over time, individuals comprising the membership of lower-risk or higher-risk behaviour categories changed somewhat from questionnaire to questionnaire.

In the UK, according to the results of the systematic review I conducted, there were no data available in regard to individual trajectories in condomless anal sex among HIV-negative GBMSM. In the Netherlands, data from 815 HIV-negative GBMSM in the ACS between 2007 and 2017 found three typical trajectories of sexual risk behaviour during the life course of GBMSM (164). Based on a sexual behaviour risk score that was predictive of HIV seroconversion, this study used *latent class growth mixture* modelling to estimate linear trajectories of sexual risk behaviour and GBMSM group membership. The three trajectories were labelled as 'low-risk' trajectory (90% of the sample), a 'falling high-risk' trajectory (6.5%), and a 'rising high-risk' trajectory (3.3%). In Victoria, Australia, data from surveillance surveys among 4,685 HIV-negative GBMSM attending visiting general practices for sexual health screening between 2007 and 2013, The Victorian Primary Care Network for Sentinel Surveillance on Bloodborne Viruses and STIs (VPCNSS), identified four distinct classes of sexual risk, labelled as 'monogamous' (26%), 'risk-minimizer' (31%), 'risk-potential' (28.5%), and 'risk-taker' (14.5%) using a *latent class model* (169). These two studies have been detailed in Chapter 2.

In the United States, the Multicenter AIDS Cohort Study (MACS) identified three sexual risk trajectories among GBMSM: 'low-risk' (63%), 'moderate-risk' (23%), and 'high-risk' (14%) (171). MACS analysed data from 419 HIV-negative GBMSM in Baltimore, Pittsburgh, Chicago, and Los Angeles between 2003 and 2011 using *group-based trajectory modelling*. Another study among 538 GBMSM (4.1% HIV-positive) who attended public STI clinics in Rhode Island between 2012 and 2014 identified four latent classes of sexual risk behaviour using *latent class analysis* (312). In this study, individuals who belong in 'Class 1' (7.35%) had the lowest rates of STIs, tended to have been previously tested for HIV, and had fewer sex partners compared to other classes. Individuals in 'Class 2' (31.6%) had less than five anal sex partners in the past 12 months and the lowest rates of drug use during sex. 'Class

3' (12.5%) included GBMSM with the highest rate of HIV and other STIs and the largest number of men who reported drugs during sex. Individuals in 'Class 4' (48.4%) had similar characteristics as 'Class 2', but men in this class more frequently reported having 5 – 10 oral and anal sex partners than any other categories. Another study using data from a longitudinal cohort study of 804 young GBMSM and transgender women in Chicago (mean age at baseline 21 years) between 2015 and 2020 (178), indicated there was a substantial within-person variation in the trajectory of reported one time partners, with a most common number of partners during most visits was zero (72.6%). This study used a series of *random-effects models.* These studies have also been described in detail in Chapter 2.

The focus of the current analysis on trajectories of CLS with two or more partners using lasagna plots, although it has offered alternative methods in terms of ease of depiction and interpretation of trajectories, is only descriptive, and comparisons with previous studies are challenging. Previous studies have mainly examined aggregate risk scores in sexual-risk behaviour or aggregated across all partner types. However, the main findings from the AURAH2 that broadly concur with many of these studies are that, while GBMSM vary in their level of risk or contact rates over time, there remains a predominance of low-risk behaviour (in AURAH2 >60% from total online questionnaires reported lower-risk behaviour). This has been mentioned as well in Chapter 2, which found that most studies that investigated trajectories of sexual behaviour reported the predominance of low-risk behaviour. For example, Wilkinson et al. (169) found that a majority of participants were identified as 'monogamous' or 'risk minimizers', and Pines et al. (171) found a majority of participants were 'low risk' in their trajectory, despite both studies indicating changes in risk over time.

5.4.4 Transitions in sexual risk behaviours among GBMSM

The lack of transition probabilities for higher-risk and lower-risk behaviours of more than 75% among men in AURAH2 suggest stability in sexual behaviour levels from one questionnaire to the next, regardless of the initial state, as also shown in the visual plots. Findings from limited previous research characterising transitions in risk behaviour among HIV-negative GBMSM have been mixed (see Chapter 2, Section *2.3.2.2*). Using *latent transition analyses* (a type of Markov model), VPCNSS reported similar results of individual transitions between states among 516 gay men to those in AURAH2 (169). Analyses from MACS also similarly demonstrated that HIV-negative men exhibit relatively stable yet distinct patterns of sexual risk behaviour over time, with more than half of the sample cohort rarely engaged in high-risk behaviours (low-risk group:63%) over the eight-year study period (171).

To my knowledge, the only longitudinal study in Europe that has investigated transitions between HIV risk levels and determinants of behaviour change among HIV-negative

GBMSM is the ACS. Based on data from 767 participants between 2008 and 2017, the study reported overall similar results with those from my analysis (313). The majority of GBMSM showed no behaviour change; however, in this study, risk levels were classified into three (based on sexual behaviour score): low (73% of visits), medium (22%), and high risk (5%). For GBMSM at low risk, the six-month probability of increasing risk was 11%. For GBMSM at medium risk, the probability of increasing to high risk was 8%, while the probability of decreasing to low risk was 33%. For GBMSM at high risk, the probability of decreasing risk was 43%. This study used biannual visits instead of quarterly visits as in AURAH2; therefore, changes were estimated for the next six months. The slight difference observed in the probability of transition to and out from high risk level to other levels was probably due to the difference in the categorisation of risk levels. In my analyses, I classified risk levels into two, based on whether men reported CLS with two or more partners or not (in the past three months). The results from this recent paper from ACS was not included in my systematic review, as this study was only identified very recently (published at the end of 2021).

Unlike in AURAH2, the Young Men's Health Study, a study among 493 young GBMSM (mean age 22 years) in Los Angeles between 2005 and 2009, reported little stability in sex risk from one wave to the next during follow-up (173). This study applied *hidden Markov modelling* and estimated that all transition probabilities for sexual risk to stay in the same class of risk (no partners; protected anal intercourse; single seroconcordant partner unprotected anal intercourse, and multiple partners/serodiscordant partner unprotected anal intercourse) were less than 65%. Data from a two-year prospective cohort of 882 gay men in three cities in the U.S between 1992 and 1995 (CDC Collaborative Seroincidence Study; CSS, articles published in 2015) observed a high level of movement between dichotomous sexual roles (insertive/receptive, with/without condom, anal/oral, and HIV status of partners) (132, 133). Using *Markov chain models* with four states (abstinent, insertive, receptive, and versatile), the study reported highly dynamic sexual roles among gay men. A similar analysis based on the Markovian process using data collected from a Netherlands cohort also demonstrated that anal sex fluctuates across six-month observation periods (study published in 1995) among gay men (314). Likely, the differences in the estimated probabilities in these studies and AURAH2 was due to the difference in characteristics of men included in the cohort (younger men) and the use of old data in CSS and the Netherlands cohort.

5.4.5 Factors associated with or explaining the transitions in sexual behaviours among GBMSM

5.4.5.1 Recreational drug use

As in AURAH2, recreational drug use, including chemsex, has been consistently linked to CLS measures in studies of GBMSM in the other UK and high-income countries (315-319). A systematic review investigating recreational drug use in GBMSM has demonstrated that chemsex use is associated with increased risky behaviour such as CLS, group sex and an increase in STIs and poor mental health symptoms (320). Polydrug use has also been reported to be associated with condomless sex and higher partner numbers in HIV-negative and HIV-diagnosed GBMSM in the UK (155, 321).

Associations between sexual behaviour trajectories and transitions between sexual risk class and substance use are also in line with previous data from MACS, ACS, and the Young men's study (164, 172, 173). MACS identified four drug use trajectories: 'consistent users' of stimulant drugs over time (9.8%), men whose use increased over time (5.4%), men whose use declined over time (6.9%) and a group of abstinent or rarely-using men (77.9%) (172). In this cohort, individuals in the increasing group reported significantly a greater number of receptive CLS partners over time, while individuals in the decreasing group also reported a reduction in the number of receptive CLS partners over time.

5.4.5.2 Younger age

There was a lack of association between age and condomless anal sex with two or more partners among men in AURAH2. Evidence from previous studies suggests that younger men are more likely to engage in condomless anal sex, including with multiple partners and partners of an unknown or sero-different HIV status. Among men in MACS, compared to low-risk group membership, high-risk group membership was associated with younger age, being White, and depression symptoms (171). In line with this, ACS reported that the 'falling high-risk' trajectory was associated with younger age at sexual debut and fewer steady partnerships (164). VPCNSS in Australia also reported that older age was significantly associated with reduced odds of membership in the 'risk potential' class (169). Other UK cross-sectional studies also showed evidence of an association between younger age and sexual risk behaviour (156, 274, 322, 323). It is possible that in AURAH2, the age associations with higher-risk sexual behaviour were affected by other socio-demographic characteristics of men attending sexual health clinics.

5.4.5.3 Other factors

In terms of other factors, findings from the AURAH2 study are similar to other UK studies of sexual behaviour among GBMSM, in which there was some evidence to suggest that ethnicity and sexual identity were not associated with multiple CLS partners and CLS partners of an unknown/sero-different HIV status (298, 315, 322, 323).

No associations found in the transition analysis between education and sexual risk in AURAH2 align with results from other international longitudinal studies (164, 169, 171). On the contrary, other UK studies reported that lower levels of educational attainment were associated with multiple CLS partners and CLS partners of an unknown/sero-different status (315, 324) (associations were also observed in AURAH2 in the cross-sectional analysis of factors associated with CLS with two or more partners).

Results from analyses of this chapter found a protective effect of less stable housing status against CLS with two or more partners (the association was not significant in the cross-sectional analysis). This is consistent with previous findings that homeless GBMSM were less likely to engage in condomless sex and had fewer sex partners (325).

In AURAH2, the use of PrEP was also associated with staying in higher-risk behaviour. The use of PrEP might have induced risk compensation, defined as increased sexual risk behaviour, which might be leading to increased diagnosis of bacterial STIs.

5.4.6 Limitations

Because men in the AURAH2 study were recruited from three sexual health clinics in urban areas in southeast England, they may not be typical of the overall GBMSM population in England and the United Kingdom. Trends in sexual behaviour and predictors of staying in or switching to higher-risk behaviours might also differ among GBMSM who are not engaged with sexual health clinics. Additionally, the sample comprised predominantly of men who were highly educated, employed, in a stable economic situation, of White ethnicity, and with access to the internet (follow-up questionnaires were only available online, therefore, to complete the questionnaires, participants needed an internet connection), which might not allow generalisability to all GBMSM living in England.

These self-reported data may show recall bias and social desirability bias; nevertheless, the study obtained sensitive and personal data through an online follow-up questionnaire, which may have decreased desirability bias (326). The online retention of participants who initially registered in the study was not optimal, which may have caused differential bias in trends over time in sexual behaviour (detailed in Chapter 9, interpretation of the results, Section 9.2).

Lasagna plots showed that one of the AURAH2 study plots' flaws was the lack of data on sexual behaviour due to some missing data and lost to follow-up. Entire-row sorting of results efficiently displayed the total number of outcomes. However, a disadvantage of sorting is that different outcomes are stacked on top of each other, which could lead to confusion. I included only two categories of sexual behaviour as including more categories in

the plot would make interpretation increasingly challenging. To complement the plots, I included tables that show changes between time points to formalise the visual information from lasagna plots. Estimation of transitional probabilities, as well as relative effects, are also important to be included.

Regarding the 'higher-risk' behaviour definition, I limited only to CLS with two or more partners, which might not reflect the true high-risk sexual behaviour in the era of TasP and widespread use of PrEP.

Finally, while Markov modelling can effectively depict changes in categorical risk behaviours over time, it is a computationally intensive technique and can be difficult to utilise when dealing with a large number of predictors, for example, due to concerns with statistical power and coefficient interpretation. Such limitations may hinder complicated model building. For introducing covariates, only data from participants with at least two consecutive follow-up data were utilised, thus limiting the capacity to relate analysis results to more descriptive transition probabilities predicted with more complete data.

5.4.7 Conclusion

In summary, CLS and CLS with two or more partners increased slightly, while other measures of sexual behaviour (group sex and chemsex) declined over time among men in the AURAH2 study. While results showed some stability in the patterns of reporting sexual risk behaviour over time, data also revealed that a small proportion of men transitioned between different categories within a short period of time. Calendar year, recreational drugs (including injection drugs and chemsex-associated drugs), the use of PrEP and PEP and bacterial STI diagnosis were associated with condomless anal sex with two or more partners.

The lasagna plots illustrated in this chapter provide a simple way to show transitions in the status of individuals observed longitudinally, and the use of Markov modelling complements the plots to characterise and capture patterns of changes in risk behaviours over time. These analytical tools can provide valuable insights into categorical variables measured on individuals at regular intervals over time.

The implications of findings from this chapter and recommendations for future research are discussed in the final conclusion chapter of this thesis (Chapter 9).

Chapter 6: The use of HIV pre-exposure prophylaxis between 2013 and 2018 and predictors of pre-exposure prophylaxis initiation among GBMSM in the AURAH2 study

6.1 Introduction

6.1.1 Background

The PROUD study, an open-label randomized controlled trial (RCT) conducted at 13 sites in England between 2014 and 2015, reported that daily oral pre-exposure prophylaxis (PrEP) with tenofovir-emtricitabine (TDF-FTC) reduced HIV infection by 86% among gay, bisexual and other men who have sex with men (GBMSM) (40). A subsequent modelling study showed that implementing a PrEP programme for GBMSM in the UK would be cost-effective and potentially cost-saving in the long run (3). The British HIV Association (BHIVA) guidelines, published in 2018, recommend PrEP for HIV-negative GBMSM at high risk of obtaining HIV through condomless sex (111).

At the time of conducting this thesis, PrEP was only freely available to people at risk of HIV in the context of the PrEP Impact Trial by the UK Health Security Agency (UKHSA), which began in October 2017 and ran for three years through October 2020 (114). All trial participants (17,700 GBMSM participated in the trial up to February 2020) received National Health Service England (NHSE) funded PrEP (115); otherwise, people could legally purchase PrEP for their use online or from some genitourinary medicine (GUM) clinics (327). A nationally commissioned PrEP programme had been agreed for England to be operational by the end of the PrEP Impact trial (114). It was crucial for the national programme to determine who could benefit most from PrEP and how much people were already aware of it. Data on trends in PrEP awareness and uptake and predictors of PrEP initiation in England was needed to inform how to roll out PrEP and target PrEP in England during the critical time.

6.1.2 Chapter aims

The specific objectives of this chapter are:

(i) to describe trends over time in awareness of PrEP and post-exposure prophylaxis (PEP) at baseline among all GBMSM enrolled in AURAH2
(ii) to assess trends in the use of PrEP and PEP in the past 12 months over the entire study period among all GBMSM enrolled in AURAH2

(iii) to identify predictors of PrEP initiation among GBMSM in AURAH2 who reported not using PrEP at baseline

(iv) to examine factors associated with reporting the use of PrEP in the past 12 months among all GBMSM enrolled in AURAH2

6.2 Methods

6.2.1 PrEP and PEP Measures

Four PrEP and PEP measures were considered for analyses in this thesis chapter, all in the previous 12 months, definitions are shown in Table 6.1:

(i) PrEP awareness

(ii) PEP awareness

(iii) PrEP use

(iv) PEP use

Information on PrEP and PEP awareness was collected at baseline only, while Information on PrEP and PEP use was collected at the baseline and annual questionnaires. To be classified as positive for having taken PrEP/PEP in the previous 12 months, at baseline or annual questionnaire, participants were required to have answered 'yes' to the question on having ever taken PrEP/PEP, and subsequently indicated use in the past year on the question on frequency of use. Missing answers to PrEP and PEP use questions were classified as no use.

Table 6.1 PrEP and PEP measures in the AURAH2 study*

Outcomes	Baseline questionnaire	Annual questionnaire
PrEP awareness	Were you aware that you can take PrEP to try to prevent HIV infection? (Yes/No)	–
PEP awareness	Were you aware that you can take PEP to try to prevent HIV infection after sex without a condom? (Yes/No)	–
PrEP use in the past 12 months	Have you ever taken PrEP? (Yes/No)	Have you taken PrEP in the past 12 months? (Yes/No)
	If Yes, approximately for how many days did you take PrEP in the last year? • Between 1 and 4 days • Between 5 and 19 days • 20 to 50 days • More than 50 days	Approximately how much of the time were you on PrEP in the last 12 months? • Less than 3 months • 3 to 6 months • 6 to 9 months • More than 9 months

PEP use in the past 12 months	Have you ever taken PEP? (Yes/No)	Have you taken PEP in the past 12 months? (Yes/No)
	If Yes, approximately how often did you take PEP in the last year? • Never • Once • 2 to 3 times • More than 3 times	Approximately how often did you take PEP in the last year? • Once • 2 to 3 times • More than 3 times
Source of PrEP	–	Where did you access PrEP from? (clinic, the internet, research study, a friend, other)

* PrEP and PEP data not collected in the 4-monthly online questionnaire

6.2.2 Socio-demographic, health and lifestyle, and other sexual/HIV-related behaviours measures

For a detailed description of the categories and definitions of each of the socio-demographic, health and lifestyle, and sexual behaviour variables used in this chapter, please see chapter 3 (thesis methods, Sections 3.6.1 – 3.6.3).

Socio-demographic variables included age group, country of birth and ethnicity, sexual identity, university education status, ongoing relationship status, employment status, financial status, and housing status.

Five measures of sexual/HIV-related behaviour were considered for this analysis: condomless anal sex (CLS), CLS with two or more partners (CLS2+), group sex, bacterial sexually transmitted infections (STI) diagnosis, and recent HIV test.

Health and lifestyle factors included recreational drug use, depressive symptoms, anxiety symptoms, and higher alcohol consumption.

Country of birth and ethnicity, sexual identity, university education status, employment status, financial status, and housing status were fixed variables derived from the baseline questionnaire, whereas age, sexual / HIV-related behaviours, and health and lifestyle factors were time-varying variables derived from baseline and annual questionnaires. As explained in Chapter 3 (thesis methods, Sections 3.5.1 and 3.5.2), missing values for variables were treated as ‘no’, except for variables: age, country of birth and ethnicity, sexual identity, financial status, and housing status, for which missing values were excluded.

6.2.3 Statistical analysis

The prevalence of and trends in PrEP and PEP awareness and use were calculated according to calendar period, using three-month periods from the first enrolment (July 2013) to the end of the AURAH2 study period (March 2018). Information from each participant's questionnaires was ascribed to the three-month period in which the questionnaire was completed. Data for the last two quarters of 2013 (July to December 2013) were combined as one calendar period because the number of men recruited between July and September 2013 was too small to be considered a separate period. To describe trends over calendar time in the proportion of participants indicating PrEP and PEP awareness, only data from baseline questionnaire were used (see Table 6.1, questions on awareness of PrEP and PEP were only asked at baseline). A chi-squared test for linear trend in proportions was done over the period of July 2013 – April 2016 (enrolment stage).

To examine trends in past 12-month PrEP and PEP use over the entire study period (July 2013 – March 2018), univariable generalized estimating equation (GEE) models with a logit link and robust standard errors (SEs) were used, accounting for multiple questionnaire responses from individual participants, using pooled data from all available baseline and annual questionnaires. To obtain a test for linear trend, calendar year was fitted as a continuous variable. Trends over time in the proportion of questionnaires for which PrEP use was reported among men who also reported CLS2+ were also investigated, including the source of obtaining PrEP (in a six-month calendar period).

Predictors of PrEP initiation during follow-up were assessed in a longitudinal analysis among those who reported not using PrEP at baseline and had completed at least one annual questionnaire. PrEP initiation was defined as the first report of PrEP (in the past 12 months) from an annual questionnaire; time to initiation was the time from baseline to the date of completion of the questionnaire on which PrEP was first reported, or baseline to end of follow-up if PrEP was not initiated. Each factor was considered separately in age-adjusted Poisson models (using age as a continuous variable) with robust SEs. The predictors considered included factors mentioned in Section 6.2.2 reported in preceding questionnaires associated with subsequent PrEP initiation. Age-adjusted incidence rate ratios (aIRRs) and their corresponding 95% CI are presented.

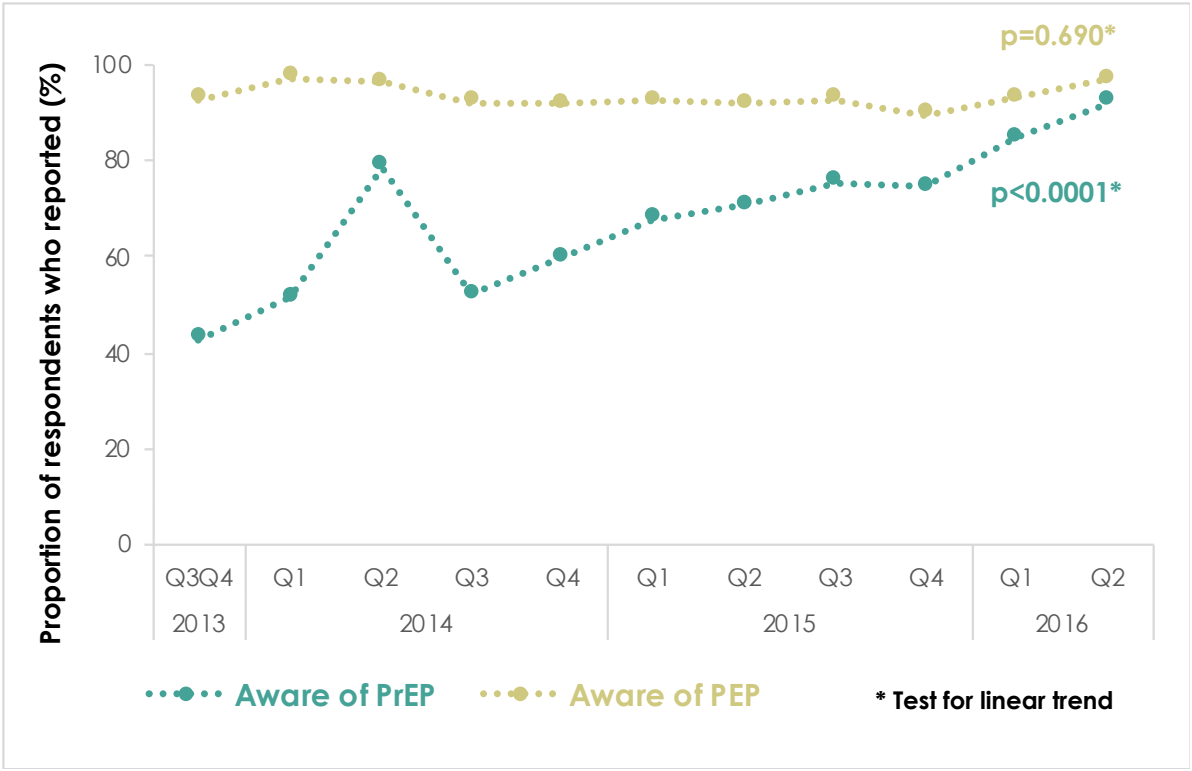
Finally, to examine the factors associated with being on PrEP in the past 12 months, generelized estimating equation (GEE) models with a logit link function, adjusted for age (as a continuous variable) were used. Age-adjusted odds ratios (aORs) and the corresponding 95% CI are presented.

6.3 Results

6.3.1 PrEP and PEP awareness over calendar time

Figure 6.1 shows PrEP and PEP awareness at enrolment by calendar period of baseline questionnaire; data from 1,161 of the 1,162 participants who completed a baseline questionnaire were used. Overall, 838 of 1,161 participants (72.2%) were aware of PrEP and 1,074 (92.5%) were aware of PEP at baseline. The proportion of men who reported PrEP awareness increased significantly over calendar time of recruitment, from 42.9% (12/28) in men recruited in July – December 2013 to 92.1% (58/63) for men recruited in April – June 2016 (*p-chi-squared test for trend*<0.001). The awareness of PEP was already high in the first period of recruitment, 92.9% (26/28) in July – December 2013, and remained so over the period given, 96.8% (61/63) in April-Jun 2016 (*p-trend*=0.690).

Figure 6.1 Prevalence of PrEP and PEP awareness over time among GBMSM in the AURAH study at enrolment, 2013 – 2016*



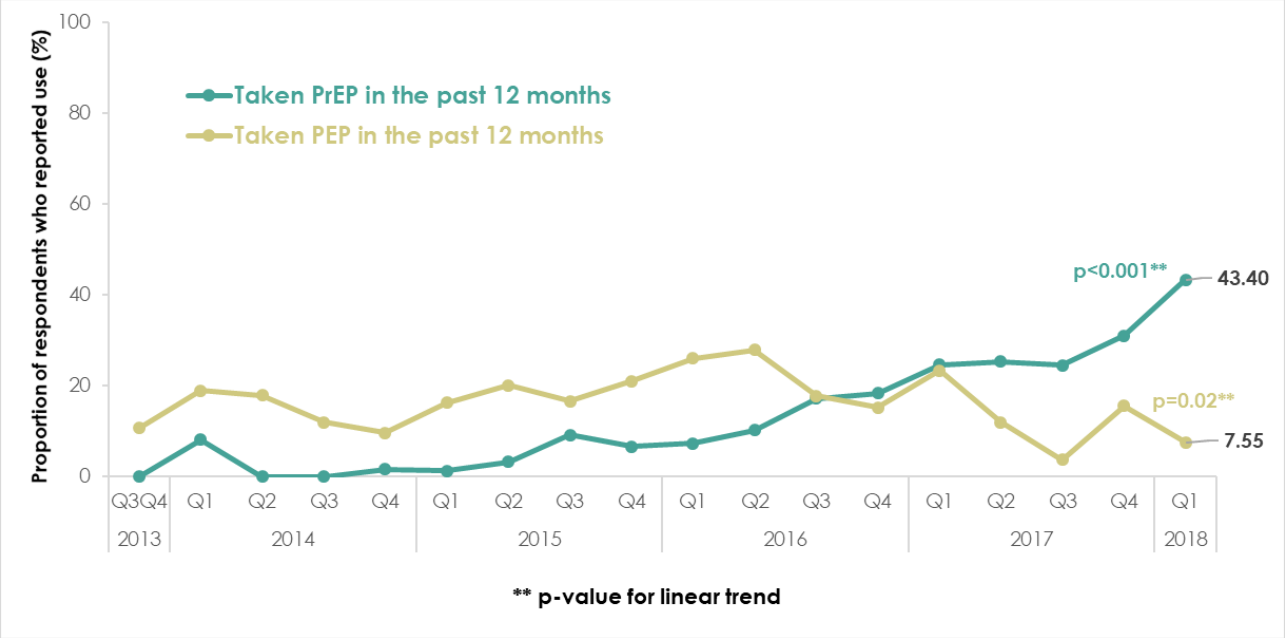
	2013	2014				2015				2016	
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Number of questionnaires	28	37	28	25	62	160	306	183	142	131	63
Aware of PrEP	12	19	22	13	37	109	216	138	106	111	58
Aware of PEP	26	36	27	23	57	149	281	170	127	122	61

*Data from baseline paper questionnaires, missing values on PrEP and PEP questions were treated as No, (N = 1161)

6.3.2 PrEP and PEP use over calendar time

Figure 6.2 shows PrEP and PEP use trends over time; data from 2,079 baseline and annual online follow-up questionnaires were used. PrEP use in the past 12 months was overall reported in 11.9% of questionnaires (248/2,079). PrEP use increased significantly from 0% in the last two quarters of 2013 to 43.4% by January – March 2018 (*p-value for linear trend from GEE-logistic model*<0.001). On the other hand, some fluctuation was seen in the trend of PEP use. The overall prevalence of PEP use was 17.8% (371/2,079). PEP use was consistently higher than PrEP use until July – September 2016; however, after reaching a peak of 27.9% in Apr-Jun 2016, the proportion reporting PEP use began to fall significantly to a low of 7.5% by January – March 2018 (*p-trend*=0.020 for the whole study period).

Figure 6.2 Prevalence of PrEP and PEP use in the past 12 months over time among GBMSM in the AURAH2 study, 2013 – 2018 *



	2013	2014				2015				2016				2017				2018
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Number of questionnaires	28	37	28	25	62	160	304	271	152	165	147	169	125	77	67	106	103	53
Taken PrEP in the past 12 months	0	3	0	0	1	2	10	25	10	12	15	29	23	19	17	26	32	23
Taken PEP in the past 12 months	3	7	5	3	6	26	61	45	32	43	41	30	19	18	8	4	16	4

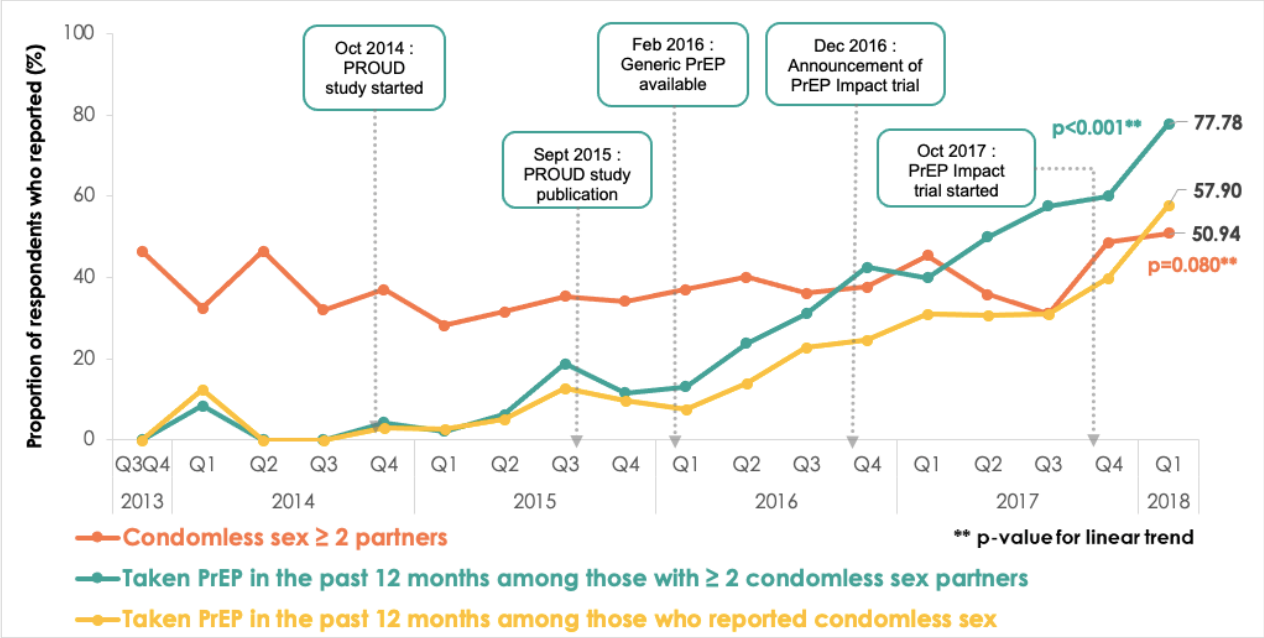
*Data from baseline and annual questionnaires, missing values on PrEP and PEP questions were treated as No (N = 1161 participants provided 2079 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment).

6.3.2.1 PrEP use among men who reported CLS with two or more partners

Figure 6.3 shows PrEP use prevalence among men who reported CLS2+ over time. From the 2,079 baseline and annual online follow-up questionnaires, 36.4% (n=755) questionnaires reported CLS2+. Of the 755 questionnaires, 25.2% (n=190 questionnaires) reported having taken PrEP. PrEP use increased dramatically among men who reported CLS2+, from 0% in July – December 2013 to 77.8% (21/27) in January – March 2018 (*p-trend*<0.001).

Data used to show the prevalence of CLS2+ shown in Figure 6.3 were from baseline and annual questionnaires (where data on PrEP were collected); therefore, there was a slight difference in the *p*-value of trend as shown in Figure 5.1 (see Chapter 5). In Chapter 5, data were analysed from all baseline, four-monthly and annual questionnaires.

Figure 6.3 Prevalence of PrEP use among men who reported condomless sex with two or more partners among GBMSM in the AURAH2 study, 2013 – 2018*



	2013	2014				2015				2016				2017				2018
	Q3Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Questionnaire reported CLS ≥2 *	13	12	13	8	23	45	96	96	52	61	59	61	47	35	24	33	50	27
Taken PrEP in the past 12 months**	0	1	0	0	1	1	6	18	6	8	14	19	20	14	12	19	30	21
Questionnaire reported CLS	18	24	16	15	32	107	178	179	103	107	101	118	85	55	49	74	78	38
Taken PrEP in the past 12 months among eligible men through CLS^	0	3	0	0	1	3	9	23	10	8	14	27	21	17	15	23	31	22

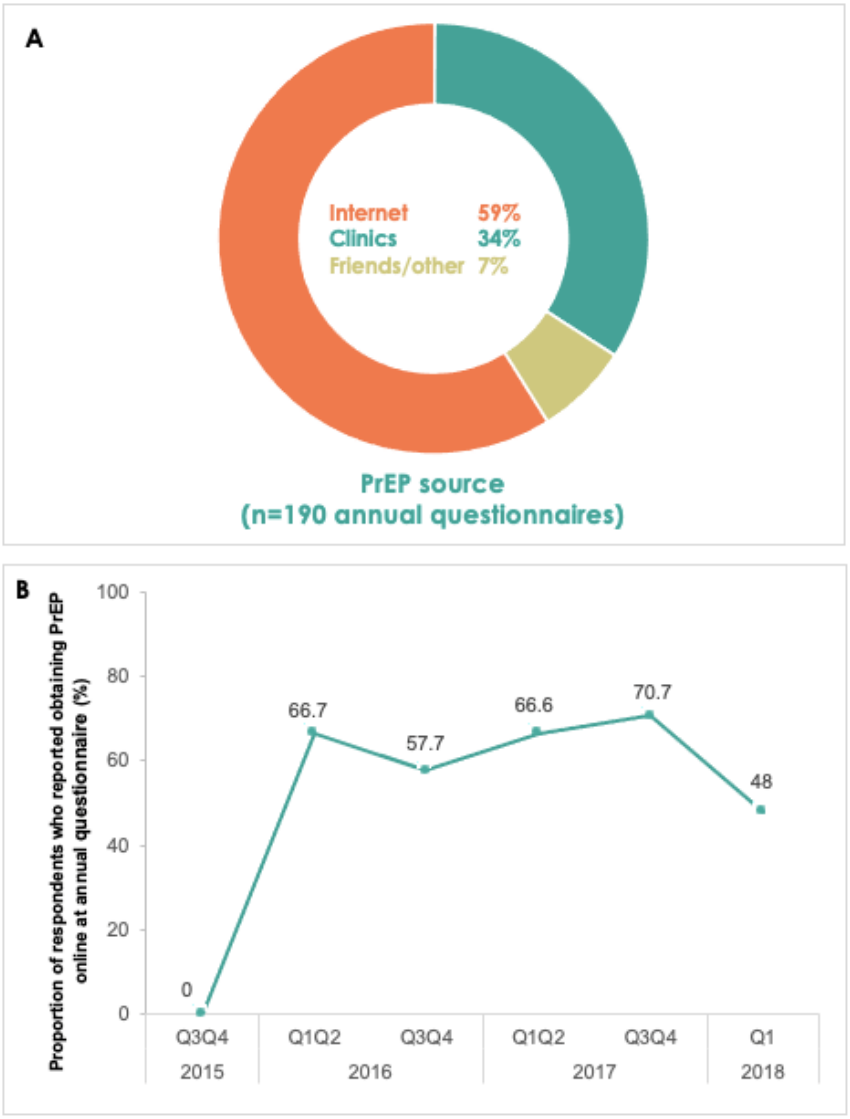
* Data from total all baseline and annual questionnaires (N = 1,161 participants provided 2079 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment)

** Data from questionnaires in which condomless sex with more than two partners was reported (n=755 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment)
^ Data from questionnaires in which condomless anal sex was reported (n=1,377 questionnaires), 227 questionnaires reported the use of PrEP

6.3.2.2 Source of PrEP

Of all available annual questionnaires that reported PrEP sources (n=190), 58.9% (112/190) indicated PrEP had been obtained from the internet, 34.2% (65/190) from clinics, and 6.8% (13/190) from friends or others (Figure 6.4A). In October 2017 – March 2018 (after the PrEP Impact Trial started), the proportion of respondents who reported sourcing PrEP from the internet was 65.5% (36/55), from a clinic was 25.5% (14/55), and from friends or other was 9.1% (5/55). Sourcing PrEP via the internet, as a percentage of all PrEP use, also increased over time. This proportion was 0% in the period of July – December 2015, after which there was a considerable increase to 66.7% (6/9) in January – June 2016, and this then remained relatively stable until December 2017: 57.7% (30/52) in July – December 2016, 66.7% (24/36) in January – June 2017, 70.7% (41/58) in July – December 2017 (the period in which the PrEP Impact Trial started), then dropped to 47.8% (11/23) in January – March 2018 (Figure 6.4B).

Figure 6.4 Source of PrEP among GBMSM in the AURAH2 study



6.3.3 Predictors of PrEP initiation

To examine factors associated with initiating PrEP, analysis was restricted to the 460 participants who reported no previous PrEP use in the baseline questionnaire and completed at least one annual follow-up questionnaire (data from 875 questionnaires).

Table 6.2 (first results column) presents age-adjusted incidence rate ratios. The PrEP initiation rate increased considerably from 2013 to 2018. Compared to calendar year of 2013–2015, aIRR was 6·69 (95%CI 3·28–13·68; *p*<0.001) for calendar year of 2016, and 21·19 (95%CI 9·48–47·35, *p*<0.001) for calendar year of 2017–2018. When considering year as a continuous variable, the age-adjusted IRR (aIRR) per calendar year was 5·91 (95%CI 3·68–9·49; *p*<0.001). Being in the older age categories of 40-44 years (unadjusted

IRR 4·25, 95%CI 1·14–15·79, *p*=0·03) and 45 years or more (unadjusted IRR 3·59, 95%CI 1·07–11·97, *p*=0·03), compared to less than 25 years were associated with a higher rate of PrEP initiation. Non-employment (aIRR 0·35, 95%CI 0·14–0·91, *p*=0·032) and unstable housing compared to being a homeowner (aIRR 0·13, 95%CI 0·02–0·95, *p*=0.044), were significantly associated with a lower rate of PrEP initiation.

Behavioural factors associated with higher rates of PrEP initiation were having had a recent HIV test (aIRR 5·17, 95%CI 1·89–14·08, *p*=0.001), reporting CLS in the previous three months (aIRR 5·01, 95%CI 2·16–11·63, *p*<0.001), CLS with two or more partners (aIRR 5·43, 95%CI 2·99–9·86, *p*<0.001), group sex (aIRR 1·69, 95%CI 1·01–2·84, *p*=0.045), the use of non-injection chemsex-related drug compared to no drug use (aIRR 2·86, 95%CI 1·67–4·91, *p*=0.002) and the use of PEP in the previous 12 months (aIRR 4·69, 95%CI 2·83–7·79, *p*<0.001).

6.3.4 Factors associated with reporting PrEP use

To assess factors associated with reporting PrEP use in the previous year, data from 2,080 questionnaires (baseline and follow-up) representing 1,162 participants were used. Results are shown in Table 6.2 (second column). The factors associated with reporting PrEP use in the previous year were similar to those associated with initiating PrEP. In particular, being older (age category of 30-34, 35-39, 40-44, and ≥45 years compared to <25 years) and later calendar year were strongly associated with higher use of PrEP, while unstable housing and poorer financial status were associated with lower use of PrEP. Behavioural factors associated with reporting the use of PrEP were having had a recent HIV test, reporting CLS, reporting CLS2+, group sex, non-injection chemsex-related drug use, and PEP use.

Country of birth and ethnicity, sexual identity, university education status, ongoing relationship status, higher alcohol use, symptoms of depression and anxiety, and bacterial STI diagnosis were not associated with the initiation of PrEP or use of PrEP (Table 6.2).

Table 6.2 Longitudinal analysis of factors associated with initiating PrEP and cross-sectional analysis of factors associated with being on PrEP in the previous 12 months among GBMSM participating in the AURAH2 study, 2013 – 2018 *

	Predictors of initiating PrEP (N=460 participants) †		**Factors associated with being on PrEP (N=1162 participants) ‡**	
	Age-adjusted IRR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value
Demographic characteristics				
Age (time-updated) per year ˜	**1·02 (1·01 – 1·04)**	**0·001**	**1·04 (1·03 – 1·05)**	**<0·001**
Age (time-updated) category ˜ <25 25-29	868 obs 1 (Ref) 1·76 (0·47 – 6·56)	**0·005**	2062 obs 1 (Ref) 1·13 (0·49 – 2·57)	**<0·001**

30-34	2·42 (0·69 – 8·45)		**2·86 (1·44 – 5·68)**	
35-39	1·93 (0·49 – 7·59)		**3·04 (1·47 – 6·29)**	
40-44	**4·25 (1·14 – 15·79)**		**3·89 (1·80 – 8·36)**	
≥45	**3·59 (1·08 – 11·97)**		**3·54 (1·77 – 7·09)**	
Country of birth & ethnicity	868 obs		2061 obs	
UK-born, White	1 (Ref)	0·421	1 (Ref)	0·520
UK-born, Other ethnicity [§]	1·52 (0·46 – 5·03)		1·74 (0·84 – 3·59)	
Non UK-born, White	1·19 (0·68 – 2·11)		1·17 (0·79 – 1·71)	
Non UK-born, Other ethnicity	1·34 (0·56 – 3·24)		1·08 (0·63 – 1·87)	
Sexual identity	868 obs		2050 obs	
Bisexual / other	1 (Ref)	0·786	1 (Ref)	0·293
Gay	1·21 (0·29 – 4·95)		1·53 (0·69 – 3·38)	
Socio-economic characteristics and partnership status				
University education status	868 obs		2062 obs	
Yes	1 (Ref)	0·240	1 (Ref)	0·626
No	0·67 (0·34 – 1·31)		0·91 (0·63 – 1·32)	
Employment status	868 obs		2062 obs	
Employed	1 (Ref)	**0·032**	1 (Ref)	0·078
Unemployed / other	**0·35 (0·14 – 0·91)**		0·58 (0·32 – 1·06)	
Financial status**	868 obs	0·542	2062 obs	**0·037**
All of the time	1 (Ref)	(*p*-trend)	1 (Ref)	(*p*-trend)
Most of the time	1·04 (0·45 – 2·37)	0·697	0·83 (0·52 – 1·32)	0·123
Sometimes / No	0·57 (0·08 – 3·86)		0·52 (0·21 – 1·31)	
Housing status	860 obs		2050 obs	
Homeowner	1 (Ref)	**0·025**	1 (Ref)	**0·031**
Renting	0·56 (0·29 – 1·07)		0·71 (0·47 – 1·06)	
Unstable / other	**0·13 (0·02 – 0·95)**		**0·36 (0·18 – 0·73)**	
Ongoing relationship	868 obs		2062 obs	
Yes	1 (Ref)	0·875	1 (Ref)	0·475
No	0·96 (0·57 – 1·61)		0·88 (0·63 – 1·24)	
Sexual / HIV-related behaviour characteristics				
Recent HIV test	868 obs		2062 obs	
No	1 (Ref)	**0·001**	1 (Ref)	**<0·001**
Yes	**5·17 (1·89-14·08)** (Yes <6 months ago)		**2·73 (1·93 – 3·87)** (Yes <3 months ago)	
CLS in the past 3 months	868 obs		2062 obs	
No	1 (Ref)	**<0·001**	1 (Ref)	**<0·001**
Yes	**5·01 (2·16 – 11·63)**		**4·57 (2·91 – 7·17)**	
CLS2+ in the past 3 months	868 obs		2062 obs	
One / none	1 (Ref)	**<0·001**	1 (Ref)	**<0·001**
2 or more	**5·43 (2·99 – 9·86)**		**5·64 (3·97 – 8·01)**	
Group sex in the past 3 months	868 obs		2062 obs	
No	1 (Ref)	**0·045**	1 (Ref)	**0·001**
Yes	**1·69 (1·01 – 2·84)**		**1·77 (1·26 – 2·47)**	
PEP use in the previous 12 months	868 obs		2062 obs	
No	1 (Ref)	**<0·001**	1 (Ref)	**0·007**
Yes	**4·69 (2·83 – 7·79)**		**1·78 (1·17 – 2·71)**	
Recreational drug use in the past 3 months	868 obs		2062 obs	
No	1 (Ref)	**0·002**	1 (Ref)	**<0·001**

Non-injection drug and non-chemsex use	0·39 (0·05 – 2·83)		0·82 (0·29 – 2·27)	
Chemsex-related drug use (non-injection)	**2·86 (1·67 – 4·91)**		**2·70 (1·91 – 3·81)**	
Injection drug use	1·00 (0·14 – 7·42)		1·76 (0·79 – 3·91)	
Bacterial STI diagnoses	868 obs		2062 obs	
No	1 (Ref)	0·808	1 (Ref)	0·726
Yes	1·07 (0·59 – 1·98)		1·07 (0·75 – 1·53)	
Health and lifestyle characteristics				
Higher risk alcohol consumption (modified WHO AUDIT-C equals ≥6)	868 obs		2062 obs	
No	1 (Ref)	0·968	1 (Ref)	0·121
Yes	1·01 (0·49 – 2·09)		0·63 (0·35 – 1·13)	
Depressive symptoms (PHQ-9 score ≥10)	868 obs		2062 obs	
No	1 (Ref)	0·76	1 (Ref)	0·109
Yes	0·87 (0·35 – 2·15)		0·62 (0·35 – 1·11)	
Anxiety symptoms (GAD7 score ≥10)	868 obs		2062 obs	
No	1 (Ref)	0·568	1 (Ref)	0·350
Yes	1·30 (0·52 – 3·24)		0·75 (0·39 – 1·41)	
Calendar year	**5·91 (3·68 – 9·49)**	**<0·001**	**2·43 (2·12 – 2·79)**	**<0·001**
Calendar year category	868 obs		2061 obs	
2013 - 2015	1 (Ref)	**<0·001**	1 (Ref)	**<0·001**
2016	**6·69 (3·28 – 13·68)**		**2·80 (2·04 – 3·84)**	
2017 - 2018	**21·19 (9·48 – 47·35)**		**7·44 (5·39 – 10·26)**	

* Ethnicity, sexual identity, education, employment, money status, and housing status are fixed variables; Age, lifestyle characteristics, and HIV-risk behaviour are time-updated variables.
** Having enough money for basic needs e.g. for food and heating
˜ IRRs and ORs for age are unadjusted, age is included as a continuous variable when adjusting for other variables.
§ Other ethnicity includes Black, Asian, Mixed, and other ethnic group.
† Total complete observations = 875 questionnaires.
‡ Total complete observations = 2080 questionnaires.

PrEP pre-exposure prophylaxis, IRR incidence rate ratio, OR odds ratio, CLS condomless anal sex, CLS2+ condomless anal sex with two or more partners, CI confidence interval, PEP post-exposure prophylaxis, STI sexually transmitted infection, AUDIT-C alcohol use disorders identification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

6.4 Discussion

6.4.1 Summary of results

The results of this chapter provided the first estimates of longitudinal trends in PrEP use and predictors of PrEP initiation using data from a prospective cohort of HIV-negative GBMSM in England. Overall, the results demonstrated that the use of PrEP increased considerably

between 2013 and 2018, especially among men who self-reported engaging in CLS with two or more partners, from 0% in 2013 to 77.8% in the first quarter of 2018. However, one in five men at high risk through condomless sex with multiple partners was still not using PrEP.

The internet was the most preferred source for obtaining PrEP; between January and March 2018, about 48% of men reporting PrEP use obtained PrEP from the internet, paid for using their own money, and online PrEP purchasing continued even after the PrEP Impact Trial started in October 2017. Men continued to purchase PrEP online likely due to the phased recruitment in the PrEP Impact Trial; many were not yet able to access PrEP. Men aged 40 – 44 years were four times more likely to start using PrEP than those younger than 25 years, and men without a job or stable housing were less likely to do so. Certain sexual behaviours within the previous three months, such as condomless sex with multiple partners, group sex, having an HIV test, and using non-injection-chemsex-related drugs, were also associated with the decision to start PrEP.

6.4.2 Trends of PrEP use in the UK and other high-income countries among GBMSM

In England, the increased level of awareness, use, and rates of initiation of PrEP in this study coincided first with the PROUD study (Nov 29, 2012, to April 30, 2014) (40), and then the initiation of the PrEP Impact implementation trial in England (114), the availability of PrEP through NHS sexual health clinics in Scotland and Wales since 2017 (328, 329), and through a pilot study in Northern Ireland (330).

The PrEP Impact trial started recruitment in 2017, and the rate of PrEP initiation among the men in AURAH2, who at least at baseline had attended these study sites, increased by more than twenty times in 2017–18 compared with before 2015. The high proportion of men accessing PrEP online despite the PrEP Impact trial opening for enrolment might have been because available places were rapidly filled, and recruitment was closed temporarily. As a result, men in need of PrEP were being turned away and had no choice but to purchase it via the internet. Substantial advocacy efforts from community-based organisations have also contributed to some men accessing PrEP online (327).

At the time of conducting analysis and publishing results from this chapter, no data had been published from longitudinal cohort studies in England to compare with, excluding those from the PROUD trial, and one study from our research group (the Attitudes to, and Understanding of Risk of Acquisition of HIV [AURAH] and AURAH2 study) that measured changes in the prevalence of sexual behaviours and PrEP use, by comparing data from the AURAH cross-sectional study with baseline data from the AURAH2 prospective cohort (155). Self-reported PrEP use was relatively low in both AURAH (3.8%) and AURAH2 (5.5%) at baseline (155) .

The increasing trend in PrEP use among men in AURAH2 between 2013 and 2018 is consistent with findings from other high-income countries conducted around the same time (see also Chapter 2, literature review, Section 2.3.5). In the Netherlands, the Amsterdam Cohort Studies (ACS) reported that PrEP use in the preceding six months increased from 2% in the second half of 2015 to 7% in the first half of 2017 (230). In Australia, the Following Lives Undergoing Change (Flux) Study (2014 – 2015) reported that the proportion of men who reported current use of PrEP increased from 0% to 18.0% at 24 months (232). In the US, data from a national probability sample of gay and bisexual men from three age cohorts reported that PrEP use increased by 90%, from 4.1% in 2016 to 7.8% in 2018 (234).

6.4.3 Factors associated with initiating or being on PrEP among GBMSM

6.4.3.1 Older age

In AURAH2, older age was an independent predictor of PrEP initiation, with the rate of initiation among men aged 40 years and older being four times higher than among those younger than 25 years. This was similar to the Amsterdam cohort that reported the median age among men initiating PrEP was 40 years (230), and an Australian cohort that found rates of PrEP initiation highest among men aged 40 years and over (232).

6.4.3.2 Socio-economic indicators

Indicators of socio-economic disadvantage: not being employed, having unstable housing status, and having less/no money for basic needs, were also found to be associated with a lower rate of initiating PrEP or being on PrEP. Previous research in the UK has shown that lower socio-economic situation (SES) is associated with poorer HIV treatment outcomes among individuals living with HIV (331).

6.4.3.3 Sexual/HIV-related behaviour

High-risk sexual behaviours such as CLS, CLS with two or more partners, group sex, and using non-injection chemsex-related drugs, were also associated with PrEP taking, indicating appropriate use of PrEP by these men. A small proportion of men (approximately 3%) reported injecting recreational drugs; PrEP use appeared lower in this group than among those using non-injection chemsex-associated drugs.

Qualitative data from the PROUD study identified that GBMSM who were already having frequent condomless sex, added PrEP as a prevention tool (332). Similar to the findings in AURAH2, a national online prospective study in Australia reported that younger age, less use of illicit party/sex drugs, lower engagement in HIV sexual risk behaviours such as group sex and any CLS were independently associated with non-uptake of PrEP (232). The study

also reported an increase in the uptake of PrEP from baseline (2014 – 2015) to 24 months of follow-up.

In AURAH2, there was no association between bacterial STI diagnoses and taking PrEP. A 2019 evidence review analysing 20 PrEP studies and trials among men who have sex with men found high incidence rates of STIs among GBMSM taking PrEP, ranging from 33.0 per 100 person-years (PYs) to 99.8 per 100 PYs (333). However, evidence as to whether PrEP use leads to higher rates of STIs remains unclear. The review generated estimates of STI incidence rates among GBMSM who engaged in high-sexual risk behaviours (the eligibility criteria to participate in PrEP studies), rather than comparing the rates among GBMSM taking PrEP versus not. A meta-analysis of 17 studies of HIV PrEP in GBMSM found that, while PrEP protected men from HIV, the proportion diagnosed with gonorrhoea, chlamydia or syphilis increased significantly in the period between starting PrEP and follow-up, with an average length of time on PrEP at follow-up of six months. The headline figures come from eight studies that recorded both STI diagnoses at both baseline and during follow-up. On average, after starting PrEP, there was an increase of 24% in diagnoses of any of these three STIs, a 39% increase in rectal STIs and a 59% increase in rectal chlamydia. All of these increases were statistically significant (310).

The PROUD study found extremely high levels of STI diagnosis but detected no difference in the occurrence of STIs between the immediate and deferred PrEP groups (40), while PrEPX Study in Australia found the incidence of STI increased during PrEP use, but that this was partly explained by increased testing frequency (334). In addition, in the PrEPX study, half of the men were not diagnosed with an STI during follow up, and STIs were highly concentrated among PrEP users experiencing repeat infections (13%), driven by number of partners and group sex (334). A few trials identified in my systematic review also reported high and stable STI incidence throughout the follow-up period of the studies; however, most studies reported no change in incidence (41, 42, 187, 207) (see Chapter 2). In a before-after cohort study of high-risk GBMSM participating in a population-based PrEP implementation project in New South Wales Australia (N=2,404 GBMSM), STI rates were high but stable among high-risk GBMSM while taking PrEP, compared with a high but increasing trend in STI positivity before commencing PrEP (335). STI positivity was 52% in the year after PrEP use with no significant trend, compared with 50% positivity in the year prior to PrEP, with an increase in quarterly STI positivity (mean RR of 1.08 per quarter, or an 8% increase per quarter $p<0.001$). Findings were similar when stratified by specific STIs and anatomical site. These findings suggest the importance of considering trends in STIs when describing how PrEP use may be associated with STI incidence (335).

6.4.3.4 Other factors

Although men with symptoms of depression were somewhat less likely to use PrEP than those without, in AURAH2, there was no evidence that anxiety was associated with reporting recent PrEP use or PrEP initiation during follow-up. In a recent Australian study, PrEP use was independently associated with lower levels of HIV anxiety among PrEP-eligible men (GBMSM at high risk of HIV infection) compared to PrEP ineligible men (GBMSM at low risk) (336).

Alongside the increase in PrEP use, there was a significant decreasing trend in PEP use between 2013 and 2018, and the use of PEP was a predictor of future PrEP initiation. This suggests that transition from PEP use to PrEP use occurred in these men. Guidelines recommend transitioning GBMSM who are at continuous risk of HIV from use of PEP towards the use of PrEP (337). Both PrEP and PEP should be a part of a combination HIV prevention strategy.

6.4.4 Limitations

Men in the AURAH2 study were recruited from three sexual health clinics which also were PROUD study sites, and they may have been better informed about PrEP than the general GBMSM population in England. Therefore, the prevalence of PrEP and PEP use in AURAH2 may overestimate the use in the GBMSM population nationwide. As noted in Chapter 5 when studying changes in sexual behaviour, recall bias and social desirability bias may be evident in this self-report data; however, sensitive and personal data were collected through an online follow-up, which may have reduced such bias (326). As with the previous results chapter, the sample characteristics of AURAH2 may not allow generalisability to all GBMSM living in England, and trends in use and predictors of PrEP initiation may also differ among GBMSM who are not engaged with sexual health clinics. No information was available on PrEP regimen, therefore, trends in the use of daily or on-demand PrEP could not be evaluated among men in AURAH2. Lastly, the online retention of participants initially registered in the study was not optimal, which may have caused differential bias in trends over time in PrEP use (detailed in Chapter 9, interpretation of the results, Section 9.2).

6.4.5 Conclusion

In summary, the results from this chapter demonstrated that PrEP use increased substantially among GBMSM attending sexual health clinics in urban areas in south-east England between 2013 and 2018, with a high proportion of PrEP being obtained via purchasing online. In 2018, PrEP use was almost 80% among men with multiple condomless sex partners. Data suggest that older men, those of higher socio-economic status, and those

engaging in sexual behaviour related to HIV risk, are more likely to start using PrEP and being on PrEP.

The implications of findings from this chapter and recommendations for future research are discussed in the final conclusion chapter of this thesis (Chapter 9).

Chapter 7: Trends in HIV incidence between 2013 – 2019 and factors associated with subsequent incident HIV among GBMSM in the AURAH2 study

7.1 Introduction

7.1.1 Background

To bring the HIV epidemic under control, there has been a massive scale-up in the treatment and prevention of HIV over the past decade that has led to a gradual decline in new HIV infections globally (49). In the United Kingdom (UK), modelling of HIV surveillance data suggests that the underlying incidence of new HIV infections has been falling steadily for more than five years (since 2012) (100). The decline has been particularly marked among gay, bisexual and other men who have sex with men (GBMSM), among whom 51% of all new HIV diagnoses occurred in the UK in 2018 (6) (see also Chapter 1, Section *1.3.3.1*).

In England, the modelled number of incident infections among GBMSM has declined by 65% since 2014, with the most rapid fall after 2016 (6). The steep declines coincided with a period when increasing numbers of men accessed pre-exposure prophylaxis (PrEP) (338), as also shown in the results in my previous chapter (Chapter 6, Section 6.3.2). In addition, during this period, there were efforts to increase uptake and frequency of HIV testing, and HIV treatment guidelines changed to recommend prompt initiation of antiretroviral therapy (ART) for people newly diagnosed with HIV. Declines in HIV incidence among GBMSM have also been reported in Melbourne in Australia between 2013 and 2017 (339), Amsterdam in the Netherlands between 2009 and 2017 (220), and San Francisco and New York City in the United States (US) (340, 341). There remains, however, limited data from UK prospective studies assessing HIV acquisition risk, associated factors, and temporal trends for incident HIV (224, 342). Such data could help provide insight regarding the risk factors driving the HIV epidemic among GBMSM in England.

7.1.2 Chapter aims

The specific objectives of this chapter are:

(i) to assess trends over calendar time in HIV incidence between 2013 and 2019 among all GBMSM enrolled in AURAH2
(ii) to identify baseline factors associated with subsequent HIV incidence among all men enrolled in AURAH2
(iii) to identify time-updated factors associated with subsequent HIV incidence among men who completed at least one online follow-up questionnaire

7.2 Methods

7.2.1 Ascertainment of incident HIV

There were two methods of ascertainment of incident HIV diagnosis during follow-up:

(i) First, records of all GBMSM enrolled in the AURAH2 study were linked to national HIV surveillance data by the UK Health Security Agency (UKHSA) (247, 248). The databases collect information on new HIV diagnoses from laboratories, genito-urinary medicine (GUM) clinics, general practitioners (GPs), and other services where HIV testing takes place in England. The data matching process was completed in November 2019. For each study participant that matched to the HIV surveillance dataset, UKHSA data were provided on date and region of HIV diagnosis, CD4 and viral load at HIV diagnosis, and if relevant, time from diagnosis to linkage to care, time from diagnosis to treatment initiation, and death. The details of the data matching process have been described in Chapter 3 (Section 3.4).

(ii) The second method of ascertainment of new HIV diagnoses was through the online follow-up questionnaires; participants were asked about the date and results of the most recent HIV test. All the participants who reported being newly diagnosed with HIV in a follow-up questionnaire were also identified as having a new HIV diagnosis in the UKHSA surveillance databases. Linkage with the UKHSA databases also identified a small number of participants who were HIV-positive at the entry to the study (n=3); these men were excluded from the analysis.

7.2.2 Socio-demographic, health and lifestyle, and other sexual/HIV-related behaviours measures

For a detailed description of the categories and definitions of each of the socio-demographic, health and lifestyle, and sexual behaviour variables used in this chapter, please see chapter 3 (thesis methods, Sections 3.6.1 – 3.6.3).

Socio-demographic variables included age group, country of birth and ethnicity, sexual identity, university education status, ongoing relationship status, employment status, financial status, and housing status. These variables were fixed variables derived from the baseline questionnaire.

Measures of sexual/HIV-related behaviour considered for this analysis were:

- for analysis of baseline factors: condomless anal sex (CLS), number of CLS partners, CLS with partners known to be HIV positive, sexual CLS role, group sex, sex for

drugs or money, fisting or sex toys use, recent HIV test, bacterial STI diagnosis, number of new sexual partners, PrEP use, and PEP use

- for analysis of time-updated factors: recent HIV test, CLS, CLS with two or more partners, sexual CLS role, group sex, bacterial STI diagnosis, PrEP use, and PEP use

Health and lifestyle factors were:

- for analysis of baseline factors: recreational drug use, smoking status, depressive symptoms, anxiety symptoms, and higher alcohol consumption.
- for analysis of time-updated factors: chemsex (a different variable from recreational drug use variable at baseline questionnaire), injection drug use, depressive symptoms, anxiety symptoms, and higher alcohol consumption.

As explained in Chapter 3 (thesis methods, Sections 3.5.1 and 3.5.2), missing values for variables were treated as 'no', except for variables: age, country of birth and ethnicity, sexual identity, financial status, and housing status, for which men with missing values were excluded from the analysis.

7.2.3 Statistical analysis

For the analyses of HIV incidence and baseline associated factors, all men enrolled in AURAH2 were included. Incident HIV infection was defined as seroconversion from HIV-negative status at baseline to HIV-positive during follow-up, confirmed by the UKHSA. Person-years (PYs) of follow-up were calculated from the date of completing the baseline questionnaire until:

(i) the date of HIV diagnosis from the UKHSA for men who seroconverted
(ii) three months before the date of data linkage with the UKHSA datasets was completed (June 30, 2019) for men who did not seroconvert

Due to the linkage with the UKHSA data for ascertainment of the endpoint, all men could be considered as remaining under follow-up over the entire period, even if follow-up questionnaires were not completed.

HIV incidence rates (IRs) were calculated as the number of new HIV infections divided by the number of PYs of follow-up, reported with 95% confidence intervals (95% CI). IRs were calculated per 100 PYs, overall and according to calendar year from 2013 until 2019. As the study started on July 30, 2013, and ended on June 30, 2019, the first two years (2013-2014) and the last two years (2018-2019) were combined.

The associations of baseline factors and current calendar year as a continuous variable with HIV incidence were analysed by calculating HIV IRs and using Cox proportional hazards

models to estimate crude hazard ratios (HR) and adjusted HRs for age at baseline, country of birth and ethnicity, sexual identity, and education, and corresponding 95% CI. Adjustment variables were determined a priori and were socio-demographic characteristics that were considered not to be influenced by HIV incidence and sexual behaviour but could have an impact on HIV incidence. To account for clustering within AURAH2 sites, factors were also analysed using two-level random-intercept proportional hazard models (343) with sexual health clinic sites defining the second level, to estimate conditional hazard ratios. The conditional distribution of the response given the random effects was assumed to be a Weibull distribution. The use of hierarchical models was chosen to take into account clustering according to clinics. Hazard ratios (HRs) with 95% CI are presented unadjusted and adjusted for socio-demographic factors that were not influenced by HIV incidence and sexual behaviour: age at baseline, country of birth and ethnicity, sexual identity, and education.

I also performed an additional longitudinal analysis among men who completed at least one online follow-up questionnaire to examine time-updated factors associated with HIV incidence. I used Poisson regression models, unadjusted and adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and education, using all available baseline and follow-up questionnaires. To account for clustering within AURAH2 sites, factors were also analysed using two-level random-intercept Poisson regression models, unadjusted and adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and education, using all available baseline and follow-up questionnaires. I present these results as incidence rate ratios (IRRs) with their corresponding 95% CI.

In the multivariable analyses, the whole statistical unit for a single individual with missing values was excluded from the analyses if a value for one of the covariates was missing (complete case analysis). There was very minimal missing data in the AURAH2 study's questionnaires (see Chapter 3, Sections 3.5.1 and 3.5.2), and initial analyses that were undertaken to investigate whether excluding missing values (when defining each variable) impacted findings, demonstrated that this was not the case.

7.3 Results

7.3.1 Trends in HIV incidence

All 1,162 men enrolled in AURAH2 were included in the UKHSA linkage to ascertain new HIV diagnoses. In total, 33 of 1,162 men (2.8%) were newly diagnosed with HIV during the period from the date of completion of their baseline questionnaire until June 2019. Of all 33 diagnoses identified by the UKHSA linkage, 15 were self-reported by the participant on one of the AURAH2 online follow-up questionnaires. There were no additional unconfirmed self-reported HIV diagnoses. The three men who did not complete a baseline questionnaire (see Chapter 4, Section 4.3) were included in the incidence analysis as data on their age, HIV status, and person-years of follow-up time were available from the UKHSA. There were no deaths recorded among the 33 men diagnosed with HIV.

With 4,618.9 PYs of follow-up time, the overall HIV incidence rate in AURAH2 was 0.71 (95% CI 0.51 – 1.00) per 100 PYs (Figure 7.1 and Table 7.1). Between 2013 and 2019, HIV incidence declined progressively, from 1.47 (95% CI 0.48 – 4.57) per 100 PYs in 2013/2014 to 0.25 (95% CI 0.08 – 0.78) per 100 PYs in 2018/2019. The incidence fell on average by 0.86-fold per year (p<0.001, modelled using Cox proportional hazard). The median (interquartile range; IQR) age at the time of new HIV diagnosis among the 33 men was 35 years (26 – 40).

Figure 7.1 HIV Incidence among GBMSM in the AURAH2 study, 2013 – 2019

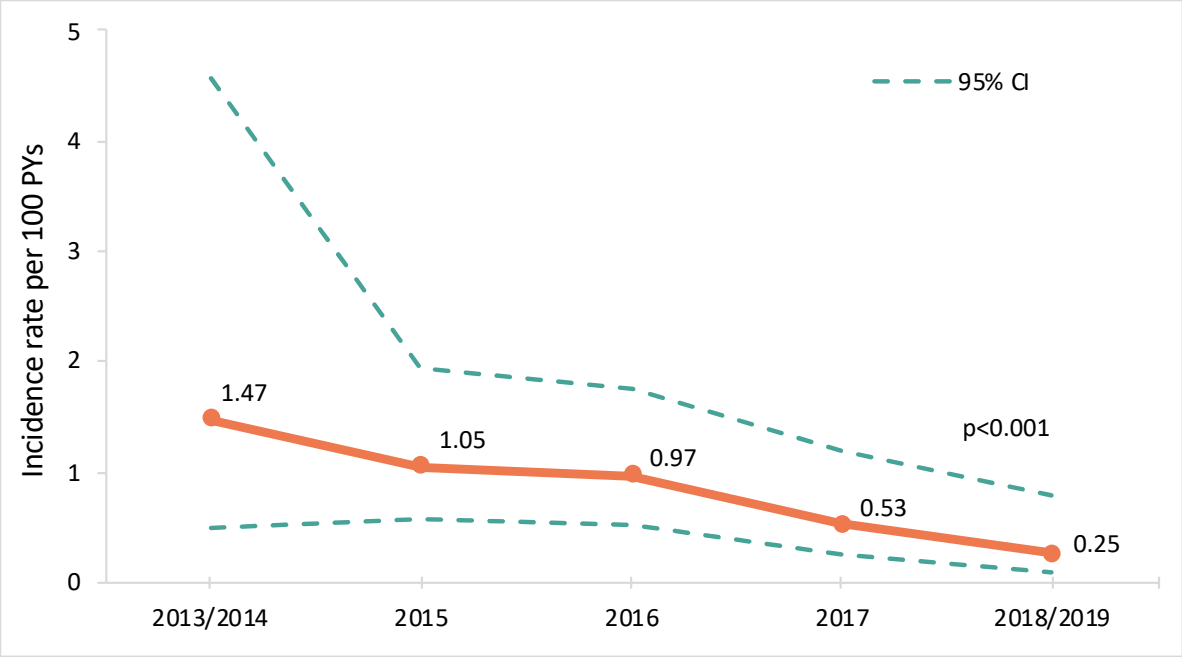


Table 7.1 HIV Incidence among GBMSM in the AURAH2 study, 2013–2019

Calendar year	PYs	No. of HIV Infections	Incidence rate per 100 PYs (95% CI)
2013/2014	203.55	3	1.47 (0.48 – 4.57)
2015	953.53	10	1.05 (0.56 – 1.95)
2016	1139.29	11	0.97 (0.53 – 1.74)
2017	1134.80	6	0.53 (0.24 – 1.18)
2018/2019	1187.69	3	0.25 (0.08 – 0.78)
Overall	**4618·86**	**33**	**0.71 (0.51 – 1.00)**

PYs person-years, CI confidence interval

7.3.2 Associations of baseline factors with subsequent incident HIV among all men in the AURAH2 study

Table 7.2 presents the association of baseline factors with incident HIV diagnosis. Adjustment for age at baseline, country of birth and ethnicity, sexual identity, and education did not materially change the associations between incident HIV and baseline factors.

In univariable Cox proportional hazard models, the strongest predictor for HIV acquisition was reporting injection drug use in the past three months, with an almost 28-fold higher rate compared to men who did not report recreational drug use (HR 27.59, 95% CI 6.89 – 110.41, *global p*<0.001). The HIV incidence rate among injection drug users was 4·74 (95%CI 2·13–10·54) per 100 PY. Having used at least one non-injection chemsex-related drug was also strongly associated with HIV acquisition (HR 6.41, 95% CI 1.83 – 22.52, compared to no drug use); the association with non-chemsex-related drugs was weaker (HR 3.74, 95% CI 0.99 – 14.11).

Other sexual/HIV-related behaviour risk factors were strongly associated with increased risk of HIV infection: CLS (HR 3·75, 95%CI 1·31–10·74, *p*=0·014); greater number of CLS partners, with increased risk for those having at least two partners (HR for 2 – 4 partners 4·06, 95%CI 1·29 – 12·77; HR for 5 – 10 partners 9.53, 95%CI 2·56 – 35·55, HR for more than 10 partners 14.15, 95%CI 4·14 – 48·34, compared with no CLS, *global p*<0.001); group sex (HR 8·80, 95%CI 3·07–25·22, *p*<0.001), and sex for drugs or money (HR 3·29, 95%CI 1·15 – 9·44, p=0.027) in the past three months; reporting a bacterial STI diagnosis in the past 12 months (HR 3·92, 95%CI 1·79–8·56, *p*=0.001), reporting more than 10 new sexual partners in the past 12 months (HR for 11 – 49 new partners 3·17, 95%CI 1·39 – 7·25, HR for 50 – 99 new partners 4.38, 95%CI 1·35 – 14·24, HR for 100 or more new partners 4.91, 95%CI 1·06 – 22·72, compared to 0 – 10 new partners, *global p*=0.009) and having used PEP in the past 12 months (HR 2·28, 95%CI 1·08–4·79, *p*=0.030).

For socio-economic and demographic characteristics, lower level of education was associated with increased risk of HIV infection (HR for no qualification 4·96, 95%CI 1·14–21·49 compared to a university degree, global *p*=0·011). There was some evidence that employed men were at greater risk of infection than non-employed (HR for non-employment 0·16, 95%CI 0·02 – 1·19, *p*=0.075).

There were no significant associations of age group, housing status, financial status, relationship status, HIV test in the past six months, fisting or sex toy use in the past three months, PrEP use in the past 12 months, smoking status, higher alcohol consumption, depressive symptoms, and anxiety symptoms at baseline with risk of HIV infection (Table 7.2).

Table 7.2 Baseline characteristics and associations with incident HIV among 1162 GBMSM in the AURAH2 prospective study, 2013 – 2019*

Baseline characteristics	Participants N (%)	HIV infections n (%)	PYs at risk	HIV incidence rate per 100 PYs (95% CI)	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio** (95% CI)	p-value
Demographic characteristics								
Age at baseline category, years							1140 observations	
<25	275 (23.9)	8 (2.9)	1087·61	0·74 (0·37 – 1·47)	1 (Ref)	0·421	1 (Ref)	0.270
25-29	207 (17.9)	3 (1.5)	839·50	0·36 (0·11 – 1·10)	0·49 (0·13 – 1·87)	0·417[t]	0.63 (0.16 – 2.47)	
30-34	227 (19.7)	5 (2.2)	896·65	0·56 (0·23 – 1·34)	0.76 (0·25 – 2·32)		0.55 (0.14 – 2.13)	
35-39	156 (13.5)	8 (5.1)	605·63	1·32 (0·66 – 2·64)	1.79 (0·67 – 4·77)		2.03 (0.73 – 5.67)	
40-44	121 (10.5)	4 (3.3)	480·92	0·83 (0·31 – 2·22)	1.14 (0·34 – 3·78)		1.40 (0.41 – 4.81)	
≥45	167 (14.5)	5 (2.9)	674·09	0·74 (0·31 – 1·78)	1.03 (0·34 – 3·14)		1.23 (0.39 – 3.88)	
Mean age (SD)	**34 (10.4)**							
Median age (IQR)	**31 (26 – 39)**							
Country of birth and ethnicity§							1140 observations	
Born in the UK, White	568 (49.4)	10 (1.8)	2296·31	0·44 (0·23 – 0·81)	1 (Ref)	0·179	1 (Ref)	0.150
Born on the UK, Other ethnicity	60 (5.2)	1 (1.7)	242·16	0·41 (0·06 – 2·93)	0·94 (0·12 – 7·37)		0.95 (0.12 – 7.48)	
Non-UK born, White	374 (32.5)	17 (4.5)	1463·62	1·16 (0·23 – 1·34)	2.63 (1·20 – 5·75)		2.67 (1.22 – 5.84)	
Non-UK born, Other ethnicity	148 (12.9)	2 (1.4)	581·72	0·34 (0·66 – 2·64)	0.77 (0·17 – 3·52)		0.80 (0.17 – 3.71)	
Sexual Identity							1140 observations	
Gay	1076 (93.6)	26 (2.4)	4291·83	0·61 (0·41 – 0·89)	1 (Ref)	0·128	1 (Ref)	0.146
Bisexual / other	74 (6.4)	4 (5.4)	291·26	1·37 (0·52 – 3·66)	2·26 (0·79 – 6·49)		2.19 (0.76 – 6.31)	
Socio-economic characteristics and partnership status								
University education status							1140 observations	
Yes	853 (74.4)	17 (1.9)	3413·05	0·49 (0·31 – 0·80)	1 (Ref)	**0·011**	1 (Ref)	**0.011**
Other qualification	272 (23.8)	11 (4.4)	1108·62	1·02 (0·56 – 1·84)	2·06 (0·97– 4·39)	**0·013[t]**	2.10 (0.98 – 4.51)	
No qualification	21 (1.8)	2 (9.5)	75·83	2·64 (0·66 – 10·55)	**4·96 (1·14– 21·49)**		**4.76 (1.08 – 20.88)**	
Employment status†							1138 observations	
Employed	952 (82.9)	29 (3.1)	3767·14	0·77 (0·53 – 1·10)	1 (Ref)	0·075	1 (Ref)	0.073
Unemployed / other	197 (17.1)	1 (0.5)	812·17	0·12 (0·01 – 0·87)	0·16 (0·02 – 1·19)		0.16 (0.02 – 1.18)	
Financial status^							1140 observations	
All of the time	896 (77.4)	24 (2.7)	3581·41	0·67 (0·45 – 1·00)	1 (Ref)	0·627	1 (Ref)	0.472
Most of the time	194 (16.8)	5 (2.6)	768·90	0·65 (0·27 – 1·56)	0·97 (0·37 – 2·53)	0·613[t]	0.89 (0.33 – 2.36)	
Sometimes / No	68 (5.9)	1 (1.5)	264·84	0·38 (0·05 – 2·68)	0.55 (0·07 – 4·09)		0.46 (0.06 – 3.48)	
Housing status ₴							1136 observations	
Renting	680 (59.3)	13 (1.9)	2707·24	0·48 (0·28 – 8·27)	1 (Ref)	0·342	1 (Ref)	0.197

Baseline characteristics	Participants N (%)	HIV infections n (%)	PYs at risk	HIV incidence rate per 100 PYs (95% CI)	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio** (95% CI)	p-value
Homeowner	314 (27.4)	14 (4.5)	1252·75	1·11 (0·66 – 1·89)	2·34 (1·10 – 4·99)	0·330[t]	3.71 (1.52 – 9.08)	
Unstable or other	153 (13.3)	3 (1.9)	611·33	0·49 (0·16 – 1·52)	1.02 (0·29 – 3·57)		1.15 (0.32 – 4.11)	
Ongoing relationship							1140 observations	
Yes, living with partner	272 (23.5)	11 (4.0)	1080·22	1·01 (0·56 – 1·84)	1 (Ref)	0·471	1 (Ref)	
Yes, not living with partner	193 (16.7)	3 (1.6)	783·15	0·38 (0·12 – 1·19)	0·38 (0·10 – 1·35)	0·191[t]	0.42 (0.12 – 1.52)	0.211
No	693 (59.8)	16 (2.3)	2755·05	0·58 (0·36 – 0·95)	0·57 (0·26 – 1·22)		0.58 (0.26 – 1.26)	
Sexual / HIV-related behaviour characteristics								
HIV test in the past 6 months							1140 observations	
No	322 (27.8)	6 (1.9)	1324·99	0·45 (0·20 – 1·01)	1 (Ref)	0·325	1 (Ref)	0.353
Yes	837 (72.2)	24 (2.9)	3293·42	0·73 (0·49 – 1·09)	1·57 (0·64 – 3·83)		1.53 (0.62 – 3.77)	
CLS in the past 3 months‡							1140 observations	
No	418 (36.1)	4 (0.9)	1704·76	0·23 (0·09 – 0·63)	1 (Ref)	**0·014**	1 (Ref)	**0.016**
Yes	741 (63.9)	26 (3.5)	2913·66	0·89 (0·61 – 1·31)	**3·75 (1·31 – 10·74)**		**3.66 (1.27 – 10.52)**	
Number of CLS partners in the past 3 months‡							1140 observations	
No CLS partners	424 (36.6)	4 (0.9)	1727·09	0·23 (0·09 – 0·62)	1 (Ref)	**<0·001**	1 (Ref)	**<0.001**
One CLS partner	325 (28.0)	3 (0.9)	1306·35	0·23 (0·07 – 0·71)	0·98 (0·22 – 4·39)	**<0·001[t]**	0.99 (0.22 – 4.47)	
2 – 4 partners	293 (25.3)	11 (3.8)	1163·99	0·95 (0·52 – 1·71)	**4·06 (1·29 – 12·77)**		**3.83 (1.21 – 12.03)**	
5 – 10 partners	60 (5.2)	5 (8.3)	212·67	2·36 (0·98 – 5·64)	**9.53 (2·56 – 35·55)**		**9.82 (2.58 – 37.35)**	
More than 10 partner	57 (4.9)	7 (12.3)	208·30	3·36 (1·60 – 7·05)	**14.15 (4·14 – 48·34)**		**13.97 (4.06 – 48.01)**	
CLS with partners known to be HIV positive in the past 3 months‡							1140 observations	
No	1012 (87.3)	16 (1.6)	4086·01	0·39 (0·24 – 0·64)	1 (Ref)	**<0·001**	1 (Ref)	**<0.001**
Yes	147 (12.7)	14 (9.5)	532·41	2·63 (1·56 – 4·44)	**6·39 (3·12 – 13·11)**		**6.56 (3.13 – 13.71)**	
Number of new sexual partners in the past 12 months~							1140 observations	
0 – 10 new partners	688 (59.4)	9 (1.3)	2772·34	0·32 (0·17 – 0·62)	1 (Ref)	**0·009**	1 (Ref)	**0.001**
11 – 49 new partners	367 (31.6)	15 (4.1)	1446·30	1·04 (0·63 – 1·72)	**3·17 (1·39 – 7·25)**	**0·001[t]**	**3.38 (1.47 – 7.80)**	
50 – 99 new partners	72 (6.2)	4 (5.6)	272·66	1·47 (0·55 – 3·91)	**4.38 (1·35 – 14·24)**		**4.37 (1.33 – 14.29)**	
100 or more new partners	32 (2.8)	2 (6.3)	127·12	1·57 (0·39 – 6·29)	**4.91 (1·06 – 22·72)**		**4.63 (0.99 – 21.58)**	
Group sex in the past 3 months							1140 observations	
No	659 (56.9)	4 (0.6)	2670·75	0·15 (0·06 – 0·39)	1 (Ref)	**<0·001**	1 (Ref)	**<0.001**
Yes	500 (43.1)	64 (12.8)	1947·67	1·33 (0·91 – 1·96)	**8·80 (3·07 – 25·22)**		**8.91 (3.10 – 25.56)**	
Fisting or sex toys use in the past 3 months							1140 observations	

Baseline characteristics	Participants N (%)	HIV infections n (%)	PYs at risk	HIV incidence rate per 100 PYs (95% CI)	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio** (95% CI)	p-value
No	745 (64.3)	16 (2.2)	2982·81	0·54 (0·33 – 0·88)	1 (Ref)	0·202	1 (Ref)	0.180
Yes	414 (35.7)	14 (3.4)	1635·61	0·86 (0·51 – 1·45)	1·60 (0·78 – 3·27)		1.63 (0.79 – 3.36)	
Sex for drugs or money in the past 3 months							1140 observations	
No	1104 (95.2)	26 (2.4)	4418·16	0·59 (0·40 – 0·86)	1 (Ref)	**0·027**	1 (Ref)	0.060
Yes	55 (4.8)	4 (7.3)	200·26	1·99 (0·75 – 5·32)	**3·29 (1·15 – 9·44)**		2.83 (0.96 – 8.44)	
PEP use in the past 12 months	919 (79.3)						1140 observations	
No	240 (20.7)	19 (2.1)	3709·52	0·51 (0·33 – 0·80)	1 (Ref)	**0·030**	1 (Ref)	0.060
Yes		11 (4.6)	908·89	1·21 (0·67 – 2·18)	**2·28 (1·08 – 4·79)**		2.06 (0.97 – 4.35)	
PrEP use in the past 12 months	1101 (95)						1140 observations	
No	58 (5.0)	27 (2.7)	4408·52	0·61 (0·42 – 0·89)	1 (Ref)	0·202	1 (Ref)	0.276
Yes		3 (5.2)	209·49	1·43 (0·46 – 4·44)	2·18 (0·66 – 7·17)		1.95 (0.59 – 6.49)	
Bacterial STI diagnoses in the past 12 months							1140 observations	
No	719 (62.0)	9 (1.3)	2936·07	0·31 (0·16 – 0·59)	1 (Ref)	**0·001**	1 (Ref)	**0.001**
Yes	440 (38.0)	21 (4.8)	1682·35	1·25 (0·81 – 1·91)	**3·92 (1·79 – 8·56)**		**3.99 (1.81 – 8.79)**	
Health and lifestyle characteristics								
Recreational drug use in the past 3 months							1140 observations	
No	464 (40.0)	3 (0.7)	1895·32	0·16 (0·05 – 0·49)	1 (Ref)	**<0·001**	1 (Ref)	**<0.001**
Non-injection drug and non-chemsex use	336 (29.0)	8 (2.4)	1350·96	0·59 (0·29 – 1·18)	3·74 (0·99 – 14·11)	**<0·001[t]**	**3.92 (1.04 – 14.86)**	
Chemsex-related drug use (no-injection)	321 (27.7)	13 (4.1)	1254·47	0·97 (0·61 – 1·79)	**6.41 (1·83 – 22·52)**		**6.78 (1.91 – 24.13)**	
Injection drug use	38 (3.3)	6 (15.8)	126·67	4·74 (2·13 – 10·54)	**27.59 (6·89 – 110·41)**		**29.41 (7.29 – 118.69)**	
Smoking status							1138 observations	
Never smoked	612 (53.1)	14 (2.3)	2452·23	0·57 (0·34 – 0·96)	1 (Ref)	0·735	1 (Ref)	0.416
Ex-smoker	290 (25.2)	8 (2.8)	1163·82	0·69 (0·34 – 1·37)	1·21 (0·51 – 2·87)		1.18 (0.49 – 2.86)	
Regular smoker	250 (21.7)	8 (3.2)	977·79	0·82 (0·41 – 1·64)	1·41 (0·59 – 3·36)		1.43 (0.59 – 3.44)	
Higher risk alcohol consumption (modified WHO AUDIT-C score of ≥6)							1140 observations	
No	935 (80.1)	25 (2.7)	3721·68	0·67 (0·45 – 0·99)	1 (Ref)	0·714	1 (Ref)	0.837
Yes	224 (19.3)	5 (2.2)	896·74	0·56 (0·23 – 1·34)	0·84 (0·32 – 2·18)		0.90 (0.34 – 2.38)	
Depressive symptoms (PHQ-9 score ≥10)							1140 observations	
No	1018 (87.8)	26 (2.6)	4064·75	0·64 (0·43 – 0·93)	1 (Ref)	0·844	1 (Ref)	0.962

Baseline characteristics	Participants N (%)	HIV infections n (%)	PYs at risk	HIV incidence rate per 100 PYs (95% CI)	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio** (95% CI)	p-value
Yes	141 (12.2)	4 (2.8)	553·67	0·72 (0·27 – 1·92)	1·11 (0·39 – 3·18)		0.97 (0.33 – 2.83)	
Anxiety symptoms (GAD7 score ≥10) No Yes	1033 (89.1) 126 (10.9)	28 (2.7) 2 (1.6)	4118·39 500·03	0·68 (0·47 – 0·98) 0·39 (0·10 – 1·59)	1 (Ref) 0·58 (0·14 – 2·43)	0·456	1140 observations 1 (Ref) 0.53 (0.12 – 2.22)	0.383
Year of enrolment							1140 observations	
2013	28 (2.4)	2 (7.1)	149.98	1.33 (0.33 – 5.33)	1 (Ref)	0.446	1 (Ref)	0.997
2014	152 (13.1)	3 (1.9)	735.62	0.4 (0.13 – 1.26)	0.27 (0.05 – 1.62)		0.31 (0.05 – 1.91)	
2015	788 (67.8)	21 (2.7)	3115.90	0.67 (0.44 – 1.03)	0.37 (0.09 – 1.58)		0.37 (0.08 – 1.63)	
2016	194 (16.7)	7 (3.6)	617.36	1.13 (0.54 – 2.38)	0.57 (0.12 – 2.76)		0.54 (0.10 – 2.78)	

* All measures were self-reported, missing data or missing questionnaire for (in the unadjusted analysis):
Age: 9 (all HIV negative); Country of birth and ethnicity, Sexuality: 12 (9 HIV negative, 3 HIV positive); University education: 16 (13 HIV negative, 3 HIV positive); Relationship status, Money status: 4 (1 HIV negative, 3 HIV positive); Employment: 13 (10 HIV negative, 3 HIV positive); Housing status: 15 (12 HIV negative, 3 HIV positive); Smoking status: 10 (7 HIV negative, 3 HIV positive);
HIV test, CLS, Number of CLS partners, New sexual partners, Group sex, Fisting or sex toys use, PEP use, PrEP use, Recreational drug use, STI diagnoses, Alcohol consumption, Depressive symptoms, and Anxiety symptoms: 3 (all HIV positive).
** adjusted for age at baseline, country of birth and ethnicity, sexual identity, and university education
[t] p-value for trend.
§ Other ethnicity includes Black, Asian, Mixed, and other ethnic group.
ê Renting housing includes private renting and renting from council or housing association; unstable or other housing includes temporary accommodation, staying with friends or family, other accommodation, and homeless.
^ Having enough money to cover basic needs e.g. for food and heating.
† Employed group includes full-time (n=845) and part-time (n=107) employment / self-employment; No group includes unemployed registered or not registered for benefits (n=60), sick or disabled (n=6), retired (n=24), and other (student or training or looking after home or dependents or other) (n=107).
‡ Condomless anal sex with men only
~ New partners include men and women

PYs person-years, SD standard deviation, IQR interquartile range, CLS condomless anal sex, STI sexually transmitted infections, PrEP pre-exposure prophylaxis, PEP post-exposure prophylaxis, CI confidence interval, PEP post-exposure prophylaxis, STI sexually transmitted infection, AUDIT-C alcohol use disorders identification test-consumption, PHQ-9 patient health questionnaire-9, GAD-7 generalised anxiety disorder assessment-7

To account for clustering within sites, baseline factors were also analysed using mixed-effects Weibull proportional hazard models. Results were similar with those of using Cox proportional hazard models (Table 7.3), the factor most strongly associated with HIV acquisition was reporting injection drug use in the past three months (HR 27·96, 95%CI 6·99–111·85, *global p*<0.001). Other sexual/HIV related behaviour factors (CLS, greater number of CLS partners, CLS with HIV-positive partners, versatile CLS role, group sex, and sex for drugs money, bacterial STI diagnoses, more than ten new sexual partners, and having used PEP were also associated with increased risk of HIV infection. When modelled using the mixed-effects Weibull proportional hazard models, the incidence declined on average by 0.85-fold per year from 2013 – 2019.

Table 7.3 Mixed-effect Weibull proportional hazard models for associations of baseline characteristics with incident HIV among 1162 GBMSM participating in the AURAH2 prospective study, 2013 – 2019*

Baseline characteristics	Unadjusted Conditional Hazard Ratio (95% CI)	p-value	Adjusted Conditional Hazard ratio** (95% CI)	p-value
Demographic characteristics				
Age at baseline category			1140 observations	
<25	1 (Ref)	0·421	1 (Ref)	0.272
25-29	0·49 (0·13 – 1·85)	0·417[t]	0.63 (0.16 – 2.45)	
30-34	0.76 (0·25 – 2·32)		0.55 (0.14 – 2.13)	
35-39	1.79 (0·67 – 4·76)		2.02 (0.72 – 5.63)	
40-44	1.13 (0·34 – 3·77)		1.40 (0.41 – 4.81)	
≥45	1.02 (0·33 – 3·12)		1.22 (0.39 – 3.86)	
Country of birth and ethnicity§			1140 observations	
Yes, White	1 (Ref)	0·176	1 (Ref)	0.145
Yes, Other ethnicity	0·94 (0·12 – 7·38)		0.95 (0.12 – 7.49)	
No, White	2.63 (1·21 – 5·76)		2.68 (1.22 – 5.86)	
No, Other ethnicity	0.78 (0·17 – 3·54)		0.81 (0.17 – 3.74)	
Sexual identity			1140 observations	
Gay	1 (Ref)	0·128	1 (Ref)	0.148
Bisexual / other	2·26 (0·79 – 6·49)		2.18 (0.76 – 6.29)	
Socio-economic characteristics and partnership status				
University education			1140 observations	
Yes	1 (Ref)	**0·014**	1 (Ref)	**0.011**
Other qualification	2·01 (0·94– 4·28)	**0·013[t]**	2.10 (0.98 – 4.50)	
No	**4·65 (1·07– 20·14)**		**4.84 (1.10 – 21.24)**	
Employment status†			1138 observations	
Employed	1 (Ref)	0·074	1 (Ref)	0.072
Unemployed / other	0·16 (0·02 – 1·19)		0.16 (0.02 – 1.18)	
Financial status^			1140 observations	
All of the time	1 (Ref)	0·627	1 (Ref)	0.469
Most of the time	0·97 (0·37 – 2·54)	0·613[t]	0.89 (0.33 – 2.36)	
Sometimes / No	0.55 (0·07 – 4·09)		0.46 (0.06 – 3.46)	
Housing status‡			1136 observations	
Home owner	1 (Ref)	0·342	1 (Ref)	0.194
Renting	2·34 (1·10 – 4·97)	0·330[t]	3.72 (1.52 – 9.09)	
Unstable / other	1.02 (0·29 – 3·58)		1.15 (0.32 – 4.13)	
Ongoing relationship			1140 observations	

Yes, living with partner Yes, not living partner No	1 (Ref) 0·38 (0·10 – 1·35) 0·57 (0·26 – 1·22)	0·200 0·191[t]	1 (Ref) 0.42 (0.12 – 1.53) 0.58 (0.26 – 1.26)	0.215
Sexual / HIV-related behaviour characteristics				
HIV test in the past 6 months No Yes	 1 (Ref) 1·57 (0·64 – 3·85)	 0·325	1140 observations 1 (Ref) 1.53 (0.62 – 3.78)	 0.350
CLS in the past 3 months‡ No Yes	 1 (Ref) **3·75 (1·31 – 10·74)**	 **0·014**	1140 observations 1 (Ref) **3.65 (1.27 – 10.51)**	 **0.016**
Number of CLS partners in the past 3 months‡ No CLS partners One CLS partner 2 – 4 partners 5 – 10 partners More than 10 partner	 1 (Ref) 0·98 (0·22 – 4·40) **4·05 (1·29 – 12·72)** **9.60 (2·58 – 35·76)** **14.04 (4·11 – 47·98)**	 **<0·001** **<0·001[t]**	1140 observations 1 (Ref) 0.99 (0.22 – 4.48) **3.81 (1.21 – 11.99)** **9.83 (2.59 – 37.39)** **13.81 (4.02 – 47.47)**	 **<0.001**
CLS with partners known to be HIV positive in the past 3 months‡ No Yes	 1 (Ref) **6·45 (3·15 – 13·22)**	 **<0·001**	1140 observations 1 (Ref) **6.60 (3.15 – 13.80)**	 **<0.001**
Sexual role CLS in the past three months‡ No CLS / didn't state which partner Always insertive Always receptive sometimes insertive, sometimes receptive	 1 (Ref) 0.98 (0.18 – 5.35) 2.06 (0.46 – 9.19) **6.35 (2.18 – 18.51)**	 **<0.001**	1140 observations 1 (Ref) 0.93 (0.17 – 5.10) 2.06 (0.45 – 9.36) **6.33 (2.16 – 18.54)**	 **<0.001**
Number of new sexual partners in the past 12 months~ 0 – 10 new partners 11 – 49 new partners 50 – 99 new partners 100 or more new partners	 1 (Ref) **3·17 (1·39 – 7·26)** **4.40 (1·35 – 14·29)** **4.84 (1·05 – 22·41)**	 **0·001** **0·001[t]**	1140 observations 1 (Ref) **3.39 (1.47 – 7.83)** **4.42 (1.34 – 14.48)** **4.55 (0.98 – 21.23)**	 **0.001**
Group sex in the past 3 months No Yes	 1 (Ref) **8·81 (3·07 – 25·24)**	 **<0·001**	1140 observations 1 (Ref) **8.89 (3.10 – 25.50)**	 **<0.001**
Fisting or sex toys use in the past 3 months No Yes	 1 (Ref) 1·59 (0·77 – 3·25)	 0·202	1140 observations 1 (Ref) 1.63 (0.79 – 3.34)	 0.185
Sex for drugs or money in the past 3 months No Yes	 1 (Ref) **3·27 (1·14 – 9·38)**	 **0·027**	1140 observations 1 (Ref) 2.81 (0.94 – 8.34)	 0.063
PEP use in the past 12 months No Yes	 1 (Ref) **2·29 (1·09 – 4·81)**	 **0·029**	1140 observations 1 (Ref) 2.07 (0.98 – 4.37)	 0.058
PrEP use in the past 12 months No Yes	 1 (Ref) 2·21 (0·67 – 7·30)	 0·190	1140 observations 1 (Ref) 2.00 (0.60 – 6.64)	 0.259
Bacterial STI diagnoses in the past 12 months			1140 observations	

No Yes	1 (Ref) **3·95 (1·81 – 8·63)**	**0·001**	1 (Ref) **4.02 (1.82 – 8.87)**	**0.001**
Health and lifestyle characteristics				
Smoking status Never smoked Ex-smoker Regular smoker	 1 (Ref) 1·20 (0·50 – 2·87) 1.41 (0·59 – 3·37)	 0·735	1138 observations 1 (Ref) 1.18 (0.49 – 2.85) 1.44 (0.60 – 3.46)	 0.409
Recreational drug use in the past 3 months No Non-injection drug and non-chemsex use Chemsex-related drug use (no-injection) Injection drug use	 1 (Ref) 3·73 (0·99 – 14·05) **6.45 (1·84 – 22·64)** **27.96 (6·99 – 111·85)**	 **<0·001** **<0·001[t]**	1140 observations 1 (Ref) **3.92 (1.04 – 14.86)** **6.83 (1.92 – 24.29)** **29.77 (7.38 – 120.02)**	 **<0.001**
Higher risk alcohol consumption (modified WHO AUDIT-C score of ≥6) No Yes	 1 (Ref) 0·83 (0·32 – 2·17)	 0·714	1140 observations 1 (Ref) 0.90 (0.34 – 2.38)	 0.837
Depressive symptoms (PHQ-9 score ≥10) No Yes	 1 (Ref) 1·12 (0·39 – 3·20)	 0·844	1140 observations 1 (Ref) 0.98 (0.34 – 2.85)	 0.971
Anxiety symptoms (GAD7 score ≥10) No Yes	 1 (Ref) 0·58 (0·14 – 2·45)	 0·462	1140 observations 1 (Ref) 0.53 (0.12 – 2.25)	 0.389
Year of enrolment 2013 2014 2015 2016	 1 (Ref) 0.29 (0.05 – 1.94) 0.43 (0.09 – 1.93) 0.67 (0.11 – 4.09)	 0.430	1140 observations 1 (Ref) 0.33 (0.05 – 2.03) 0.43 (0.10 – 1.88) 0.60 (0.12 – 3.06)	 0.913

*All measures were self-reported, missing data or missing questionnaire for (in the unadjusted analysis):
Age: 9 (all HIV negative); Country of birth and ethnicity, Sexuality: 12 (9 HIV negative, 3 HIV positive); University education: 16 (13 HIV negative, 3 HIV positive); Relationship status, Money status: 4 (1 HIV negative, 3 HIV positive); Employment: 13 (10 HIV negative, 3 HIV positive); Housing status: 15 (12 HIV negative, 3 HIV positive); Smoking status: 10 (7 HIV negative, 3 HIV positive);
HIV test, CLS, Number of CLS partners, New sexual partners, Sexual CLS role, Group sex, Fisting or sex toys use, PEP use, PrEP use, Recreational drug use, STI diagnoses, Alcohol consumption, Depressive symptoms, and Anxiety symptoms: 3 (all HIV positive).
** adjusted for age at baseline, country of birth and ethnicity, sexual identity, and university education
[t] p-value for trend.
§ Other ethnicity includes Black, Asian, Mixed, and other ethnic group.
ê Renting housing includes private renting and renting from council or housing association; unstable or other housing includes temporary accommodation, staying with friends or family, other accommodation, and homeless.
^ Having enough money to cover basic needs e.g. for food and heating
† Employed group includes full-time (n=845) and part-time (n=107) employment / self-employment; No employment group includes unemployed registered or not registered for benefits (n=60), sick or disabled (n=6), retired (n=24), and other (student or training or looking after home or dependents or other) (n=107).
‡ Condomless anal sex with men only
~ New partners include men and women

PY person-years; CLS condomless anal sex; STI sexually transmitted infections, PE: post-exposure prophylaxis PrEP pre-exposure prophylaxis; AUDIT-C alcohol use disorders identification test-consumption; PHQ-9: patient health questionnaire - 9; GAD–7: generalised anxiety disorder-7

7.3.3 Association of time-updated factors with subsequent incident HIV among men who completed at least one online follow-up questionnaire

Among the 622 men who completed an online follow-up questionnaire, 19 were diagnosed with HIV during the period from the date of completion of their baseline questionnaire until 30 June 2019. With a total of 2,495 PYs of follow-up time, the overall HIV incidence rate among the online cohort was 0.76 (95% CI 0.49 – 1.19) per 100 PYs, similar to the overall incidence rate among all men enrolled AURAH2 (0.71 per 100 PYs, 95% CI 0.51 – 1.00).

Table 7.4 shows unadjusted and adjusted IRRs from Poisson models for factors associated with HIV incidence among these men. In this analysis, age, partnership status, sexual/HIV related behaviours, PrEP and PEP use, and health and lifestyle variables were time-updated; whereas ethnicity and country of birth, education, employment, sexual identity, financial status, and housing status were fixed variables that were only asked at baseline questionnaires. Predictors for HIV incidence among these men were quite similar to those among the 1,162 men, in particular, injection drug use (unadjusted IRR 21.67, 95% CI 4.15 – 113.09, p<0.001), chemsex use, CLS with two or more partners, group sex (all in the previous three months), bacterial STI diagnosis (in the previous 12 months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires), and calendar year.

Table 7.4 Association of time-updated factors with subsequent incident HIV among 622 GBMSM who completed at least one online follow-up questionnaire, 2013 – 2018*

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted€ IRR (95% CI)	p-value
Demographic characteristics				
Age (time-updated) per year	3785 obs 1.01 (0.96 – 1.05)	0.839	3770 obs 1.02 (0.97 – 1.07)	0.412
Age (time-updated) category <25 25-29 30-34 35-39 40-44 ≥45	3785 obs 1 (Ref) 0.22 (0.02 – 1.93) 0.41 (0.07 – 2.23) 0.72 (0.16 – 3.23) 0.35 (0.04 – 3.14) 0.86 (0.23 – 3.20)	0.675	3770 obs 1 (Ref) 0.65 (0.21 – 1.92) 0.61 (0.22 – 1.97) 1.05 (0.22 – 4.99) 0.45 (0.05 – 4.41) 1.30 (0.29 – 5.79)	0.412
Country of birth and ethnicity Yes, White Yes, Other ethnicity No, White No, Other ethnicity	3782 obs 1 (Ref) 1.64 (0.21 – 13.18) 0.97 (0.28 – 3.30) 0.74 (0.09 – 6.02)	0.953	3770 obs 1 (Ref) 1.77 (0.21 – 14.68) 1.01 (0.29 – 3.45) 0.79 (0.09 – 7.09)	0.906
Sexual identity Gay Bisexual / other	3793 obs 1 (Ref) 1.63 (0.21 – 12.50)	0.638	3770 obs 1 (Ref) 1.82 (0.19 – 17.44)	0.603
Socio-economic characteristics and partnership status				
University education Yes	3805 obs 1 (Ref)	0.923	3770 obs 1 (Ref)	0.931

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted[€] IRR (95% CI)	p-value
No	0.94 (0.29 – 3.06)		0.95 (0.29 – 3.04)	
Employment status	3772 obs		3760 obs	
Employed	1 (Ref)	0.305	1 (Ref)	0.299
Unemployed / other	0.34 (0.05 – 2.64)		0.29 (0.03 – 3.02)	
Financial status^	3805 obs		3770 obs	
All of the time	1 (Ref)	<0.001	1 (Ref)	0.805
Most of the time	1.29 (0.29 – 5.83)		1.43 (0.30 – 7.06)	
Sometimes / No	**0.10 (0.05 – 0.18)**		0.12 (0.05 – 0.25)	
Housing status	3750 obs		3738 obs	
Home owner	1 (Ref)	0.611	1 (Ref)	0.724
Renting	0.56 (0.17 – 1.85)		0.66 (0.13 – 3.32)	
Unstable / other	0.97 (0.19 – 4.81)		1.13 (0.21 – 6.04)	
Ongoing relationship **	1536 obs		1522 obs	
Yes	1 (Ref)	0.402	1 (Ref)	0.424
No	0.63 (0.21 – 1.87)		0.64 (0.22 – 1.88)	
Sexual / HIV-related behaviour characteristics				
Recent HIV test[†]	3699 obs		3651 obs	
No	1 (Ref)	0.340	1 (Ref)	0.317
Yes	1.87 (0.51 – 6.80)		1.90 (0.54 – 6.69)	
CLS in the past 3 months	3821 obs		3770 obs	
No	1 (Ref)	0.871	1 (Ref)	0.189
Yes	1.09 (0.38 – 3.14)		2.71 (0.61 – 11.96)	
CLS2+ in the past 3 months	3819 obs		3770 obs	
One / none	1 (Ref)	**<0.001**	1 (Ref)	**0.004**
2 or more	**6.19 (1.73 – 22.15)**		**9.39 (2.04 – 43.35)**	
Group sex in the past 3 months	3819 obs		3770 obs	
No	1 (Ref)	**0.042**	1 (Ref)	**0.032**
Yes	**2.98 (1.03 – 8.60)**		**3.51 (1.12 – 11.01)**	
PEP use in the past 12 months**	1530 obs		1512 obs	
No	1 (Ref)	0.971	1 (Ref)	0.885
Yes	1.04 (0.12 – 8.84)		1.16 (0.14 – 9.41)	
PrEP use in the past 12 months**	1532 obs		1512 obs	
No	1 (Ref)	0.995	1 (Ref)	0.997
Yes	0.96 (0.12 – 7.72)		0.99 (0.13 – 7.51)	
Chemsex use in the past 3 months	3819 obs		3770 obs	
No	1 (Ref)	**0.012**	1 (Ref)	**0.005**
Yes	**3.90 (1.35 – 11.21)**		**4.81 (1.60 – 14.47)**	
Injection drug use in the past 3 months**	1536 obs		1518 obs	
No	1 (Ref)	**<0.001**	1 (Ref)	**0.001**
Yes	**21.67 (4.15 – 113.09)**		**18.96 (3.56 – 100.80)**	
Bacterial STI diagnoses[‡]	3819 obs		3770 obs	
No	1 (Ref)	**0.005**	1 (Ref)	**0.002**
Yes	**4.46 (1.57 – 12.68)**		**5.93 (1.89 – 18.58)**	
Health and lifestyle characteristics				
Recreational drug use in the past 3 months**	1536 obs		1518 obs	
No	1 (Ref)	0.152	1 (Ref)	0.095
Yes	4.80 (0.56 – 41.11)		5.84 (0.73 – 46.38)	
Higher risk alcohol consumption (modified WHO AUDIT-C equals ≥6)**	1536 obs		1521 obs	
No	1 (Ref)	0.258	1 (Ref)	0.357

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted€ IRR (95% CI)	p-value
Yes	2.10 (0.58 – 7.60)		1.91 (0.48 – 7.52)	
Depressive symptoms (PHQ-9 score ≥10)**	1536 obs		1521 obs	
No	1 (Ref)	0.818	1 (Ref)	0.696
Yes	1.28 (0.15 – 10.64)		1.53 (0.17 – 13.31)	
Anxiety symptoms (GAD7 score ≥10)**	1537 obs		1526 obs	
No	1 (Ref)	0.559	1 (Ref)	0.684
Yes	1.88 (0.23 – 15.58)		2.06 (0.23 – 18.30)	
Calendar year as a continuous variable	3821 obs **0.52 (0.35 – 0.77)**	**0.001**	3769 obs **0.47 (0.28 – 0.78)**	**0.004**
Calendar year category	3821 obs		3769 obs	
2013 – 2014	1 (Ref)	**0.040**	1 (Ref)	**0.026**
2015	0.26 (0.07 – 1.05)		**0.17 (0.03 – 0.89)**	
2016	0.35 (0.10 – 1.19)		0.20 (0.03 – 1.06)	
2017 – 2018	**0.06 (0.01 – 0.54)**		**0.05 (0.00 – 0.47)**	

* total complete observations: 3,821 questionnaires; sexual/HIV related behaviour data was based on the last time man asked; number of new sexual partners, fisting or sex toys, sex for drugs or money, and smoking status were not included in the analysis because they were only asked at the baseline questionnaire

** data were not collected at the four-monthly questionnaire (only baseline and annual questionnaires)

† in the past six months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires

‡ in the past 12 months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires

^ Having enough money to cover basic needs e.g. for food and heating

€ adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and university education

CI, confidence interval; CLS, condomless anal sex; GAD-7, generalised anxiety disorder-7;; IRR, incidence rate ratio; PEP, postexposure prophylaxis; PHQ-9, patient health questionnaire-9; PrEP, preexposure prophylaxis; STI, sexually transmitted infection; AUDIT-C, alcohol use disorders identification test-consumption.

When factors were analysed using mixed-effect models, results remained the same, in particular, injection drug use (unadjusted IRR 21·67, 95% CI 3·96 – 118·30, p<0.001), chemsex (3.89, 95% CI 1.35 – 11.22, p=0.012), CLS with two or more partners, versatile CLS role, group sex (all in the previous three months), bacterial STI diagnosis (in the previous 12 months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires), and calendar year were all the predictors (Table 7.5).

Table 7.5 Mixed-effect Poisson models for association of time-updated factors with subsequent incident HIV among 622 GBMSM who completed at least one online follow-up questionnaire, 2013 – 2018*

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted€ IRR (95% CI)	p-value
Demographic characteristics				
Age (time-updated) per year	3785 obs 1.00 (0.96 – 1.05)	0.843	3770 obs 1.02 (0.97 – 1.06)	0.400
Age (time-updated) category <25 25-29 30-34 35-39 40-44 ≥45	3785 obs 1 (Ref) 0.22 (0.02 – 1.93) 0.41 (0.07 – 2.23) 0.72 (0.16 – 3.23) 0.35 (0.04 – 3.14) 0.86 (0.23 – 3.21)	0.676	3770 obs 1 (Ref) 0.65 (0.21 – 1.92) 0.61 (0.22 – 1.97) 0.99 (0.19 – 5.17) 0.49 (0.05 – 4.92) 1.21 (0.28 – 5.21)	0.325
Country of birth and ethnicity Born in the UK, White Born in the UK, Other ethnicity Non-UK born, White Non-UK born, Other ethnicity	3782 obs 1 (Ref) 1.63 (0.20 – 13.29) 0.97 (0.28 – 3.31) 0.74 (0.09 – 6.03)	0.953	3770 obs 1 (Ref) 1.77 (0.21 – 15.04) 1.00 (0.29 – 3.46) 0.79 (0.09 – 6.54)	0.905
Sexual identity Gay Bisexual / other	3793 obs 1 (Ref) 1.63 (0.21 – 12.54)	0.639	3770 obs 1 (Ref) 1.82 (0.23 – 14.34)	0.569
Socio-economic characteristics and partnership status				
University education Yes No	3805 obs 1 (Ref) 0.94 (0.29 – 3.06)	0.923	3770 obs 1 (Ref) 0.95 (0.29 – 3.09)	0.932
Employment status Employed Unemployed / other	3772 obs 1 (Ref) 0.34 (0.04 – 2.64)	0.305	3760 obs 1 (Ref) 0.29 (0.03 – 2.32)	0.243
Financial status^ All of the time Most of the time Sometimes / No	3805 obs 1 (Ref) 1.29 (0.29 – 5.83) 0.10 (0.05 – 0.18)	0.744	3770 obs 1 (Ref) 1.43 (0.30 – 7.06) 0.12 (0.05 – 0.25)	0.829
Housing status Home owner Renting Unstable / other	3750 obs 1 (Ref) 0.56 (0.17 – 1.85) 0.97 (0.19 – 4.82)	0.611	3738 obs 1 (Ref) 0.66 (0.16 – 2.71) 1.12 (0.18 – 6.81)	0.701
Ongoing relationship ** Yes No	1536 obs 1 (Ref) 0.63 (0.36 – 1.08)	0.094	1522 obs 1 (Ref) 0.65 (0.36 – 1.17)	0.148
Sexual / HIV-related behaviour characteristics				
Recent HIV test† No Yes	3699 obs 1 (Ref) 1.87 (0.51 – 6.80)	0.340	3651 obs 1 (Ref) 1.90 (0.52 – 6.92)	0.329
CLS in the past 3 months No Yes	3821 obs 1 (Ref) 1.09 (0.38 – 3.14)	0.871	3770 obs 1 (Ref) 2.71 (0.60 – 12.23)	0.196
CLS with two or more partners One / none 2 or more	3819 obs 1 (Ref) **6.19 (1.72 – 22.17)**	**0.005**	3770 obs 1 (Ref) **9.39 (2.07 – 42.66)**	**0.004**
Sexual role CLS in the past three months No CLS / didn't state which partner	3803 obs 1 (Ref)	0.705	3752 obs 1 (Ref)	**0.016**

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted[€] IRR (95% CI)	p-value
Always insertive Always receptive Versatile (sometimes insertive, sometimes receptive)	- 0.95 (0.18 – 4.88) 1.79 (0.60 – 5.32)		- 2.47 (0.35 – 17.67) **4.55 (1.01 – 21.11)**	
Group sex in the past 3 months No Yes	3819 obs 1 (Ref) **2.98 (1.03 – 8.61)**	**0.043**	3770 obs 1 (Ref) **3.51 (1.14 – 10.77)**	**0.029**
PEP use in the past 12 months** No Yes	1530 obs 1 (Ref) 1.04 (0.12 – 8.90)	0.971	1512 obs 1 (Ref) 1.16 (0.13 – 10.11)	0.888
PrEP use in the past 12 months** No Yes	1532 obs 1 (Ref) 0.96 (0.12 – 7.81)	0.970	1512 obs 1 (Ref) 0.99 (0.13 – 7.51)	0.999
Bacterial STI diagnoses[‡] No Yes	3819 obs Ref **4.46 (1.57 – 12.68)**	**0.005**	3770 obs Ref **5.93 (1.95 – 18.03)**	**0.002**
Health and lifestyle characteristics				
Recreational drug use in the past 3 months** No **Yes**	1536 obs 1 (Ref) 4.81 (0.56 – 41.26)	0.152	1518 obs 1 (Ref) 5.83 (0.66 – 50.97)	0.111
Chemsex in the past 3 months No Yes	3819 obs 1 (Ref) **3.89 (1.35 – 11.22)**	**0.012**	3770 obs 1 (Ref) **4.81 (1.57 – 14.74)**	**0.006**
Injection drug use in the past 3 months** No Yes	1536 obs 1 (Ref) **21.67 (3.96 – 118.30)**	**<0.001**	1518 obs 1 (Ref) **18.99 (3.39 – 106.14)**	**0.001**
Higher risk alcohol consumption (modified WHO AUDIT-C equals ≥6)** No Yes	1536 obs 1 (Ref) 2.10 (0.58 – 7.63)	0.260	1521 obs 1 (Ref) 1.91 (0.51 – 7.08)	0.335
Depressive symptoms (PHQ-9 score ≥10)** No Yes	1536 obs 1 (Ref) 1.28 (0.15 – 10.64)	0.818	1521 obs 1 (Ref) 1.53 (0.17 – 13.31)	0.701
Anxiety symptoms (GAD7 score ≥10)** No Yes	1537 obs 1 (Ref) 1.88 (0.23 – 15.60)	0.559	1526 obs 1 (Ref) 2.06 (0.23 – 18.30)	0.681
Calendar year as a continuous variable	3821 obs **0.52 (0.45 – 0.59)**	**<0.001**	3769 obs **0.47 (0.28 – 0.78)**	**0.004**
Calendar year category 2013 – 2014 2015 2016 2017 – 2018	3821 obs 1 (Ref) 0.26 (0.07 – 1.05) 0.35 (0.10 – 1.19) **0.06 (0.01 – 0.54)**	0.053	3769 obs 1 (Ref) **0.17 (0.04 – 0.82)** **0.20 (0.05 – 0.83)** **0.05 (0.01 – 0.44)**	**0.010**

* total complete observations: 3821 questionnaires; sexual/HIV related behaviour data was based on the last time man asked; number of new sexual partners, fisting or sex toys, sex for drugs or money, and smoking status were not included in the analysis because they were only asked at the baseline questionnaire

** data were not collected at the four-monthly questionnaire (only baseline and annual questionnaires)

Characteristics	Unadjusted IRR (95% CI)	p-value	Adjusted€ IRR (95% CI)	p-value

† in the past six months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires
‡ in the past 12 months at the baseline questionnaire, and in the past three months at the four-monthly and annual questionnaires
^ Having enough money to cover basic needs e.g. for food and heating
€ adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and university education

GBMSM: gay, bisexual, and other men who have sex with men; IRR: incidence rate ratio; CLS: condomless anal sex; STI: sexually transmitted infections; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; WHO-AUDIT: world health organization – alcohol use disorders identification test; PHQ-9: patient health questionnaire - 9; GAD–7: generalised anxiety disorder-7

7.3.4 The use of condomless anal sex with two or more partners as the main measure of 'higher-risk' sexual risk behaviour

As stated in Chapter 5 (Section 5.2.3), in this thesis, CLS2+ was used as the main measure of 'higher-risk' sexual behaviour considering the U=U period and the relatively low PrEP use in the UK during the data collection period of the AURAH2 study. Condomless sex with one partner was supposed to be less likely to represent behaviour potentially linked to a high risk of acquisition of HIV because this may occur in the context of a long-term relationship where HIV status is known with more confidence. CLS with an HIV-positive partner when the HIV-positive partner is taking antiretroviral drugs with good adherence and has a fully suppressed viral load is also not a high-risk behaviour because the risk of HIV transmission through anal sex is zero in this context (32, 33). Guidelines from WHO published in 2018 also include as criteria for PrEP to be indicated unprotected sex with multiple partners in the past six months (344).

It is possible that CLS2+ does not reflect 'true' high-risk sexual behaviour. However, as can be seen from the findings in this chapter, CLS2+ was strongly associated with a subsequent HIV incidence, with a stronger association between time-updated CLS2+ and HIV incidence among men in the online cohort (N=622, aIRR 9.39, 95% CI 2.04 – 43.35, *p*=0.004). The population attributable fraction (PAF) for the effect of CLS2+ on subsequent HIV incidence was estimated as 75.6% (95% CI 12.1 % – 93.2%) among men in the online cohort. Among all men enrolled in AURAH2, the PAF estimate was 64.3% (31.3% – 81.4%). These estimates were calculated using the ***punaf*** procedure in Stata 15 (345). These fractions represent HIV incidence reduction in the population that would occur if CLS2+ could be eliminated, assuming that age, sexual identity, education level and ethnicity remain the same. We see that 75.6% of new HIV incident cases could have been prevented by eliminating CLS2+. The PAF estimates for other sexual behaviours were lower than CLS2+; for example, for group sex, the PAF estimate was 43.4%, recent HIV test was 36.4%, condomless anal sex was 53.3%, and bacterial STI diagnosis was 44.7%.

7.4 Discussion

7.4.1 Summary of results

The results of this chapter demonstrated a substantial decline in HIV incidence among a prospective cohort of HIV-negative GBMSM in England, from 1.47 per 100 PYs to 0.25 per 100 PYs between 2013 and 2019. Injection drug use, chemsex use, and measures of high-risk sexual behaviour such as condomless sex with multiple partners and group sex were strongly associated with incident HIV.

7.4.2 Decline in HIV incidence in the UK and other high-income countries among GBMSM

The results of an earlier report from England's national STI surveillance system also estimated that the annual HIV incidence among men who have sex with men attending English sexual health clinics decreased from 1·90 per 100 PY in 2012/2013 to 0·79 per 100 PY in 2016/2017 (338). Based on the CD4 back-calculation model that was used to estimate HIV incidence among GBMSM living in England based on data on new HIV diagnoses, incidence began to fall in 2012 (98, 100).

The substantial decline in HIV incidence in AURAH2 was also described in some other countries (220, 223). It may be attributed to important behavioural changes within GBMSM populations. The dramatic decline in HIV infection rates in AURAH2 coincided with declines in the proportion of individuals reporting group sex and recreational drug use since 2013 and diagnosis of bacterial STIs since 2015 (see Chapter 5). In contrast to these trends in STIs, group sex and drug use overall, in AURAH2, a slight increase in the prevalence of CLS and CLS2+ and a stable prevalence of injection drug use between 2013 and 2018 were observed. Therefore, the decline in HIV incidence was unlikely to be solely explained by changes in sexual behaviour during this period.

Lower levels of infectious HIV in the community due to more timely HIV diagnosis and earlier treatment among those accessing HIV care are likely to have had a role in declining incidence, in line with the previous prediction (1, 2). A longitudinal cohort study in Australia, the Treatment with Antiretrovirals and their Impact on Positive And Negative men (TAIPAN) study, demonstrated that the decrease in community-level HIV viraemia (≥200 copies/mL) from 28·6% in 2012 to 12·8% in 2017 among HIV-positive gay and bisexual men was significantly associated with decreasing HIV incidence in New South Wales and Victoria (from 0·88 per 100 PYs in 2012 to 0·22 per 100 PYs in 2017) (339).

PrEP use during follow-up may also have impacted on declining HIV incidence. An important finding from AURAH2 was that the fall in HIV incidence coincided with a major increase in the proportion of men reporting the past 12-month PrEP use over time (see Chapter 6) (346). In AURAH2, baseline and longitudinal reported PrEP use was not associated with reduced HIV incidence. At baseline, only 5% of men reported PrEP use in the past 12 months, and possibly these men were early PrEP takers having high-risk sexual behaviour, putting them at particularly high risk of HIV infection. It is possible that no clear association was observed due to opposing factors operating – PrEP use decreasing the risk of HIV acquisition on the one hand, and PrEP use acting as an indicator of very high-risk behaviour (similar to the other markers of CLS) on the other. Moreover, past 12-month PrEP use was only asked at baseline and annual questionnaires; therefore, I do not have a complete picture of PrEP use during follow-up or adherence and consistency in using PrEP. Taken together, results from this chapter are consistent with the hypothesis that the benefits of ART in reducing HIV transmission in combination with increased uptake of PrEP has had a substantial impact in reducing HIV incidence in the GBMSM population.

7.4.3 Predictors of HIV incidence among GBMSM

7.4.3.1 Recreational drug use

Recreational drug use was one of the strongest factors associated with HIV incidence among men in AURAH2. HIV incidence was especially high among men who reported the use of injection drugs, 4·8 per 100 PY; almost 28-fold higher than the incidence among men who did not report any recreational drugs. The use of non-injection chemsex-related drugs also increased the risk of HIV incidence more than 6-fold. A 2019 systematic review investigating recreational drug use in GBMSM demonstrated that chemsex use is associated with increased risky behaviour such as CLS and group sex, as well as with an increase in STIs and poor mental health symptoms (320). Concerning injection drug use, data among GBMSM in the UK and Europe are limited. Findings from the 2014 Gay Men's Sex Survey, an online survey of 14,464 GBMSM living in the UK, suggested that injection drug use (amphetamine, crystal methamphetamine, heroin, mephedrone, GHB/GBL, and ketamine) is significantly associated with CLS with multiple partners (347). The survey also found that injecting was most common among those who were of age 30 – 59 years, lived in London, and were HIV seropositive (347). Data from Australian and Canadian GBMSM cohorts also observed strong associations between injecting drugs and sexual risk behaviours (348, 349).

7.4.3.2 Sexual/HIV-related behaviour

The risk of acquiring HIV was higher among GBMSM who reported high-risk sexual behaviours (CLS with multiple or HIV positive partners, group sex, greater number of new

sexual partners, versatile CLS role, and sex for drugs or money), and bacterial STI diagnoses. Risk was particularly high among men reporting group sex and those with higher number of CLS partners in the past three months. This is consistent with findings from other cohort studies in the UK and other countries (224, 342, 350).

7.4.3.3 Socio-demographic and other factors

In AURAH2, most demographic and socioeconomic factors were not associated with incident HIV; however, a higher incidence rate among men with non-university level of education was observed. This might be explained by the higher prevalence of high-risk sexual behaviours in this subgroup of men, and it seems that some men could not afford to pay to buy PrEP. The prevalence of past three-month CLS at baseline was significantly higher among men with no educational qualifications, at 86% (p=0.038), compared to men with university level education and other qualification (Appendix 13). A lower educational level has been reported to be associated with risk-taking behaviours and with an increased risk of HIV seroconversion in European studies (128, 351). There was no evidence that high alcohol use, smoking, or symptoms of depression or anxiety associated with incident HIV in the baseline or time-updated analysis, although confidence intervals were wide for some factors. It has previously been reported that the relationship of mental health symptoms with sexual behaviour may be complex and operate in both directions (352).

7.4.4 Limitations

The strengths of this study include the prospective design, and HIV status confirmation of all 1,162 participants enrolled in AURAH2 through linkage with national HIV surveillance data. This allows for optimum use of available information to estimate HIV incidence and trends for all men in the cohort and means that the main analysis is not subject to potential bias due to loss to follow-up. Before data linkage, I presented the interim results from AURAH2 data restricted to men under follow-up with the questionnaire (353), adopting the single random point method to decide HIV infection dates between self-reported first HIV positive test results and last HIV negative test results (354). A significant decline over time was also observed among 622 men who completed at least an online questionnaire; however, trends were only able to be calculated from 2015 until 2018 (online follow-up period), and a number of diagnoses were missed that were identified after linking the AURAH2 data with data from the UKHSA.

There are some limitations to this study. Men in this cohort were recruited from three sexual health clinics in urban areas of London and Brighton that were recruiting sites for the PROUD study, the PARTNER study (assessing the risk of transmission in sero discordant

couples in which condom was not consistently used) and offer special clinics for chemesex. Participants in the AURAH2 study are predominantly highly educated, employed, in a stable economic situation, and of White ethnicity. These men may not be representative of the broader GBMSM population in England and the UK. It is possible that the incidence estimates, and risk factors identified are not generalizable to GBMSM who do not attend sexual health clinics or who live in more rural areas. The small number of HIV infections in each calendar year among men in this study has resulted in relatively wide confidence intervals of incidence rates; therefore, incidence rates and associations with factors must be interpreted carefully. In addition, assessment of trends over time in sexual behaviour may be subject to 'regression to the mean' as the clinic visit at which recruitment occurred may have been specifically prompted by a recent period of higher risk. For risk factors analysis, I focused on baseline factors in order to include all data from the whole cohort, which may have underestimated the associations between sexual/HIV-related behaviours and HIV incidence, including the impact of PrEP. However, I observed similar results when the analysis was restricted to the 622 men who contributed to the follow-up and for which time-updated variables could be used. In terms of the time-updated analysis, the online retention of participants who initially registered in the study was not optimal. Results from this chapter may be sensitive to specific recall bias and social desirability bias in men's responses in the baseline questionnaire. Data linkage to surveillance systems using pseudo-anonymised identifiers potential for mismatches or missing seroconversions, however this has been minimised by the UKHSA data triangulation; all self-reported seroconversions were validated by the UKHSA data. Lastly, this study would not include seroconversions that were not diagnosed or those that were diagnosed outside the UK.

7.4.5 Conclusion

In summary, the results from this chapter provided evidence of a substantial decline in HIV incidence among a cohort of GBMSM attending sexual health clinics in England. Data suggest that GBMSM reporting the use of recreational drugs, in particular injection drug use and chemsex drug use, high risk sexual behaviours such as CLS with multiple partners, CLS with HIV positive partners, group sex, and those with a bacterial STI, are at increased risk of HIV acquisition. HIV infections are also significantly higher among those with lower levels of education at baseline. Temporal trends in sexual risk behaviours and drug use in the cohort over the study period were mixed, but the marked decrease in incidence coincided with a substantial increase in PrEP use, and decreases in proportion reporting group sex and chemsex (see Chapter 5). Given similar findings from recent data among GBMSM in the UK and other countries, it is likely that the observed decline is largely related to the increase in testing and earlier ART initiation from 2013 onward and the scale-up of PrEP.

The implications of findings from this chapter and recommendations for future research are discussed in the final conclusion chapter of this thesis (Chapter 9).

Chapter 8: Behaviour changes following HIV diagnosis among GBMSM in the era of Treatment as Prevention: Methods and Results from the Guy's and St. Thomas' Hospital observational study

8.1 Introduction

This chapter comprises both the methods and results sections from the Guy's and St. Thomas' hospital observational study. I detail the content of this chapter in the Chapter aims section (Section 8.1.2).

8.1.1 Background

Treatment as Prevention (TasP) for HIV was recommended following results from the HPTN052 randomised controlled trial that was published in 2011, which showed that treatment was efficacious in reducing the risk of HIV transmission to a sexual partner (355, 356). The evidence that HIV-positive people who are receiving antiretroviral therapy (ART) and are virally suppressed cannot sexually transmit the virus in the context of sero-different same sex male couples was published in 2016 while the Guy's and St. Thomas' study took place (2015 – 2018) and led to the launch of Undetectable = Untransmittable (U=U) campaign (32-34) and changes in the message given to people living with HIV.

The effect of an HIV diagnosis on the subsequent sexual behaviour of gay, bisexual, and other men who have sex with men (GBMSM) in the era of U=U is unclear. Although there was concern historically that optimism towards ART use could increase risk-taking within high-risk populations (357), and therefore transmission of HIV, it is now known that any increase in condomless sex (CLS) for an HIV-positive person on ART will not impact HIV transmission risk to HIV-negative partners if the HIV-positive person has an undetectable viral load. In some specific situations, however, such as during a period of low ART adherence or during the initial treatment period when viral load is still detectable, there may be a risk of HIV transmission. Men engaging in CLS shortly after HIV diagnosis will be infectious unless they have started ART and already have an undetectable viral load. In addition, CLS is associated with the risk of other sexually transmitted infections (STIs), irrespective of ART or viral load status.

Longitudinal cohorts outside of the UK have reported that GBMSM reduced sexual risk behaviours at the time of HIV diagnosis; however, the decreases were temporary (236, 239, 358). Data also showed that condomless sex tended to increase over calendar time (358). In the UK, where GBMSM accounted for more than 50% of total new HIV diagnoses in 2018

(6), the longitudinal trends in sexual behaviour post-HIV diagnosis are less clear (143). Understanding the pattern of sexual behaviours among HIV-positive GBMSM following HIV diagnosis is crucial to assess the potential risk of HIV spread in the community and give insight into the risk of transmission of other STIs.

8.1.2 Chapter aims

The specific objectives of this chapter are:

(i) to outline the design and methodology of the Guy's and St. Thomas' observational study and provide an overview of the data management of the study tasks completed as part of this thesis
(ii) to describe the characteristics of participants included in the analyses
(iii) to describe the prevalence of the various measures of sexual behaviour (condomless sex, seroconcordant condomless sex, serodiscordant condomless sex and number of partners), overall, and at each time point: baseline, 12 weeks, and 48 weeks, and trends over one year of follow-up since baseline in the prevalence of sexual behaviour among newly diagnosed GBMSM
(v) to assess within-person changes in sexual behaviour measures after HIV diagnosis
(vi) to examine factors associated with measures of sexual behaviour in the initial period after an HIV diagnosis (week 12 and week 48 after enrolment in the study)

8.2 Methods

8.2.1 Guys and St. Thomas' study

8.2.1.1 Aims and rationale for the study

The primary aim of the study was to estimate the direct and indirect cost of people with newly diagnosed HIV infection (see the study protocol, Appendix 14). This study was prompted by the increase in the number of people living with HIV (PLHIV) globally, due to the increased life expectancy of PLHIV on ART. Evaluation of the use and cost incurred by PLHIV in the first 12 months following HIV diagnosis will provide policymakers and other stakeholders with more robust and up to date information on the total cost of services contributed by this group of patients.

I present a secondary analysis with the specific objective to determine the change in sexual behaviour following HIV diagnosis. Evaluation of changes in sexual behaviour post-HIV diagnosis will enable policymakers, health professionals and civil society members, including people living with HIV, to improve the effectiveness and efficiency of the response to the HIV

epidemic in London and the UK. This will facilitate resource planning for both HIV prevention and the management of HIV infection.

The study was sponsored by the Guy's and St. Thomas' National Health Service (NHS) Foundation Trust and funded by the Gilead Sciences. The Chief investigator of this study was Dr Julie Fox.

8.2.1.2 Study design

The Guy's and St. Thomas's study was a prospective observational study of people newly diagnosed with HIV and attending Guy's and St. Thomas' NHS Trust, with a one-year follow-up. Participants were eligible for inclusion into the study if they:

(i) were male or female over 18-years old

(ii) newly diagnosed with HIV-1 diagnosis within the previous four months and attending St. Thomas' Hospital

(iii) able to understand and consent to study and able to comply with the study protocol (Appendix 14)

Participants were excluded if they were detected with HIV-2 Ab. People recruited in the study could withdraw from it at any point in time. They were asked permission to continue collecting laboratory measurements, and their data would be included in the analysis unless they requested otherwise.

8.2.1.3 Recruitment

Patients were recruited from the genito-urinary medicine (GUM) / HIV department at Guy's and St. Thomas' NHS trust and enrolled in the study between February 2015 and April 2017 and were followed up for one year. Depending on how well the individual was coping after receiving their HIV diagnosis, individuals were approached anytime between diagnosis and four months following this (as assessed by the study team) during one of the visits. During the first four months of any HIV diagnosis, individuals attended the unit on approximately three occasions to see a health advisor, clinic nurse and clinic doctor, during which routine data were collected. Therefore, there were approximately three occasions to approach individuals about participation in the study.

There were no potential risks to the participants. The HIV clinician carried out the routine HIV care of the individual, and study visits were arranged around these. The NHS staff referred individuals to the research unit and consented to the study by either the study nurse or doctor. Due to the time taken to complete the forms, patients were reimbursed £10 per visit.

8.2.1.4 Participants consent and ethics approval

Individuals could consent immediately or after a more extended consideration and they were offered the opportunity to contact the GUM / HIV department. Consent included permission to contact individual general practitioner (GP) practices to provide information on the encounters with the patients for the six months before and the 12 months since the patient was diagnosed with HIV (see Appendix 15). The study protocol and amendments were reviewed and approved by the National Research Ethics Service (NRES) Committee London – Surrey Borders.

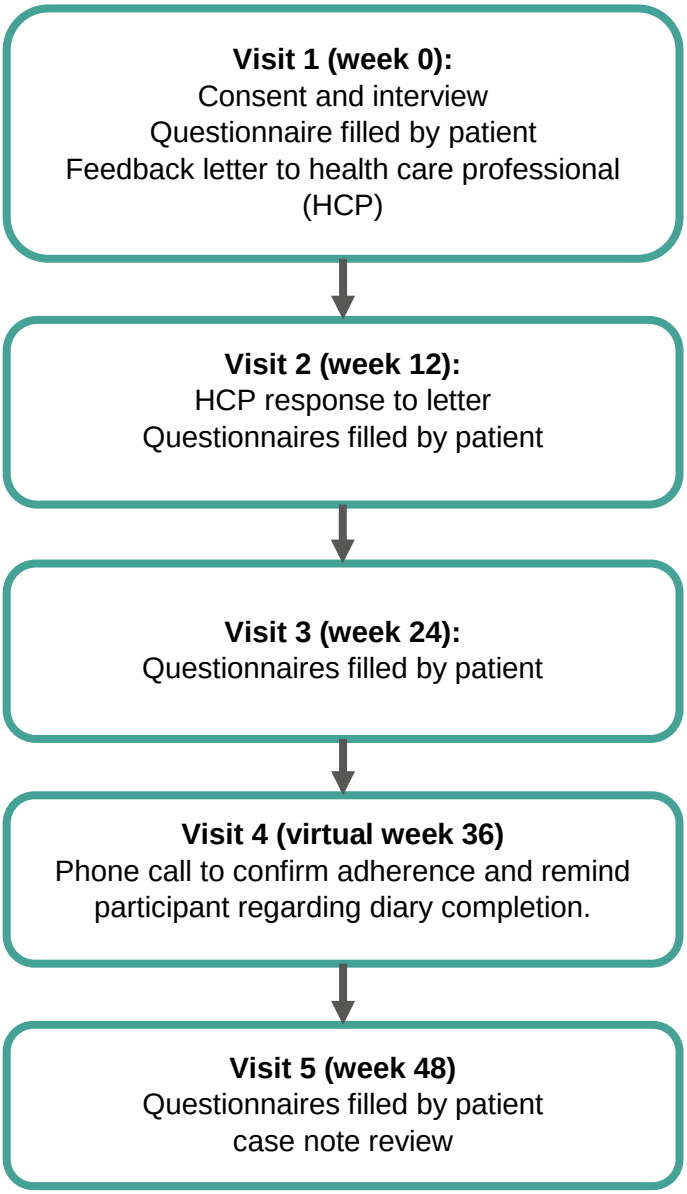
8.2.1.5 Sample size

The study aimed to recruit a minimum of 125 individuals newly diagnosed with HIV during the study period. On average, ten newly HIV diagnosed patients were recruited per month out of 25 new diagnoses that on average occurred at St. Thomas Hospital when the study was designed. The anticipated recruitment time was approximately 12 months.

8.2.1.6 Data collection

In this study, data were collected through patient questionnaires (Appendix 16). Individuals self-completed a questionnaire (on paper or electronically, depending on participant preference) at weeks 0 (baseline), 12, 24 and week 48. The time taken to complete these questionnaires is approximately 25 minutes. Those with poor literacy or English as a second language were asked permission to complete questionnaires with a health care assistant. Individuals were also asked to complete the diary for the entire duration of the study (12 months) with support from a research nurse. Stamped addressed envelopes were provided for individuals to send diaries on a monthly basis. As a reminder to complete the diaries, monthly text messages, emails or phone calls were used depending on the patients' preference. The visit schedule for participants can be seen in Figure 8.1.

Figure 8.1 Flow chart of visit schedule for participants



Data collected at each visit and the timing of questionnaires are shown in Table 8.1. Sexual behaviour data were only collected at baseline (week 0), week 12, and week 48. With exception to some socio-demographic queries that were only obtained at baseline, all other questions were collected at each questionnaire.

Table 8.1 Timing of questionnaires and activities for participants in the Guy's and St. Thomas' observational study

Content of questionnaire	Week number			
	0	12	24	48
General information: • ethnicity • born in the UK • first move to the UK • education • presumed mode of HIV transmission • HIV testing history • date of first of positive test • STIs screening history	√	–	–	–
General information: • employment status • housing status • difficulty to pay for heating cost in winter • receive benefits • return cost to hospital	√	–	√	√
Patient and HIV: • disclosure to other • feeling about HIV testing • relationship status • have a partner with HIV • have children	√	√	√	√
Views on HIV transmission risk: Agree or not to the following statements: • *In my opinion, because of improvements in HIV treatments, people are more willing to take a chance of getting infected or infecting someone else with HIV* • *In my opinion, a person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load* • *In my opinion, if an HIV-positive person's viral load is undetectable, it is not necessary to use a condom to prevent transmission of HIV*	√	√	√	√
Health and wellbeing: • receive treatment for depression • receive treatment for other mental health • Memorial Symptom Assessment Scale (MSAS) • Patient Health Questionnaire (PHQ-9) • Health outcome (EQ-5D) • Social support (DUKE UNC functional social)	√	√	√	√
Lifestyle: • CAGE questionnaire • recreational drug use	√	√	√	√
HIV treatment: • receive ART • reasons starting ART	√	√	√	√

• condition after taking ART • changing regimen • current HIV treatment • adherence for those on ART				
Sexual behaviour: • STI diagnosis • Hepatitis C history • sex with women (and the frequency) • sex with women without condom • sex with men (and the frequency) • sex with men without condom • sexual condomless sex role • number of condomless sex partners • reasons for not using condoms • pregnancy (for women)	√	√	–	√
• type of partners (seroconcordant / serodiscordant)	–	√	–	√

The questionnaires used a recall period of the past three months, except for STIs history at baseline that used a recall period of the past two years.

Besides patient questionnaires, other methods of data collection in this cohort study were diaries with monthly reminders, case note reviews, data download on the whole cohort for all investigations carried out at Guys and St. Thomas' NHS Trust, and GP provided information on encounter data, referrals and hospital attendances. Patients were also asked information on use of all medical or social services, formal or informal used either in the community, hospital(s) or both daily on a diary. Information obtained from the case review can be seen in Appendix 17. Information on Capturing the Use and Cost of Community and Hospital Services can be seen in Appendix 18.

8.2.2 Data management of the Guys and St. Thomas' study

The Guy's and St. Thomas' study datasets were received in four batches between August 2020 and December 2021. First, I was provided with a cleaned-raw excel dataset containing all participants' questionnaires responses by Dr Julie Fox, the chief investigator of the Guy's and St. Thomas' study, in August 2020. In September 2020, I was provided with another excel spreadsheet dataset containing a database of costing study and viral load data (at baseline and week 48 only). In January 2021, Ms Alice Sharp, the Guy's and St. Thomas study administrator, provided me with another excel dataset containing the date of diagnosis of every patient. Finally, in December 2021, I was provided with another locked-excel dataset containing a database of laboratory results, including viral load and CD4 count at each visit. The datasets that I received containing data on all HIV patients, not just GBMSM. I stored these datasets on an encrypted memory stick, with a backup on the UCL Data Safe

Haven, a secure service owned by UCL that allows for the secure storage and exchange of sensitive personal data (250). Preparing Stata datasets for analysis and variable derivation were my responsibility.

There was very minimal missing data in the study, <1% of the data for questions utilised in the analysis was missing, and most variables had no missing data. In this study, observations with missing data were excluded from the analysis. Missing data items were mentioned in the specific table or figure results.

8.2.3 Variable definitions in the Guy's and St. Thomas' study

Table 8.2 summarizes the categories and recall period of each of the variables used in this thesis, including demographic, socio-economic and partnership status, sexual and other HIV-related behaviour, and health and lifestyle characteristics.

Table 8.2 Socio-demographic, sexual and HIV related behaviours, and health and lifestyle variables in the Guy's and St. Thomas' observational study

Characteristics	Variables	Categories	Recall period
Demographic	Age group	<25; 25 – 29; 30 – 34; 35 – 39; 40 – 44; and ≥45 years	current
	Ethnicity	White; Other ethnicity	
	Country of birth	UK; Outside the UK	
Socio-economic and partnership status	University education status	Yes; No	current
	Employment status	Full time / part-time employment; Unemployed / other	current
	Housing status	Homeowner; Renting; Other	current
	Difficulty to pay for heating cost	Yes; No or not applicable	current
	Receive benefits	Yes; No	current
	In relationship status	Yes – living with partner; Yes – not living with partner; No	current
	Have a partner with HIV	Yes; No	
Disclosure HIV status and ART	Disclosure of HIV status to others	Yes; No	current
	Ever taken ART at baseline	Yes; No	at baseline
Views on HIV transmission risk	Agree to statement: A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load	Yes; No	current
	Agree to statement: If an HIV positive person's viral load is	Yes; No	current

	undetectable, it is not necessary to use a condom		
Sexual and other HIV related behaviour	any sex	Yes; No	past 3 months
	Condomless sex	Yes; No	past 3 months
	Condomless sex with HIV-negative or unknown status partners	Yes; No	past 3 months
	Condomless sex with HIV-positive partners	Yes; No	past 3 months
	Number of partners	one regular partner; one casual partner; 2–4 partners; 5–10 partners; and >10 partners.	past 3 months
	STI diagnosis	Yes; No	past 3 months
Health and lifestyle	Recreational drug use	Yes; No	past 3 months
	Depressive symptoms	Yes; No	past two weeks
	Alcohol dependency symptoms	Yes; No	ever

8.2.3.1 Sexual behaviour measures

The following measures of sexual behaviours during the previous three months were considered:

(i) any sex
(ii) condomless sex (CLS)
(iii) condomless sex with HIV sero-concordant (HIV-positive) partner(s) only (CLS-C)
(iv) condomless sex with at least one HIV-discordant (HIV-negative or unknown status) partner(s) (CLS-D)
(v) the number of sexual partners.
(vi) CLS-D with risk of HIV transmission (CLS-D-HIV-risk) at weeks 12 and 48 after diagnosis, which was defined as CLS-D plus at least one of the following: not on ART; most recent (within the past three months) documented plasma viral load (VL) > 200 copies/mL; no documented VL within the past three months

Measures of any sex, CLS, and number of sexual partners were collected at baseline, week 12, and week 48, while CLS-C and CLS-D data were only collected at week 12 and week 48. Due to the recall period at the baseline questionnaire may covering a period of being HIV-positive and a period of being HIV-negative, questions on serodiscordant or discordant CLS are difficult to interpret.

The number of sexual partners was classified as: one regular partner; one casual partner; 2–4 partners; 5–10 partners; and >10 partners. All other sexual behaviour measures were assessed as dichotomous measures (yes; no).

8.2.3.2 Other variables

Socio-demographic and partnership status characteristics included:

(i) age group
(ii) ethnicity
(iii) country of birth
(iv) university education status
(v) employment status
(vi) housing status
(vii) relationship status
(viii) difficulty to pay for the heating cost
(ix) receive benefits

Health and lifestyle factors included:

(i) recreational drug use in the past three months
(ii) alcohol dependency symptoms (a score of ≥2 on the CAGE score) (241)
CAGE questions for alcohol use are:
- Have you ever felt you needed to Cut down on your drinking?
- Have people Annoyed you by criticizing your drinking?
- Have you ever felt Guilty about drinking?
- Have you ever felt you needed a drink first thing in the morning (Eye-opener) to steady your nerves or to get rid of a hangover?

(iii) depressive symptoms (a score of ≥10 on the Patient Health Questionnaire-9 [PHQ-9]) (244)

Other behavioural and HIV-related covariates included:

(i) STI diagnosis
(ii) disclosure of HIV status to others apart from health care staff
(iii) having had an HIV-positive partner
(iv) ever taken ART (at baseline)
(v) views on HIV transmission risk (agree or not to two statements about HIV transmission:
- '*A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load'*
- *'If an HIV positive person's viral load is undetectable, it is not necessary to use a condom to prevent transmission of HIV'*

All variables were collected at baseline and subsequent questionnaires at week 12 and week 48 (in the preceding three months unless stated otherwise), except for data on ethnicity, country of birth, level of education, and ever taken antiretroviral treatment that were only obtained at baseline questionnaire (fixed variables).

8.2.4 Statistical analysis

Analysis in this chapter focussed on GBMSM whose baseline visit was within three months of HIV diagnosis. The prevalence of the various measures of sexual behaviour, overall, and at each time point: baseline, 12 weeks, 48 weeks were first calculated as the proportion of men who reported the sexual behaviours out of the total number who completed questionnaires in each visit. Trends over one year of follow-up since baseline in the prevalence of sexual behaviour were then assessed using univariable logistic regression models fitted using generalized estimating equations (GEE), taking into account repeated data within-subjects (359). The follow-up visit was fitted as a continuous variable to obtain a test for linear trend.

To assess within-individual changes in sexual behaviours after diagnosis, data from the same individuals who completed all three visits were used. Longitudinal changes were presented as the proportion who reported and did not report sexual behaviours among those who reported sexual behaviours in the previous visit. The same was done among those who did not report sexual behaviours in the previous visit.

Associations of the follow-up visit and other characteristics with any sex, CLS, CLS-C, and CLS-D, were examined using GEE logistic models, using questionnaires from week 12 and week 48. Factors were also assessed separately at weeks 12 and 48, including factors associated with stopping CLS in week 12 among those who reported CLS at baseline, using logistic regression models. Analyses were conducted unadjusted and adjusted for age, ethnicity, country of birth, and education level, and results are presented as odds ratios (ORs) with their corresponding 95% CI. All analyses were conducted using Stata SE statistical software (version 15.1). Missing values were excluded from analyses.

8.3 Results

8.3.1 Characteristics of the participants

Between February 2015 and April 2017, 121 participants (112 men and nine women) were enrolled in the study and completed a baseline questionnaire, of whom 96 were GBMSM. To evaluate patterns in sexual behaviour shortly after diagnosis, analysis focussed on GBMSM whose baseline visit was within three months of diagnosis. Of the 96, six (6.2%) men had been diagnosed with HIV for more than three months at the time of study enrolment, so these men were excluded. In total, data from 90 (93.8%) men, who contributed data on 250 questionnaires in total, were used in the analyses. Baseline questionnaires were completed a mean of 29 days (median 22 days) after HIV diagnosis (Table 8.3).

At baseline, the mean age of participants was 36 years (standard deviation [SD]: 9.6), 83.3% were of white ethnicity, 42.2% were UK-born, 64.4% had a university degree, and 85.6% reported being employed. Almost all men (97.8%) had a detectable viral load (>200 copies/mL), 78.9% had disclosed their HIV status to others additional to health care staff, 7.8% were in a relationship with an HIV-positive partner, 14.9% had already started taking ART, 67.8% of men reported recreational drug use, and 47.8% reported having an STI diagnosed when diagnosed with HIV. The prevalence of depressive symptoms at baseline was 24.4%, and the majority of men (84.4%) were aware and believed that '***a person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load' (U=U).***

Of the 90 men who completed a baseline questionnaire, 93.3% (84/90) completed a follow-up questionnaire at week 12, and 84.4% (76/90) at week 48. There were 73 (81.1% of 90) men who completed all three questionnaires (baseline, week 12, and week 48).

Table 8.3 Baseline characteristics among 90 newly diagnosed with HIV GBMSM participating in the Guy's and St. Thomas' Hospital observational study*

Characteristics	n	%
Total sample	**90**	**100**
Age category, years		
< 25	7	7.8%
25 – 29	20	22.2%
30 – 34	17	18.9%
35 – 39	13	14.4%
40 – 44	16	17.8%
≥ 45	17	18.9%
Mean age (SD)	**36 (9.6)**	
Ethnicity[§]		
White	75	83.3%
Other ethnicity	15	16.7%

Characteristics	n	%
Country of birth		
UK	38	42.2%
Outside the UK	52	57.8%
University education status		
Yes	58	64.4%
No	32	35.6%
Employment status†		
Full time / part time employment	77	85.6%
Unemployed / other	13	14.4%
Housing status‡		
Homeowner	20	22.2 %
Renting	65	72.2%
Other	4	4.5%
Difficulty to pay for the heating cost in winter		
Yes	15	16.7%
No or not applicable	75	83.3%
Receive benefits		
Yes	5	5.6%
No	85	94.4%
Relationship status		
Yes, living with partner	29	32.2%
Yes, not living with partner	15	17.7%
No	46	51.1%
Have a partner with HIV		
Yes	7	7.8%
No	83	92.2%
Disclosure of HIV status to others		
Yes	71	78.9%
No	19	21.1%
Ever taken ART		
Yes	13	14.9%
No	74	85.1%
Recreational drugs use in the past 3 months		
Yes	61	67.8%
No	29	32.2%
STI diagnoses in the past 3 months		
Yes	43	47.8%
No	47	52.2%
Any sex in the past 3 months		
Yes	77	85.6%
No	13	14.4%
Condomless sex in the past 3 months		
Yes	56	62.2%
No	34	37.8%
Number of partners in the past 3 months		
0 or no sex	13	14.4%
1 – regular or long-term partner	15	16.7%
1 – casual or short-term partner	7	7.8%
2 – 4 partners	30	33.3%
5 – 10 partners	11	12.2%
> 10 partners	14	15.6%

Characteristics	n	%
Depressive symptoms (PHQ-9 score ≥10)		
Yes	22	24.4%
No	68	75.6%
Mean PHQ-9 score (SD)	6.9 (6.8)	
Median PHQ-9 score (IQR)	4 (2 – 10)	
Alcohol dependency symptoms (CAGE score >=2)		
Yes	7	7.8%
No	83	92.2%
Views on HIV transmission risk		
Agree to statement: *A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load.*	76	84.4%
Agree to statement: *If an HIV positive person's viral load is undetectable, it is not necessary to use a condom to prevent transmission of HIV*	16	17.8%
HIV viral load (VL) at diagnosis		
≤ 200 copies/mL	2	2.2%
> 200 copies/mL	88	97.8%
Mean days of VL measurement since diagnosis (SD)	14 days (16.4)	
Median days of VL measurement since diagnosis (IQR)	8 days (4 – 18)	
Time from diagnosis to baseline completion		
≤ 14 days	26	28.9%
15 – 30 days	36	40.0%
31 days – 3 months	28	31.1%
Mean days from diagnosis to baseline (SD)	29 days (23.2)	
Median days from diagnosis to baseline (IQR)	22 days (14 – 36)	

*There were no missing data except for: housing status: 1; ever taken ART: 3
§ Other ethnicity includes Black, Asian, Mixed, and other ethnic group
† Unemployed or other group includes student, retired and disabled or sick
‡ Other housing status includes temporary accommodation, staying with partner, and homeless

SD standard deviation, IQR interquartile range, STI sexually transmitted infection, PHQ-9 patient health questionnaire-9, CAGE alcohol questionnaire

8.3.2 Prevalence of sexual behaviour following HIV diagnosis

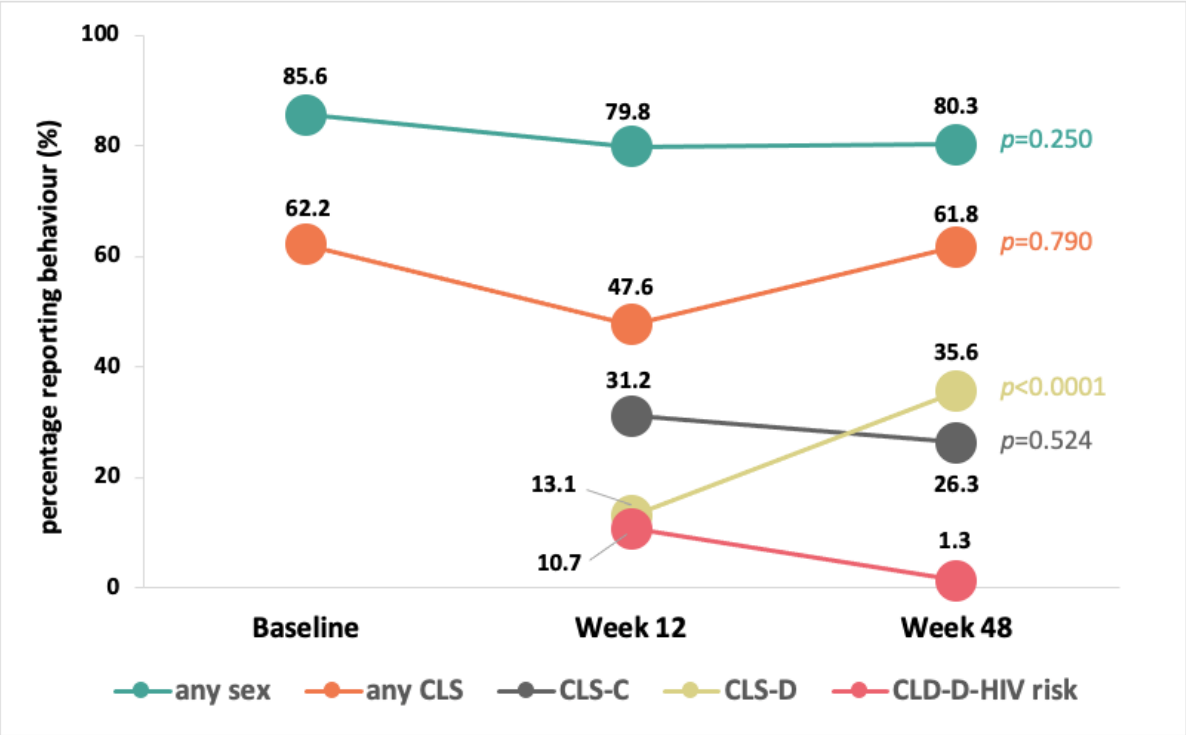
Figure 8.2 presents trends in the prevalence of any sex, CLS, CLS-C, and CLS-D according to visit. Any sex in the previous three months remained stable throughout the 48 weeks follow-up period: 85.6% (77/90) at baseline, 79.8% (67/84) at week 12 and 80.3% (61/76) at week 48 (*p-value for linear trend from GEE logistic model=0.*250*)*. CLS was reported by 62.2% (56/90) of men at baseline, dropped to 47.6% (40/84) at week 12, increased again to 61.8% (47/76) at week 48 (*p-trend=0.*790).

The proportion of men who reported CLS-C declined slightly, from 31.2% (25/80) at week 12 to 26.3% (20/76) at week 48, but this was not significant (*p-trend=0.*524), while the

proportion of men who reported CLS-D increased considerably from 13.1% (11/84) at week 12 to 35.6% (27/76) at week 48 (*p-trend*<0.001).

The prevalence of detectable viral load (>200 copies/mL) at week 12 was 48.8% (41/84), at week 48 was 7.9% (6/76). The prevalence of CLS-D-HIV risk at week 12 was 10.7% (9/84), which means that nine of 11 (81.8%) men who reported CLS-D were at high risk of infecting their partners. The prevalence of CLS-D-HIV risk at week 48 after diagnosis was only 1.3% (1/76), as 26 of the 27 men who reported CLS-D at week 48 were on ART with the last viral load (within the last three months) <50c/mL.

Figure 8.2 Prevalence of any sex, seroconcordant condomless sex, and serodiscordant condomless sex over time*



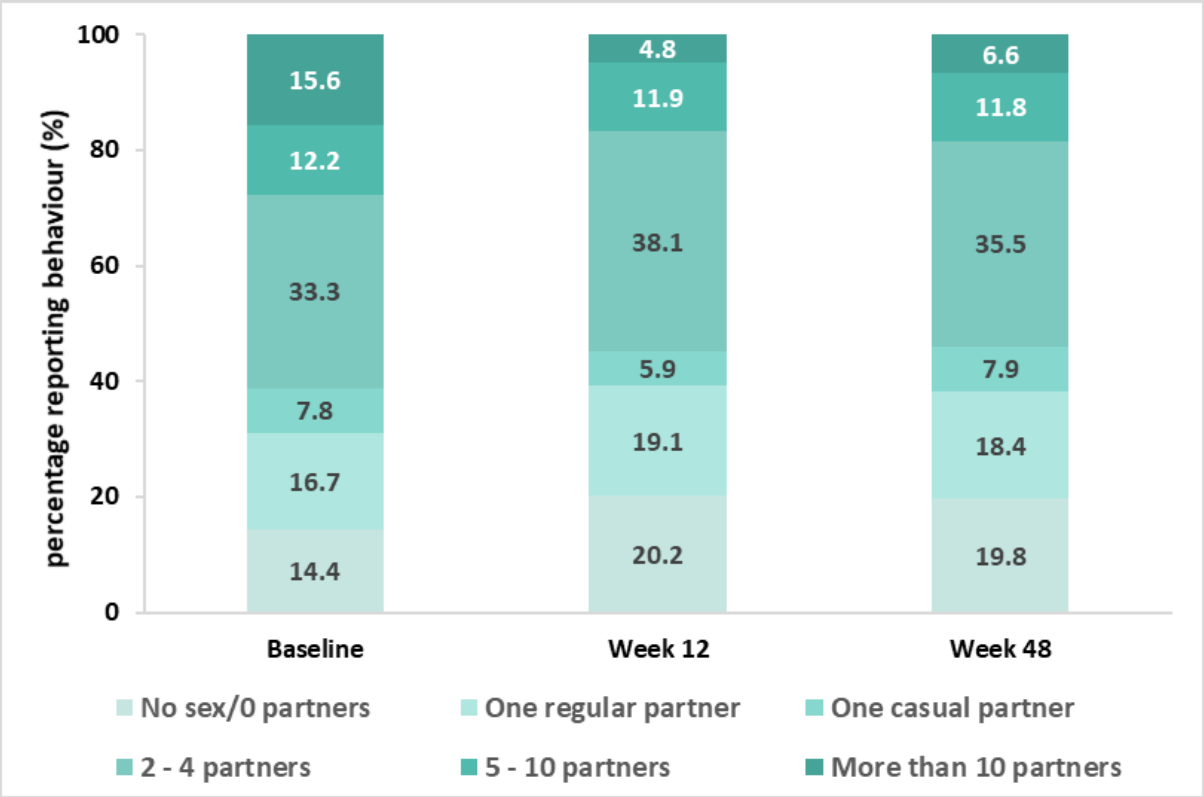
	Baseline	Week 12	Week 48
Detectable VL	97.8% (88/90)	48.8% (41/84)	7.9% (6/76)

* Trends over one-year follow-up period, sample sizes at baseline: 90 men, week 12: 84 men, week 48: 76 men; CLS-C and CLS-D data were not available at baseline, three missing questionnaires on CLS-C. Prevalence of sexual behaviours in the past three months at baseline corresponds to three months pre-diagnosis – diagnosis day.

Concerning the number of sexual partners per three months, the most common category for number of sexual partners reported was 2-5 partners (35.6%; 89/250) across three visits. Figure 8.3 presents trends in number of sexual partners. There were no changes in the proportion reporting one regular partner (*p-trend*=0.563), one casual partner (*p-trend*=0.915), 2–5 partners (*p-trend*=0.842), and 5–10 partners (*p-trend*=0.935) from baseline to week 48.

The proportion of men who reported more than ten partners decreased from 15.6% at baseline to 6.6% at week 48 (*p-trend*=0.101).

Figure 8.3 Reported number of sexual partners over time*



* * Trends over one-year follow-up period, sample sizes at baseline: 90 men, week 12: 84 men, week 48: 76 men, no missing questionnaires. Prevalence of sexual behaviours in the past three months at baseline corresponds to three months pre-diagnosis – diagnosis.

8.3.3 Within-person changes in sexual behaviour

Among the 73 men who completed all three visits, the general tendency for reporting any sex and CLS was that levels of sexual behaviour fell from baseline to week 12, and then sexual activity tended to increase again by one year after baseline (Figure 8.4A and Figure 8.4B). A slight decreasing individual trend was observed from week 12 to week 48 in CLS-C (Figure 8.4C) and an increase at week 48 in the within-individual frequency of CLS-D (Figure 8.4D).

When considering within-person changes in sexual behaviour (in the past three months), Figure 8.4A shows that 87.7% of men (64/73) reported any sex at baseline; 69.9% (51/73) continued to report any sex at week 12, while 17.8% (13/73) stopped reporting any sex. Among the nine men who did not report any sex at baseline (12.3% of 73), five men (6.8% of 73) started reporting any sex at week 12, while four men continued to not report any sex at

week 12 (5.5% of 73). The total prevalence of reporting any sex among 73 men at week 12 was 76.7% (56 men). At week 48, 51 of 56 men who reported any sex at week 12 continued to report any sex at week 48 (69.9%, or 51 from a total of 73 men at baseline), and four men (4/73, 5.5%) stopped reporting it. Among the 17 men of 73 men who did not report any sex at week 12 (23.3%), seven men (7/73, 9.6%) reported any sex at week 48, while ten men of the 73 (13.7%) continued not to report any sex. The total prevalence of reporting any sex among 73 men at week 48 was 79.5%. 45 of 73 men (61.6%) reported CLS at baseline, of whom 28 of 73 (38.4%) continued to report CLS in week 12, while 17 men (23.3%) stopped reporting CLS. Among 28 men who did not report CLS at baseline (38.4%), five men (6.8%) started reporting CLS at week 12, while 23 men continued not to report CLS at week 12 (31.5%). From the total 33 of 73 men (45.2%) who reported CLS at week 12, 28 men (38.4%) continued to report CLS at week 48, and five men (6.8%) stopped reporting it. Among the 40 of 73 men who did not report CLS at week 12 (54.8%), 17 men (23.3%) reported CLS at week 48, while 23 men (31.5%) continued not to report CLS. The total prevalence of CLS among the 73 men at week 48 was 61.6% (Figure 8.4B).

CLS-C showed a slight decreasing trend from week 12 to week 48. For the analysis of CLS-C, I only used data from 70 men (three missing responses) who completed both questionnaires. Of 70, 20 men reported CLS-C at week 12 (28.6%), and of these 20, ten men (14.3%) continued to report CLS-C at week 48, while ten men (14.3%) did not report CLS-C. 50 men out of 70 (71.4%) did not report CLS-C at week 12; of these, eight men (11.4%) reported CLS-C at week 48, and 42 men (60.1%) continued not to report CLS-C. The total reported CLS-C at week 48 was 25.7% (Figure 8.4C).

An increase at week 48 was seen in the within-individual frequency of CLS-D. Of 73, ten men (13.7%) reported CLS-D at week 12, of whom seven men (9.6%) continued to report CLS-D at week 48, three men (4.1%) stopped reporting this behaviour. 63 men out of 73 (86.3%) did not report CLS-D; of these, 19 men (26.0%) reported CLS-D at week 48, 44 men (60.3%) continued not to report CLS-D. The total prevalence of CLS-D at week 48 was 35.6% (Figure 8.4D).

The tendency to report one regular partner, one casual partner, two to four partners, and 5–10 partners from baseline until week 48 was stable (Figure 8.5A, 8.5B, 8.5C, and 8.5D); however, men tended to reduce reporting more than ten partners after HIV diagnosis (Figure 8.5E), as also already shown in Figure 8.3.

Figure 8.4 Within-person changes in the frequency of any sex (panel A), condomless sex (panel B), seroconcordant condomless sex (panel C) and serodiscordant condomless sex (panel D) over time

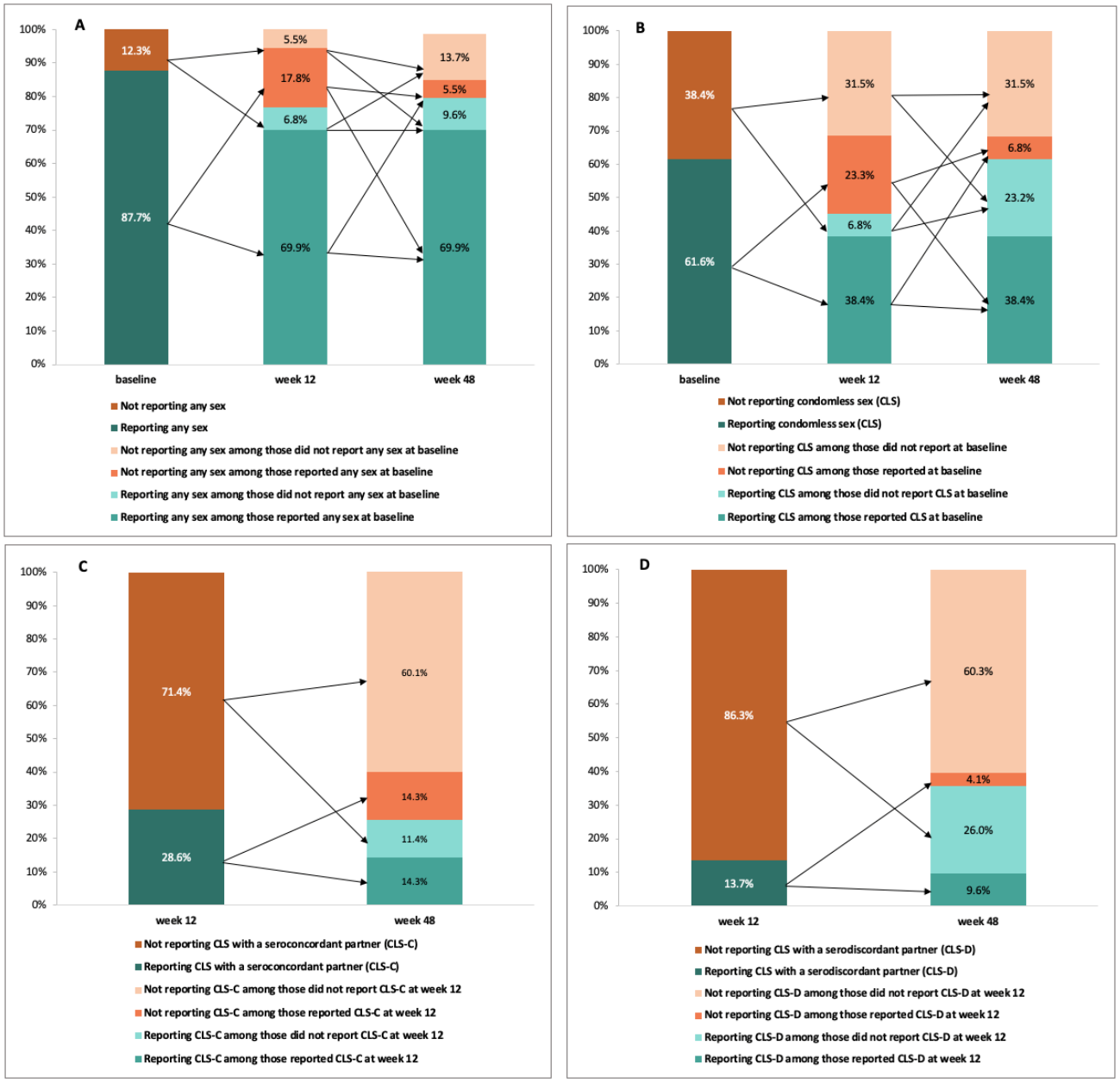
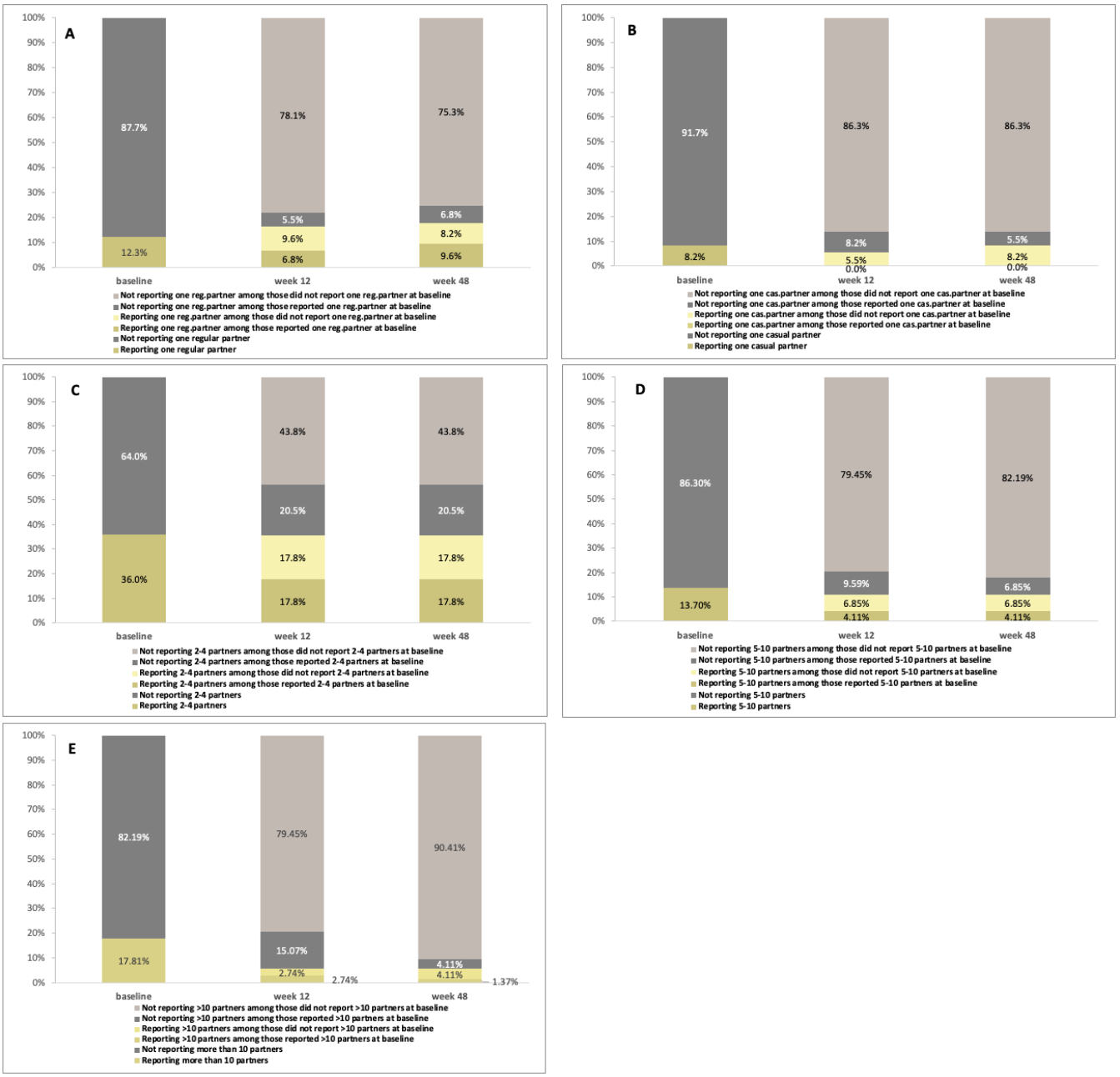


Figure 8.5 Within-person changes in frequency of reporting (A) one regular partner, (B) one casual partner, (C) 2–4 partners, (D) 5–10 partners, and (E) more than 10 partners over time



8.3.4 Factors associated with sexual behaviour at week 12 and 48

The unadjusted association of factors with any sex, CLS, CLS-C, and CLS-D are shown in Table 8.4. I did not include baseline data (total questionnaires used 160) because CLS-C and CLS-D were not measured at baseline and to focus the associations during the initial period after diagnosis (three months – one year).

When compared to men who reported no recreational drug use, the odds of having any sex (OR 2.90, 95% CI 1.39–6.05, p<0.001), CLS (OR 3.04, 95% CI 1.48–6.22, p=0.002), and CLS-C (OR 4.29, 95% CI 1.59–11.62, p=0.004), was significantly greater in men who reported recreational drug use. Participants who viewed that 'condoms are not necessary when HIV viral load is undetectable' had an increased odds of having any sex (OR 2.43, 95% CI 1.33–4.47, p=0.004), CLS (OR 3.33, 95% CI 1.56–7.10, p=0.002), and CLS-D (OR 2.99, 95% CI 1.36 –6.56, p=0.006). The odds of having CLS (OR 1.83, 95% CI 1.12–2.99, p=0.017) and CLS-D (OR 3.59, 95% CI 1.80–7.17, p<0.001) increased at week 48 compared to week 12. Men who reported STI diagnosis also had greater odds of reporting any sex (OR 1.82, 95% CI 1.00–3.30, p=0.050). Not having started ART yet at baseline (OR 4.76, 95% CI 1.04–21.77, p=0.044) was associated with CLS-C. The odds of having CLS-D was also greater in more recent year (OR for the year 2017/2018 versus 2015 4.13, 95% CI 1.21 – 14.08, global p=0.050).

The associations remained statistically significant after adjustment for age, ethnicity, country of birth, and education (Table 8.5). There were no significant associations of age group, ethnicity, country of birth, employment, housing status, difficulty to pay for the heating cost, benefits, disclosure of HIV status to others, depressive symptoms, and alcohol dependency symptoms, with any sex, any CLS, CLS-C, and CLS-D (Table 8.4 and Table 8.5**)**.

When factors were analysed separately for week 12 and week 48, similar results were observed (Table 8.6). Recreational drug use was associated with CLS and CLS-C both at week 12 and week 48. A view that it is unnecessary to use a condom if viral load is undetectable was associated with increased odds of reporting CLS and CLS-D at week 48. Having an HIV partner was associated with increased odds of reporting CLS at week 12. No factors were found to be significantly associated with CLS-D at week 12.

Table 8.4 Unadjusted associations of factors with any sex, condomless sex, seroconcordant condomless sex, and serodiscordant condomless sex among 90 newly diagnosed HIV-positive men who have sex with men in the Guy's and St. Thomas' observational study (n=160 observations from week 12 and week 48)*

Characteristics	Any sex†		Condomless sex†		CLS-C‡		CLS-D§	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age								
< 25	ref	0.604	ref	0.786	ref	0.266	ref	0.513
25 – 29	0.35 (0.01 – 10.16)		0.31 (0.05 – 1.95)		0.31 (0.06 – 1.49)		0.83 (0.19 – 3.64)	
30 – 34	0.58 (0.18 – 18.71)		0.41 (0.06 – 2.95)		0.64 (0.13 – 3.23)		0.56 (0.09 – 3.18)	
35 – 39	0.30 (0.01 – 9.76)		0.37 (0.05 – 2.60)		0.25 (0.05 – 1.34)		1.38 (0.29 – 6.60)	
40 – 44	0.38 (0.01 – 13.44)		0.32 (0.04 – 2.51)		0.66 (0.12 – 3.52)		0.31 (0.04 – 2.45)	
≥ 45	0.35 (0.01 – 11.34)		0.39 (0.05 – 2.89)		0.25 (0.05 – 1.32)		1.15 (0.24 – 5.54)	
Ethnicity								
White	ref	0.316	ref	0.904	ref	0.274	ref	0.132
Other ethnicity	1.99 (0.52 – 7.74)		1.06 (0.43 – 2.58)		0.55 (0.18 – 1.61)		2.10 (0.80 – 5.51)	
Country of birth								
UK	ref	0.620	ref	0.993	ref	0.707	ref	0.733
Outside the UK	1.20 (0.49 – 3.28)		0.99 (0.48 – 2.08)		1.17 (0.51 – 2.66)		0.87 (0.38 – 1.95)	
University education status								
Yes	ref	0.485	ref	0.709	ref	0.973	ref	0.559
No	0.71 (0.27 – 1.86)		0.86 (0.39 – 1.89)		0.98 (0.42 – 2.30)		0.76 (0.30 – 1.90)	
Employment status								
Full time / part time employment	ref	0.632	ref	0.711	ref	0.563	ref	0.676
Unemployed / other	1.31 (0.43 – 3.96)		1.20 (0.46 – 3.16)		1.33 (0.50 – 3.54)		0.78 (0.24 – 2.52)	
Housing status								
Homeowner	ref	0.369	ref	0.277	ref	0.508	ref	0.125
Renting	0.67 (0.24 – 1.92)		0.66 (0.29 – 1.51)		0.60 (0.23 – 1.61)		1.01 (0.32 – 3.13)	
Other	1.36 (0.30 – 6.06)		1.55 (0.39 – 6.13)		0.42 (0.07 – 2.38)		4.25 (0.83 – 21.84)	
Difficulty to pay for heating cost								
Yes	ref	0.272	ref	0.661	ref	0.385	ref	0.755
No	1.56 (0.70 – 3.45)		1.18 (0.56 – 2.52)		1.59 (0.55 – 4.59)		0.86 (0.32 – 2.27)	
Receive benefits								

Characteristics	Any sex†		Condomless sex†		CLS-C‡		CLS-D§	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Yes	ref	0.268	ref	0.839	ref	0.904	ref	0.509
No	2.35 (0.52 – 10.71)		1.16 (0.27 – 5.06)		1.14 (0.14 – 9.37)		2.26 (0.20 – 25.35)	
In relationship status								
No	ref	0.488	ref	0.997	ref	0.272	ref	0.315
Yes, living with partner	1.66 (0.64 – 4.31)		0.97 (0.44 – 2.13)		1.59 (0.71 – 3.56)		0.55 (0.24 – 1.24)	
Yes, not living with partner	1.44 (0.66 – 3.09)		1.00 (0.41 – 2.48)		0.70 (0.24 – 2.03)		1.02 (0.38 – 2.73)	
Have a partner with HIV								
No	ref		ref	0.069	ref	0.095	ref	0.872
Yes	1 (success perfectly)		4.05 (0.89– 18.36)		2.91 (0.83 – 10.22)		1.13 (0.26 – 4.79)	
Disclosure of HIV status to others								
Yes	ref	0.167	ref	0.186	ref	0.626	ref	0.225
No	0.57 (0.25 – 1.27)		0.53 (0.21 – 1.35)		0.80 (0.33 – 1.95)		0.49 (0.16 – 1.54)	
Ever taken ART at baseline								
Yes	ref	0.113	ref	0.285	ref	**0.044**	ref	0.531
No	2.66 (0.79 – 8.95)		1.80 (0.61 – 5.29)		**4.76 (1.04 – 21.77)**		0.72 (0.26 – 2.00)	
Recreational drug use in the past 3 months								
No	ref	**0.004**	ref	**0.002**	ref	**0.004**	ref	0.631
Yes	**2.90 (1.39 – 6.05)**		**3.04 (1.48 – 6.22)**		**4.29 (1.59 – 11.62)**		1.21 (0.55 – 2.67)	
STI diagnosis in the past 3 months								
No	ref	**0.050**	ref	0.707	ref	0.565	ref	0.921
Yes	**1.82 (1.00 – 3.30)**		1.16 (0.53 – 2.53)		1.26 (0.57 – 2.77)		0.95 (0.39 – 2.35)	
Depressive symptoms (PHQ-9 score ≥10)								
No	ref	0.778	ref	0.182	ref	0.114	ref	0.623
Yes	1.26 (0.25 – 6.45)		0.47 (0.15 – 1.43)		0.30 (0.07 – 1.33)		0.73 (0.22 – 2.50)	
Alcohol dependency symptoms (CAGE score ≥2)								
No	ref	0.717	ref	0.742	ref	0.985	ref	0.960
Yes	0.76 (0.18 – 3.28)		1.22 (0.37 – 4.06)		0.99 (0.29 – 3.41)		1.03 (0.35 – 3.05)	
Views on HIV transmission risk								

Characteristics	Any sex†		Condomless sex†		CLS-C‡		CLS-D§	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Agree to statement: A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load								
No	ref	0.637	ref	0.370	ref	0.806	ref	0.307
Yes	0.85 (0.43 – 1.67)		1.63 (0.56 – 4.79)		0.85 (0.24 – 3.05)		2.45 (0.44 – 13.66)	
Agree to statement: If an HIV positive person's viral load is undetectable, it is not necessary to use a condom								
No	ref	**0.004**	ref	**0.002**	ref	0.458	ref	**0.006**
Yes	**2.43 (1.33 – 4.47)**		**3.33 (1.56 – 7.10)**		1.32 (0.63 – 2.78)		**2.99 (1.36 – 6.56)**	
Visit								
12 weeks	ref	0.694	ref	**0.017**	ref		ref	
48 weeks	1.11 (0.65 – 1.91)		**1.83 (1.12 – 2.99)**		0.82 (0.45 – 1.49)	0.524	**3.59 (1.80 – 7.17)**	**<0.001**
Calendar Year								
2015	ref	0.403	ref	0.808	ref	0.192	ref	**0.050**
2016	0.62 (0.27 – 1.41)		1.20 (0.68 – 2.14)		0.89 (0.44 – 1.79)		2.11 (0.71 – 6.31)	
2017 / 2018	0.82 (0.30 – 2.22)		1.22 (0.55 – 2.72)		0.42 (0.15 – 1.15)		**4.13 (1.21 – 14.08)**	

*Ethnicity, country of birth, education, ever taken ART were fixed variables derived from baseline questionnaires: all other variables were time-updated variables at week 12 and 48

† Total complete observations for any sex and CLS: 160; housing status: 154 observations; difficulty to pay for heating and ever taken ART: 156 observations. No missing data for the other variables in the table

‡ Total complete observations for CLS-C: 156; housing status: 150 observations; difficulty to pay for heating and ever taken ART: 152 observations

§ Total complete observations for CLS-D: 160; housing status: 154 observations; difficulty to pay for heating and ever taken ART: 156 observations

OR odds ratio, CI confidence interval, CLS condomless sex, STI sexually transmitted infection, PHQ-9 patient health questionnaire-9, CAGE alcohol questionnaire

Table 8.5 Adjusted associations of factors with any sex, condomless sex, seroconcordant condomless sex, and serodiscordant condomless sex among 90 newly diagnosed HIV-positive men who have sex with men in the St. Thomas observational study (n=160 observations from week 12 and week 48)*

Characteristics	Any sex†		condomless sex†		CLS-C‡		CLS-D§	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Age					156 obs			
< 25	ref	0.692	ref	0.775	ref	0.272	ref	0.611
25 – 29	0.33 (0.02 – 6.91)		0.30 (0.04 – 2.02)		0.38 (0.08 – 1.82)		0.58 (0.12 – 2.74)	
30 – 34	0.59 (0.03 – 13.18)		0.40 (0.05 – 2.97)		0.73 (0.14 – 3.88)		0.44 (0.07 – 2.79)	
35 – 39	0.33 (0.01 – 7.92)		0.37 (0.05 – 2.73)		0.27 (0.05 – 1.51)		1.21 (0.25 – 5.77)	
40 – 44	0.39 (0.01 – 10.22)		0.31 (0.04 – 2.62)		0.67 (0.11 – 3.85)		0.30 (0.04 – 2.17)	
≥ 45	0.38 (0.02 – 8.89)		0.38 (0.05 – 3.08)		0.25 (0.05 – 1.36)		1.09 (0.23 – 5.21)	
Ethnicity					156 obs			
White	ref	0.535	ref	0.831	ref	0.241	ref	0.102
Other ethnicity	1.54 (0.39 – 6.07)		1.11 (0.42 – 2.90)		0.51 (0.17 – 1.56)		2.39 (0.84 – 6.83)	
Country of birth								
UK	ref	0.773	ref	0.952	ref	0.849	ref	0.853
Outside the UK	1.16 (0.42 – 3.24)		0.98 (0.45 – 2.09)		1.09 (0.45 – 2.62)		0.93 (0.42 – 2.06)	
University education status								
Yes	ref	0.611	ref	0.652	ref	0.764	ref	0.735
No	0.77 (0.29 – 2.06)		0.82 (0.35 – 1.92)		0.87 (0.36 – 2.11)		0.84 (0.31 – 2.28)	
Employment status								
Full time / part time employment	ref	0.543	ref	0.669	ref	0.369	ref	0.574
Unemployed / other	1.42 (0.46 – 4.39)		1.24 (0.46 – 3.33)		1.56 (0.59 – 4.12)		0.70 (0.21 – 2.39)	
Housing status								
Homeowner	ref	0.687	ref	0.959	ref	0.212	ref	0.265
Renting	0.52 (0.16 – 1.61)		0.61 (0.24 – 1.56)		0.45 (0.13 – 1.49)		1.07 (0.27 – 4.22)	
Other	1.02 (0.18 – 5.82)		1.38 (0.29 – 6.45)		0.27 (0.03 – 2.76)		4.56 (0.55–37.79)	
Difficulty to pay for heating cost								
Yes	ref	0.322	ref	0.687	ref	0.375	ref	0.671
No	1.52 (0.66 – 3.49)		1.17 (0.55 – 2.49)		1.62 (0.56 – 4.75)		0.81 (0.30 – 2.18)	
Receive benefits								
Yes	ref	0.431	ref	0.941	ref	0.900	ref	0.510
No	1.86 (0.39 – 8.65)		1.06 (0.23 – 4.94)		0.86 (0.09 – 8.19)		2.31 (0.19–27.79)	

Characteristics	Any sex†		condomless sex†		CLS-C‡		CLS-D§	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
In relationship status								
No	ref	0.255	ref	0.930	ref	0.260	ref	0.109
Yes, living with partner	1.69 (0.65 – 4.35)		0.96 (0.43 – 2.13)		1.64 (0.71 – 3.79)		0.52 (0.24 – 1.13)	
Yes, not living with partner	1.46 (0.62 – 3.45)		1.00 (0.41 – 2.48)		0.77 (0.26 – 2.22)		0.92 (0.35 – 2.46)	
Have a partner with HIV								
No	1 (success	-	ref	0.066	ref	0.108	ref	0.730
Yes	perfectly)		4.19 (0.91– 19.35)		2.75 (0.80 – 9.44)		1.25 (0.35 – 4.53)	
Disclosure of HIV status to others								
Yes	ref	0.143	ref	0.189	ref	0.699	ref	0.157
No	0.54 (0.23 – 1.23)		0.53 (0.21 – 1.36)		0.83 (0.32 – 2.13)		0.45 (0.15 – 1.36)	
Ever taken ART at baseline								
Yes	ref	0.097	ref	0.225	ref	**0.025**	ref	0.431
No	2.88 (0.82 – 10.03)		2.02 (0.65 – 6.31)		**6.37 (1.27 – 32.03)**		0.63 (0.20 – 1.96)	
Recreational drug use in the past 3 months								
No	ref	**0.005**	ref	**0.003**	ref	**0.004**	ref	0.626
Yes	**3.03 (1.40 – 6.54)**		**3.03 (1.47 – 6.24)**		**4.56 (1.62 – 12.76)**		1.22 (0.54 – 2.74)	
STI diagnosis in the past 3 months								
No	ref	**0.038**	ref	0.715	ref	0.638	ref	0.938
Yes	**1.80 (1.03 – 3.15)**		1.15 (0.53 – 2.52)		1.21 (0.54 – 2.69)		1.04 (0.39 – 2.71)	
Depressive symptoms (PHQ-9 score ≥10)								
No	ref	0.738	ref	0.200	ref	0.115	ref	0.628
Yes	1.32 (0.26 – 6.85)		0.47 (0.15 – 1.49)		0.30 (0.07 – 1.34)		0.72 (0.18 – 2.77)	
Alcohol dependency symptoms (CAGE score ≥2)								
No	ref	0.918	ref	0.650	ref	0.930	ref	0.793
Yes	0.92 (0.19 – 4.42)		1.35 (0.37 – 4.95)		1.06 (0.29 – 3.89)		1.17 (0.36 – 3.86)	
Views on HIV transmission risk								
Agree to statement: A person on HIV treatment who has an undetectable viral load is less likely to transmit								

Characteristics	Any sex†		condomless sex†		CLS-C‡		CLS-D§	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
HIV to a sexual partner than someone with a high viral load								
No	ref	0.643	ref	0.384	ref	0.842	ref	0.354
Yes	0.85 (0.42 – 1.72)		1.63 (0.54 – 4.92)		0.87 (0.23 – 3.36)		2.39 (0.38–15.05)	
Agree to statement: If an HIV positive person's viral load is undetectable, it is not necessary to use a condom								
No	ref	**0.004**	ref	**0.002**	ref	0.369	ref	**0.008**
Yes	**2.55 (1.34 – 4.86)**		**3.41 (1.58 – 7.38)**		1.42 (0.66 – 3.07)		**3.02 (1.33 – 6.84)**	
Visit								
12 weeks	ref	0.696	ref	**0.016**	ref	0.603	ref	**<0.001**
48 weeks	1.11 (0.65 – 1.92)		**1.84 (1.12 – 3.02)**		0.85 (0.46 – 1.56)		**3.58 (1.78 – 7.21)**	
Calendar Year								
2015	ref	0.683	ref	0.607	ref	0.127	ref	**0.030**
2016	0.62 (0.27 – 1.40)		1.22 (0.68 – 2.19)		0.91 (0.44 – 1.87)		2.11 (0.69 – 6.40)	
2017 / 2018	0.81 (0.29 – 2.21)		1.24 (0.56 – 2.80)		0.45 (0.15 – 1.30)		**3.85 (1.08–13.69)**	

*OR adjusted for age, ethnicity, country of birth, and education.

† Total complete observations for any sex and CLS: 160; housing status: 154 observations; difficulty to pay for heating and ever taken ART: 156 observations. No missing data for the other variables in the table.

‡ Total complete observations for CLS-C: 156; housing status: 150 observations; difficulty to pay for heating and ever taken ART: 152 observations.

§ Total complete observations for CLS-D: 160; housing status: 154 observations; difficulty to pay for heating and ever taken ART: 156 observations.

aOR adjusted odds ratio, CI confidence interval, CLS condomless sex, STI sexually transmitted infection, PHQ-9 patient health questionnaire-9, CAGE alcohol questionnaire

Table 8.6 Factors associated with CLS, CLS-C and CLS-D at week 12 and week 48 among 90 newly diagnosed HIV-positive men who have sex with men in the St. Thomas observational study *

Characteristics	CLS at week 12†		CLS at week 48‡		CLS-C at week 12§		CLS-C at week 48₴		CLS-D at week 12€		CLS-D at week 48£	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age												
< 25	ref	0.552	ref	0.691	ref	0.386	ref	0.699	ref	0.893	ref	0.237
25 – 29	0.35 (0.05 – 2.49)		0.44 (0.04 – 5.09)		0.23 (0.03 – 1.79)		0.40 (0.02 – 7.63)		1.07 (0.01 – 13.02)		0.40 (0.02 – 7.63)	
30 – 34	0.44 (0.06 – 3.15)		0.80 (0.21 – 3.06)		0.70 (0.11 – 4.59)		0.43 (0.02 – 9.56)		0.31 (0.02 – 6.07)		0.67 (0.03 – 14.3)	
35 – 39	0.22 (0.03 – 1.77)		1.40 (0.26 – 7.67)		0.30 (0.04 – 2.37)		0.17 (0.01 – 3.97)		0.42 (0.02 – 8.19)		1.33 (0.07 – 26.4)	
40 – 44	0.90 (0.12 – 6.86)		1.50 (0.32 – 7.06)		0.86 (0.12 – 6.02)		0.62 (0.03 – 12.65)		0.83 (0.06 – 11.59)		0.08 (0.01 – 2.66)	
≥ 45	0.44 (0.06 – 3.15)		0.52 (0.11 – 2.30)		0.25 (0.03 – 1.95)		0.23 (0.01 – 4.94)		1.07 (0.09 – 13.02)		0.78 (0.04 – 15.0)	
Ethnicity												
White	ref	0.518	ref	0.526	ref	0.116	ref	0.894	ref	0.100	ref	0.444
Other ethnicity	0.69 (0.22 – 2.15)		1.47 (0.45 – 4.79)		0.28 (0.06 – 1.37)		0.92 (0.26 – 3.28)		3.22 (0.79 – 12.98)		1.55 (0.50 – 4.82)	
Country of birth												
UK	ref	0.599	ref	0.646	ref	0.625	ref	1.00	ref	0.767	ref	0.659
Outside the UK	1.27 (0.52 – 3.05)		0.80 (0.31 – 2.06)		1.28 (0.48 – 3.41)		0.98 (0.35 – 2.77)		1.22 (0.32 – 4.58)		0.81 (0.31 – 2.09)	
Education												
University	ref	0.217	ref	0.086	ref	0.629	ref	0.597	ref	0.140	ref	0.352
In between secondary level and university	2.58 (0.88 – 7.53)		0.37 (0.12 – 1.15)		1.69 (0.57 – 4.98)		0.78 (0.20 – 2.65)		2.72 (0.72 – 10.28)		0.44 (0.12 – 1.55)	
Secondary or high school	1.11 (0.27 – 4.64)		0.25 (0.05 – 1.19)		1.01 (0.17 – 5.87)		0.34 (0.04 – 3.07)		1.00 ~		0.48 (0.09 – 2.62)	
Employment status												
Full time / part time employment	ref	0.859	ref	0.753	ref	0.696	ref	0.615	ref	0.604	ref	0.884
Unemployed / other	1.11 (0.33 – 3.82)		1.27 (0.29 – 5.57)		1.30 (0.34 – 4.98)		1.47 (0.33 – 6.59)		0.56 (0.06 – 4.92)		0.89 (0.20 – 3.95)	
Housing status												
Homeowner	ref	0.698	ref	0.533	ref	0.776	ref	0.727	ref	0.742	ref	0.661
Renting	0.64 (0.23 – 1.79)		0.64 (0.19 – 2.19)		0.68 (0.23 – 2.07)		0.59 (0.16 – 2.13)		0.76 (0.17 – 3.31)		1.00 (0.29 – 3.45)	
Other	0.82 (0.09 – 7.11)		1.50 (0.22 – 10.45)		0.57 (0.05 – 6.71)		0.67 (0.09 – 4.64)		1.89 (0.14 – 25.18)		2.0 (0.34 – 11.69)	
Difficulty to pay for heating cost												
Yes	ref	0.883	ref	0.323	ref	0.474	ref	0.477	ref	0.333	ref	0.744
No	0.92 (0.29 – 2.91)		1.79 (0.56 – 5.73)		1.67 (0.41 – 6.73)		1.65 (0.41 – 6.69)		0.48 (0.11 – 2.11)		1.22 (0.37 – 4.08)	
Receive benefits												
Yes	ref	0.728	ref	0.862	ref	0.784	ref	0.781	ref		ref	0.936
No	1.39 (0.22 – 8.88)		0.80 (0.07 – 9.43)		1.38 (0.13 – 14.2)		0.70 (0.06 – 8.34)		1.00		1.10 (0.09 – 13.0)	
In relationship status												
No	ref	0.979	ref	0.933	Ref	0.201	ref	0.718	ref	0.193	ref	0.845
Yes, living with partner	0.97 (0.37 – 2.51)		0.87 (0.31 – 2.43)		2.46 (0.86 – 7.01)		1.04 (0.34 – 3.14)		0.14 (0.02 – 1.18)		0.84 (0.29 – 2.39)	
Yes, not living with partner	1.10 (0.32 – 3.76)		0.79 (0.21 – 3.03)		1.07 (0.24 – 4.89)		0.52 (0.09 – 2.83)		0.67 (0.12 – 3.63)		1.26 (0.33 – 4.84)	
Have a partner with HIV												
No	ref	**0.030**	ref	0.730	ref	0.060	ref		ref	0.402	ref	0.671
Yes			0.61 (0.03 – 10.31)				1.00		2.09 (0.37 – 11.81)		1.85 (0.11 – 31.32)	

Characteristics	CLS at week 12†		CLS at week 48‡		CLS-C at week 12§		CLS-C at week 48ǂ		CLS-D at week 12€		CLS-D at week 48£	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
	10.75 (1.26–91.50)				4.33 (0.94 – 20.03)							
Disclosure of HIV status to others Yes No	ref 0.56 (0.17 – 1.84)	0.336	ref 0.58 (0.13 – 2.56)	0.473	ref 0.85 (0.24 – 3.07)	0.813	ref 0.93 (0.17 – 5.07)	0.929	ref 0.46 (0.05 – 3.98)	0.482	ref 0.57 (0.11 – 3.09)	0.518
Ever taken ART at baseline Yes No	ref 2.90 (0.70–11.94)	0.140	ref 1.63 (0.48 – 5.52)	0.431	ref 4.91 (0.58 – 41.7)	0.145	ref 5.43 (0.65 – 45.46)	0.119	ref 1.64 (0.19 – 14.43)	0.656	ref 0.61 (0.18 – 2.07)	0.431
Recreational drug use in the past 3 months No Yes	ref **5.14 (1.53–17.23)**	**0.008**	ref **4.77 (1.75 – 13.01)**	**0.002**	ref **11.67 (1.44–94.52)**	**0.021**	ref **3.47 (1.02 – 11.78)**	**0.046**	ref 1.47 (0.29 – 7.53)	0.642	ref 1.93 (0.71 – 5.29)	0.198
STI diagnosis in the past 3 months No Yes	ref 2.33 (0.88 – 6.21)	0.090	ref 1.52 (0.35 – 6.46)	0.573	ref 1.38 (0.48 – 3.91)	0.547	ref 1.23 (0.28 – 5.37)	0.778	ref 2.37 (0.64 – 8.73)	0.195	ref 1.24 (0.32 – 4.91)	0.753
Depressive symptoms (PHQ-9 score ≥10) No Yes	ref 0.43 (0.12 – 1.54)	0.197	ref 0.45 (0.11 – 1.84)	0.264	ref 0.39 (0.08 – 1.96)	0.253	ref 0.31 (0.04 – 2.74)	0.296	ref 0.51 (0.06 – 4.40)	0.539	ref 0.89 (0.20 – 3.95)	0.884
Alcohol dependency symptoms (CAGE score >2) No Yes	ref 0.81 (0.17 – 3.90)	0.794	ref 1.27 (0.29 – 5.57)	0.753	ref 1.11 (0.19 – 6.56)	0.909	ref 0.78 (0.15 – 4.14)	0.768	ref 1.00 (empty observations)		ref 1.53 (0.37 – 6.31)	0.556
Views on HIV transmission risk Agree to statement: A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner No Yes Agree to statement: If an HIV positive person's viral load is undetectable, it is not necessary to use a condom No Yes	ref 1.10 (0.31 – 3.97) ref 2.70 (0.99 – 7.37)	0.878 0.053	ref 1.69 (0.31 – 9.10) ref **6.52 (1.95 – 21.83)**	0.540 **0.002**	ref 0.49 (0.13 – 1.80) ref 1.69 (0.58 – 4.88)	0.283 0.335	ref 1.86 (0.20 – 17.24) ref 1.20 (0.42 – 3.45)	0.583 0.735	ref 1.00 (omitted due to collinearity) ref 1.62 (0.42 – 6.22)	 0.479	ref 1.11 (0.19 – 6.57) ref **4.48 (1.63 – 12.35)**	0.908 **0.004**

*Ethnicity, country of birth, education, and ever taken ART were derived from baseline questionnaires: all other variables were time-updated variables at week 12 and week 48; multivariable models adjusted for age, ethnicity, country of birth, and education did not change the associations.

Characteristics	CLS at week 12†		CLS at week 48‡		CLS-C at week 12§		CLS-C at week 48⁼		CLS-D at week 12€		CLS-D at week 48£	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value

† housing status: 83 observations; difficulty to pay for heating: 83 observations; ever taken ART: 82 observations; other variables no missing questionnaires
‡ housing status: 71 observations; difficulty to pay for heating: 73 observations; ever taken ART: 74 observations; other variables no missing questionnaires
§ housing status and difficulty to pay for heating: 79 observations and ever taken ART: 78 observations; other variables no missing questionnaires
⁼ housing status: 71 observations; difficulty to pay for heating: 73 observations and ever taken ART: 74 observations; other variables no missing questionnaires
€ housing status and difficulty to pay for heating: 83 observations; received benefits: 79 observations; ever taken ART: 82 observations; CAGE score: 77 observations; other variables no missing questionnaires
£ housing status: 71 observations; difficulty to pay for heating: 73 observations; ever taken ART: 74 observations; other variables no missing questionnaires
˜ omitted due to collinearity

OR odds ratio, CI confidence interval, CLS condomless sex, STI sexually transmitted infection, PHQ-9 patient health questionnaire-9, CAGE alcohol questionnaire

8.3.5 Factors associated with stopping CLS at week 12

Data from 52 men who reported CLS at baseline (56 men indicated CLS at baseline) and completed a questionnaire at week 12 were used for this analysis. Of the 52, 21 men reported no CLS at week 12. The only factor significantly associated with stopping CLS at week 12 was not reporting the use of recreational drugs in the previous three months (OR for reporting drug use versus no 0.21, 95% CI 0.05–0.86, *p*=0.030) (Table 8.7).

Table 8.7 Factors associated with stopping condomless sex at week 12 among 52 men who reported condomless sex at baseline in the St. Thomas observational study*

Characteristics	Stopping condomless sex at week 12**	
	OR (95% CI)	p-value
Age category, years		
< 25	ref	0.555
25 – 29	1.00 (0.18 – 5.45)	
30 – 34	0.80 (0.14 – 4.61)	
35 – 39	1.50 (0.25 – 8.98)	
40 – 44	0.17 (0.01 – 1.95)	
≥ 45	1 (empty observations) ~	
Ethnicity		
White	ref	0.259
Other ethnicity	2.33 (0.54 – 10.16)	
Country of birth		
UK	ref	0.090
Outside the UK	3.11 (0.84 – 11.55)	
Education		
University	ref	0.326
In between secondary level and university	0.33 (0.08 – 1.41)	
Secondary or high school	0.80 (0.11 – 5.53)	
Employment		
Full time / part time employment	ref	0.688
Unemployed / other	1.35 (0.31 – 5.85)	
Housing status		
Homeowner	ref	0.523
Renting	2.28 (0.52 – 9.98)	
Other	3.00 (0.13 – 66.25)	
Difficulty to pay for heating cost		
Yes	ref	0.570
No	1.67 (0.29 – 9.70)	
Receive benefits		
Yes	ref	0.331
No	0.29 (0.02 – 3.51)	
In relationship status		
No	ref	0.696
Yes, living with partner	1.56 (0.43 – 5.67)	
Yes, not living with partner	1.78 (0.39 – 8.02)	
Have a partner with HIV		
No	ref	0.098

Characteristics	Stopping condomless sex at week 12**	
	OR (95% CI)	p-value
Yes	0.16 (0.02 – 1.40)	
Disclosure of HIV status to others		
Yes	ref	0.941
No	1.07 (0.16 – 7.19)	
Ever taken ART at baseline		
Yes	ref	0.316
No	0.38 (0.06 – 2.53)	
Recreational drug use in the past 3 months		
No	ref	**0.030**
Yes	**0.21 (0.05 – 0.86)**	
STI diagnosis in the past 3 months		
No	ref	0.746
Yes	0.82 (0.24 – 2.75)	
Depressive symptoms (PHQ-9 score ≥10)		
No	ref	0.150
Yes	2.33 (0.73 – 7.40)	
Alcohol dependency symptoms (CAGE score >2)		
No	ref	
Yes	(omitted due to collinearity)	
Views on HIV transmission risk		
Agree to statement: *A person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner*		
No	ref	0.544
Yes	0.59 (0.10 – 3.29)	
Agree to statement: *If an HIV positive person's viral load is undetectable, it is not necessary to use a condom to prevent transmission of HIV*		
No	ref	0.482
Yes	0.64 (0.18 – 2.24)	

*Ethnicity, country of birth, education, and ever taken ART were derived from baseline questionnaires: all other variables were time-updated in week 12, education classified into three
** housing status: 51 observations; CAGE score: 49 observations.
~ omitted due to collinearity

OR odds ratio, CI confidence interval, CLS condomless sex, STI sexually transmitted infection, PHQ-9 patient health questionnaire-9, CAGE alcohol questionnaire

8.4 Discussion

8.4.1 Summary of results

Using data collected from a prospective cohort of 90 GBMSM attending Guy's and St. Thomas' NHS Foundation Trust in London, the sexual behaviour of newly diagnosed GBMSM over a one-year follow-up period was examined, and factors associated with sexual behaviours after being diagnosed with HIV were assessed. The results of this chapter demonstrated that a high proportion of GBMSM with new HIV diagnoses continued to have sex, with the majority having CLS. The prevalence of CLS tended to return to baseline levels within 48 weeks, and a substantial increase in CLS-D was observed from week 12 to week 48. The proportion of men having CLS-D while not receiving ART or with the most recent documented plasma viral load (VL) >200c/mL at a year after an HIV diagnosis was low (1.3%); however, at week 12, the proportion was almost 11%.

Condomless sex was associated with recreational drug use and an understanding that condom use is not required when the viral load is undetectable. This coincided with U=U publications and increased over the duration of the study.

8.4.2 Changes in sexual behaviour post-HIV diagnosis in the UK and other high-income countries among GBMSM in the era of TaSP and U=U

To my knowledge, this study provides the first longitudinal analysis of changes in sexual behaviour among GBMSM in the first year of their HIV diagnosis in England and the UK. A cohort study published in 2009 among 98 GBMSM in England with primary HIV infection showed an increase in the proportion of men always using condoms during anal intercourse and an overall shift towards fewer sexual partners in the 12 weeks following an HIV diagnosis (143). However, in the study, there were no data on HIV transmission risk behaviour (defined as CLS with regular or casual partners of unknown or negative HIV status or incident STI) after three months of follow-up (143).

Findings in this chapter complement prior international longitudinal and cross-sectional studies, which together suggest a pattern of evolving sexual behaviour following HIV diagnosis (236, 239, 358, 360). The US cohorts reported that men rapidly and profoundly decreased behaviours likely to transmit HIV infection in the period immediately following diagnosis and increased serosorting and main partnering (145, 361). Studies from the pre-TasP era (the early 2000s) also reported that the rebound of CLS practice was after nine months with HIV-negative partners (360, 362).

In the Guy's and St. Thomas GBMSM cohort, there was a reduction in CLS practice and any sex in the three months following men's enrolment in the study by only approximately 10%. This is concerning, as it is likely that the viral load would still be detectable for a significant proportion of men during this time, which confirmed by the data that at week 12, almost 11% of men who reported CLS with HIV-negative partners also had a detectable viral load. This perhaps reflects men's greater confidence in HIV treatment due to the increasing publicity around U=U. The Guy's and St. Thomas' study was conducted at around the same time the results from the PARTNER study were published (presented in 2014, the paper published in 2016), and the U=U consensus statement was launched in 2016 (32, 33, 93). Therefore, participants might have been more informed and aware of the effectiveness of ART in reducing transmission. Baseline data confirms that more than 80% of men were aware of U=U. The interpretation is that the TasP and U=U concepts make people more confident and comfortable having sex without using condoms.

There seemed to be no reduction in number of sex partners in this study at an individual level, except for reporting more than ten partners. This might be caused by the 'regression to the mean' effect, i.e. participants were selected at the point when they were more likely to have a high prevalence of recent multiple sex partners, then, over time, the prevalence of this behaviour would regress towards the prevalence in the unselected population or decline as the study progressed (363). A longitudinal study in 1,044 MSM participating in the Multicenter AIDS Cohort Study, MACS, (348 seroconverting, 348 seronegative, and 348 seroprevalent participants matched on demographics, recruitment cohort, and study visits) previously reported in 2018 that there was no evidence for abrupt or substantial changes in risky behaviours post-seroconversion, including number of sexual partners (227). However, there was substantial variation at the individual level, with the factors underlying this variation not well understood.

8.4.3 Factors associated with sexual behaviour post-HIV diagnosis among GBMSM

Perhaps among factors influencing sexual behaviour, the most important one among men in this study was an understanding of the reduced risk of HIV transmission due to the suppressive effect of ART on the viral load, which was significantly associated with increased odds of reporting any sex, CLS, and serodiscordant CLS. Results from a French cohort, the ANRS-PRIMO (2000-2017, N=1,364), have previously reported that among men followed prospectively since a primary infection, the main reason for not using condoms was '*being on ART or having undetectable viral load*', suggesting that the HIV-positive GBMSM population was aware of treatment as prevention (358). The cohort also observed an increase in CLS, regardless of the HIV status of sexual partners over calendar time.

Even before it was demonstrated that the risk of HIV transmission in a person with undetectable viral load is zero, limited longitudinal studies had suggested a complex relationship between people's perception of viral load or other treatment-related optimism and individual decisions to engage in sexual risk-taking (236, 364, 365). Previous data from the ANRS-PRIMO cohort (2000-2009) reported that men with detectable viral loads reported sexual risk behaviours as frequently as those with undetectable viral loads (365). A longitudinal study of treatment optimism and HIV acquisition and transmission risk behaviours among 1,515 Black GBMSM who were recruited between 2009 and 2010 in six US cities (HPTN 061) reported that treatment-related optimism was independently associated with subsequent condomless anal sex with a serodiscordant male partner among HIV infected men (364). A study of 206 GBMSM seroconverters participating in the Amsterdam Cohort Study (ACS) between 1984 and 2008 reported that rebound of sexual risk behaviour seemed evident in the combination ART (cART) era, and the period of condom use during anal sex after HIV diagnosis was significantly shorter than that in the pre-cART period (236). However, in a cross-sectional study carried out in the UK in 2011–2012, GBMSM with self-reported detectable viral load tended to be less likely to report condomless sex with serodiscordant partners than their counterparts self-reported undetectable viral load (366). A desirability bias might have led to underestimating at-risk behaviours when viral load was detectable in this study.

In line with previous cross-sectional and longitudinal findings in the UK, recreational drug use was associated with condomless sex among HIV-positive men (321, 367). The prevalence of recreational drug use was overall high (68.4%, 171/250) and higher than a study of UK GBMSM living with HIV carried out at a similar time and that involved a larger number of clinics across England (ASTRA study, 51%) (321). Recreational drug use was not associated with CLS-D at week 12 or week 48 among men in this study. This is consistent with results from the ASTRA study which found that recreational drug use linked to serosorting (313).

Unlike this study that found no evidence of a link between depressive symptoms and sexual behaviour, associations between depression and risky behaviours have been shown in some US studies of HIV-positive GBMSM cohorts (368-370). The overall prevalence (baseline until week 48) of depressive symptoms among men in the Guy's and St.Thomas study was twice as high as the general population (17.6%, 44/250), while the ASTRA study reported a prevalence of 27.1% (371). An online survey among 278 HIV-positive GBMSM in the UK and Ireland found that both anxiety and depression were positively predicted by internalised and enacted stigma, suggesting the continued psychological burden associated with HIV infection among GBMSM, even as community support services are available in the UK

(372). The results point to the need for clinicians and policymakers to implement stigma reduction interventions among this population.

8.4.4 Limitations

The main strengths of this study are its longitudinal nature, the high retention rate, and the relatively few missing data for sexual behaviour and other socio-demographic or lifestyle variables.

Regarding the study limitations, the relatively small number of participants in this study means that results should be interpreted carefully. Power is limited to assess associations, and some confidence intervals are very wide. The findings may not be generalisable to all GBMSM living in the UK, as data were collected in a single clinical site in London, with White ethnicity dominating the sample. Sexual behaviour data over the prior three months were self-reported, which can be subject to recall bias and social desirability bias. However, this was minimised by the survey being completed confidentially and not with a health care staff (unless they asked for support). In addition, whether the increases in sexual behaviours are sustained over the longer term cannot be determined due to the relatively short follow-up.

Because there is a gap in risk behavior data (weeks 12–36), it is unknown when GBMSM returned to baseline levels of risk behavior. This information is crucial for the timing of interventions aimed at lowering risk behavior after HIV diagnosis, and it should be acquired in future studies. Furthermore, sexual behaviour questions at baseline referred to ‘past three months’ rather than ‘since diagnosis’, which has made the data hard to interpret as it referred to a period that was only partly before diagnosis. Therefore, in this analysis, factors were assessed for associations at weeks 12 and 48. Finally, participants' data on the type of STIs and recreational drugs (i.e. chemsex, injection drugs, other drugs) are not available; these relevant factors associated with sexual behaviours and modes to intervene need to be better characterised in further studies.

8.4.5 Conclusion

Despite the limitations, results from this chapter provide compelling evidence that highlights the existence of a relatively small proportion of men engaging in high-risk behaviour after HIV diagnosis despite not having undetectable viral load levels. Strong associations were found between condomless sex and recreational drug use and an understanding that condoms are unnecessary when viral load is undetectable (despite viral load not actually being undetectable in these men).

The implications of findings from this chapter and recommendations for future research are discussed in the final conclusion chapter of this thesis (Chapter 9).

Chapter 9: Implications of the thesis, directions for future research and final conclusion

9.1 Main thesis findings

Identifying those at the most significant risk of HIV and the situations in which HIV prevention strategies could have the most significant impact among gay, bisexual, and other men who have sex with men (GBMSM) remains a challenge. This PhD thesis aims to address these gaps in understanding, assist GBMSM to be aware of the possible risks, including the options of HIV prevention, and inform the delivery of HIV prevention interventions among GBMSM in the UK.

This thesis provides the first evidence from a longitudinal study in the UK regarding transitions between the different levels of sexual behaviour and predictors of transitions four months later among GBMSM attending sexual health clinics in England between 2015 and 2018. Using data from the same cohort of GBMSM, this thesis also provides important data regarding the longitudinal trends in PrEP use between 2013 and 2018, before PrEP was made freely available through the National Health Service England (NHSE) (4), source of PrEP and predictors of PrEP initiation. Furthermore, this thesis contains data on current trends in HIV incidence between 2013 and 2019 and characteristics predictive of HIV acquisition among GBMSM in England. Finally, this thesis presents the first data on longitudinal changes in sexual behaviour among newly diagnosed HIV GBMSM in the UK, from the time of diagnosis to one year after diagnosis, and the factors that influence these behaviours.

Having discussed the findings in the context of existing literature published from other countries and the UK in each relevant results chapter (Chapter 4 to 8), in this final chapter, I address the main findings of this thesis in terms of implications and recommendations for policy and future research.

9.1.1 Minor transitions between sexual behaviour levels among HIV-negative GBMSM

In Chapter 5, I characterized longitudinal patterns of sexual behaviour among HIV-negative GBMSM and determined the transitions between sexual behaviour levels based on participants' reported condomless anal sex with two or more partners, which I defined as 'higher-risk' and 'lower-risk' (one or no CLS partners). Results demonstrated that men exhibited a variation in the trajectory of condomless anal sex with two or more partners within an individual over time, with the tendency to remain consistent over time, and the

majority of men reported lower-risk behaviour over time during the online follow-up phase of the study (62%).

In the next four months, the estimated probability of engaging in higher-risk behaviour among men who reported higher-risk behaviour was 78% compared to only 12% for men who reported lower-risk behaviour. Calendar time, recent HIV tests, the use of PrEP and post-exposure prophylaxis (PEP) were the predictors of staying in higher-risk behaviour, while less stable housing status was a determinant of switching to lower-risk behaviour. Among men who reported lower-risk behaviour, the estimated probability of engaging in the same behaviour in the next four months was higher (88%) than the probability of engaging in the same behaviour among men who reported higher-risk behaviour. Less stable housing status was the predictor of staying in lower-risk behaviour, while recent HIV tests, PrEP and PEP use, recreational drugs, chemsex-associated drug and injection drugs, and bacterial STIs diagnosis in the past three months were the determinants of switching from lower-risk behaviour to higher-risk behaviour.

9.1.2 Considerable increase in PrEP use among HIV-negative GBMSM

In Chapter 6, I assessed trends in the use of PrEP between 2013 and 2018 before PrEP was available for free from the NHSE and predictors of PrEP initiation. The results demonstrated that the use of PrEP increased considerably between 2013 and 2018. A dramatic increase in PrEP use was also seen among men who self-reported engaging in CLS with two or more partners. Older age was an independent predictor of PrEP initiation, with the rate of initiation among men aged 40 years and older four times higher than among those younger than 25 years. Not being employed, having an insecure housing situation, and having less/no money for basic requirements were linked to a lower rate of starting PrEP or being on PrEP.

Certain sexual behaviours, such as condomless sex with numerous partners, group sex, taking an HIV test, and using non-injection-chemsex-related substances, were also linked to the choice to take PrEP in the prior three months. The rates of PrEP initiation among GBMSM in the AURAH2 study increased by more than 20 times in 2017/2018, when the PrEP Impact trial started the recruitment in 2017, compared with before 2015. The high proportion of men accessing PrEP online before the availability of the free PrEP programme in England was also due to the substantial advocacy efforts from community-based organisations and start-up websites such as PrEPster and IwantPrEPnow, that offered clear guidelines on where to obtain PrEP and how to take PrEP safely (327, 373).

9.1.3 Substantial decline in HIV incidence among GBMSM

In Chapter 7, I investigated trends over the calendar year in HIV incidence and predictors of HIV incidence. I found that among all men enrolled in the AURAH2 study, HIV incidence decreased substantially between 2013 and 2019, consistent with previous data from the UK Health Security Agency (UKHSA), attributed to the increase in testing and earlier ART initiation from 2013 onward and the scale-up of PrEP (6). Recreational drug use was one of the strongest factors associated with HIV incidence among men in AURAH2. HIV incidence was exceptionally high among men who reported the use of injection drugs, almost 28-fold higher than the incidence among men who did not report any recreational drugs. The use of non-injection chemsex-related drugs more than six-fold enhanced the risk of HIV infection. PrEP use was not associated with lower HIV incidence among men in AURAH2, which could be due to opposing factors operating, such as PrEP use lowering the risk of HIV acquisition on the one hand, and PrEP use acting as an indicator of very high-risk behaviour (similar to the other CLS markers) on the other. The fact that the decline in HIV incidence coincided with a significant increase in the proportion of men reporting prior 12-month PrEP use across time was an important result in this thesis.

9.1.4 HIV-positive GBMSM continue to engage in condomless anal sex

In Chapter 8, I assessed among newly HIV diagnosed GBMSM in London, trends over one year of follow-up since baseline in the prevalence of sexual behaviour measures, within-person changes in sexual behaviour measures and factors associated with sexual behaviour measures in the initial period after an HIV diagnosis. The findings of this chapter revealed that a large proportion of GBMSM with new HIV diagnoses had sex, with CLS being the most common in the year following their diagnosis. However, CLS did decline in the months immediately after the diagnosis to then return to baseline levels within 48 weeks, and similarly, serodiscordant CLS (CLS-D) increased significantly from week 12 to week 48. The percentage of men with CLS-D who were not on antiretroviral therapy (ART) or had a plasma viral load (VL) >200c/mL at three months after being diagnosed with HIV was 10.7% (9/84), which means that nine of 11 (81.8%) men who reported CLS-D at week 12 were at risk of infecting their partners. The percentage of men with CLS-D-HIV risk a year after being diagnosed with HIV was very low (1.3%). Condomless sex was linked to recreational drug use and a belief that condoms are unnecessary when the virus load is undetectable. This grew during the course of the follow-up, coinciding with U=U publications (93).

9.2 Strength and weakness of the research design

This thesis' findings should be interpreted in light of its limitations. Limitations of the findings have been explicitly referred to in each relevant results chapter. In this section, I describe how the design of the AURAH2 study and the Guy's and St. Thomas' study affected how the study results are interpreted.

9.2.1 Limitations of the AURAH2 study and interpretation of the results

The strengths of the AURAH2 study include the relatively large sample size and the longitudinal nature of the study. The online data collection phase made it relatively easy to collect longitudinal data on an individual level since it did not require multiple clinic visits. There is a suggestion that collecting sensitive and personal information on sexual behaviour and drug use online may reduce social desirability bias (326). However, there are several limitations to cohort studies that must be considered. Repeat questionnaires were used in the study, which may have intervention-like effects on participants by causing them to reflect or change their behaviour due to repeated questioning. Evidence suggests that participating in questionnaires that encourage behaviour reflection may have contributed to study participants becoming more aware of the consequences of their choices, which could have resulted in behaviour change (311), and may help to explain the decline in some lifestyle measures, including chemsex and bacterial STI diagnoses seen in this cohort.

The results of Chapter 4 (the AURAH2 study's loss to follow-up) revealed certain flaws that could alter how the results of the succeeding results chapter are interpreted. Despite using an online approach to retain participants, which is likely to have improved completion rates of online questionnaires and GBMSM engagement in the study, the AURAH2 study was not as successful as hoped in retaining young and less educated people, or those who used chemsex and alcohol, until the end of the study. Men who dropped out of the study, either early or later, and those who completed the study showed differences. Compared to those who were retained, dropouts were more vulnerable (younger, less educated, had less secure socioeconomic status, belonged to a minority group, and were bisexual), which implies some degree of differential bias. As a result, these men's sub-groups were not adequately assessed in terms of the outcomes, and there could be a bias in trends over time in sexual behaviours or PrEP and PEP use. This is because the trends represented the trends in the group rather than the overall trends among those men recruited. It is possible that the estimates of PrEP use and the decline in chemsex among GBMSM in the AURAH2 were overestimated.

The enrollment of participants at sexual health clinics was another potential weakness of the AURAH2 study, and this limits the generalizability of the results in this thesis to the GBMSM in the general population, as explained in Chapters 5–7. Because the three sexual health clinics that participated in the AURAH2 were sites of the PROUD trial, the estimates of PrEP use among men in the AURAH2 may be exaggerated. The three AURAH2 sites were also in metropolitan areas with large GBMSM communities, and these clinics offered special services for chemsex so that they might attract more men at higher risk into the study. However, a substantial number of new HIV diagnoses among GBMSM occur in clinics in London and Brighton, and specifically in the clinics involved in the study, which made the successful completion of the study feasible.

9.2.2 Limitations of the Guy's and St. Thomas' observational study and interpretation of the results

As noted in Chapter 8 (Section 8.4.4), the longitudinal aspect of this study, the high retention rate, and the very few missing data for sexual behaviour and other socio-demographic or lifestyle characteristics are the study's key strengths. However, due to the relatively small number of participants in this study, the results should be regarded with caution, as this may prevent the conclusions drawn from being extrapolated (374), especially when data were also analysed from a single site in London. The sexual behaviour questions at baseline referred to the 'past three months' rather than 'since diagnosis,' making it difficult to evaluate the data because we do not know if the sexual activity occurred before or after diagnosis.

9.3 Implications for practice and policy

9.3.1 Implications for the development and delivery of HIV prevention interventions among GBMSM

Based on the lessons learned in the PrEP Impact Trial and following the UK government investment and action by providers, local authorities, and National Health Service England and NHS Improvement (NHSEI), from October 2020, oral PrEP is provided in specialist sexual health services in England (4, 375). A plan for providing PrEP in settings beyond sexual and reproductive health services, such as drug and alcohol services and pharmacies, is under development (375). The results of the transition probabilities analysis indicate that the majority of GBMSM are at low risk for HIV acquisition, though they experience short periods in which they are at higher risk. This means, these men might benefit from PrEP as a tool that can be used for that short period of the enhanced risk. All of the markers of transitions to higher-risk behaviour discovered in Chapter 5's research might be used to

identify GBMSM who are likely to increase their risk in the next four months. This information might be used by nurses and clinicians so that they can ensure these men are aware of all the prevention tools at their disposal.

In Chapter 6, indicators of socioeconomic disadvantage and low-risk sexual behaviours were associated with a lower rate of initiating PrEP or being on PrEP. During the data collection period of the AURAH2, PrEP was not entirely available for free on the NHSE, and it cost £30 per month if it was sourced through the Internet; therefore, uptake might be low among those men. The results highlighted the need for PrEP to be available for free. In line with the UK government's commitment to supporting the system to continue improving access to PrEP for key population groups and monitoring the progress through a monitoring and evaluation framework (375), no one must be left behind in terms of access to PrEP. Efforts should be maintained and improved to ensure that individuals who need PrEP have equitable access.

Based on the 2018 BHIVA/BASHH guidelines on the use of PrEP (111), within the PrEP Impact Trial, individuals are eligible for PrEP if they are:

(1) Men (cisgender and transgender women) who:
    (i) have sex with men
    (ii) have had an HIV-negative test during an earlier episode of care in the preceding year
    (iii) report condomless sex in the previous three months
    (iv) affirm their likelihood of having condomless sex in the next three months
(2) HIV-negative partners of an HIV-positive person when:
    (i) the HIV-positive partner is not known to be virally suppressed (<200 copies/mL for six months or more)
    (ii) condomless sex is anticipated before treatment of the HIV-positive partner takes effect
(3) Other HIV-negative persons who are clinically assessed and considered to be at high risk of HIV acquisition as those with a serodiscordant partner who is not known to be virally suppressed (this may include people having condomless sex (excluding oral) with partners from parts of the world where HIV is common (such as Southern Africa, Southeast Asia and the Caribbean), and commercial sex workers or their clients who report regular condomless sex (376).

Findings from analysis in Chapter 7 of this thesis indicate that, in addition to the above criteria, the current guidelines may be improved with other characteristics strongly associated with HIV incidence among GBMSM, such as condomless sex with multiple partners, multiple new sexual partners, chemsex-associated drugs use, injection drugs use or group sex. The first data presented from the PrEP Impact Trial (data from the start of the

Impact Trial until 29 February 2020, 17,770 GBMSM enrolled) also indicated that the 'markers of higher risk' needed to be further developed to identify better those who may benefit from PrEP (115).

In the Impact Trial, participants were compared with a group of non-PrEP users, which were 97,908 cisgender gay and bisexual men who attended sexual health clinics at least twice while the trial was happening and would have been eligible for PrEP based on their HIV risk (primarily due to having had condomless anal sex in the previous three months). The study concluded that PrEP substantially reduced HIV incidence in GBMSM attending sexual health clinics in England, with 87% fewer HIV infections in men taking PrEP (115). However, the markers of the higher-risk group used in the PrEP Impact Trial (having had a diagnosis of a rectal bacterial STI, having sought PEP, having had at least two HIV tests, having engaged in sex work, and having had sex with someone with HIV or syphilis during the previous year) failed to identify 29% of the non-PrEP users who could benefit from PrEP. Most of the men taking part in the trial had markers of higher risk (92%), compared with 71% in the non-PrEP comparison group (29% had none). In these 'higher-risk' men, the efficacy of PrEP was similar, with 85.5% fewer infections in Impact Trial participants than in non-PrEP users. Although there were fewer men in the lower-risk group and therefore fewer HIV infections, HIV incidence in lower-risk men was higher than in the higher-risk group, in both the trial participants and non-PrEP users. Among the trial participants (PrEP users), the incidence among 'lower-risk' men (two infections among 568 men) was over eight times that of 'higher-risk' men. In the non-PrEP users, the incidence was two and a half times the incidence in supposedly higher-risk men (193 infections among 28,415 lower-risk men). Results observed might be because some of the factors seen as indicating higher risk, such as seeking HIV tests and PEP, may be markers of greater self-care, as much as those of greater risk (115).

To improve the acceptability, uptake and adherence to PrEP, the introduction of new PrEP options should be considered, including injectable PrEP versions (377). Evidence on the effectiveness of long-acting injectable cabotegravir (CAB-LA) has become available. A randomized controlled trial (RCT) showed that CAB-LA, administered every eight weeks, provided high efficacy compared to daily oral TDF-FTC in preventing HIV infection among GBMSM and transgender women (377). Because it is only given every two months, the long-acting PrEP eliminates the need to carry around medicine, making it a viable alternative that could help with adherence issues. However, the long-acting option also raises questions in regard to drug resistance. If people stop receiving injections, they will be vulnerable to HIV unless they use another HIV prevention method. Because of the long half-life, people will have a considerable period of time to build treatment resistance if they contract HIV. Only in

cases like this, where there is some HIV medication in the blood but not enough to completely suppress an infection, can drug resistance emerge (381). More research is needed to maximize the exceptional prophylactic potential of the long-acting PrEP against HIV infection in the real-world setting, taking into account not just efficacy but also tolerability, long-term safety, and patients' preferences.

There may be a particular benefit of long-acting injectable PrEP to improve adherence for those who find taking pills regularly challenging, for example, people who inject drugs (PWID). Studies examining the use of PrEP to prevent HIV transmission among PWID have not been adequately summarized (378), and no studies were conducted specifically among GBMSM injecting drugs. Among men in AURAH2, 26.3% of men who reported using injection drugs also reported using PrEP. The Bangkok Tenofovir Study (BTS), a randomized, double-blind, placebo-controlled trial among HIV-negative people aged 20 – 60 years in Bangkok (N=2,306 participants), was the first study to specifically examine the efficacy of PrEP among people who inject drugs (379, 380). The study showed that taking tenofovir daily as pre-exposure prophylaxis (PrEP) can reduce the risk of HIV infection by 49% in people who inject drugs (391). In an extension to the trial where participants were offered one year of open-label tenofovir, the study reported that adherence to daily PrEP was low overall; almost half (47%) had less than 10% adherence, and only 25% had high (>90%) adherence (380). Although analyses of behavioural data showed that the categorical factors associated with high levels of adherence were male sex, imprisonment, and injecting midazolam, no clear picture emerges of whether adherence was increased relative to higher or lower risk behaviour for HIV acquisition. For example, whether participants took PrEP during the period of recorded sexual activity or drug use. The results from the study point out the need for a more detailed assessment of factors motivating PrEP use and adherence among PWID. With persistently high rates of new infections, ongoing risk, and limited access to prevention strategies, PWID need access to all effective HIV prevention technologies, including PrEP, which should be part of a comprehensive combination prevention approach that includes harm reduction, drug treatment, and HIV treatment. PrEP alone should not be considered sufficient to prevent or reverse epidemics of HIV infection among PWID. Commitment to research assessing PrEP implementation approaches also needs to be developed further, including the context of injecting partnerships, social networks, and a more straightforward delivery method.

Although PrEP has sparked concerns that it could contribute to a new epidemic of STIs other than HIV, it is unclear if PrEP leads to increases in other STIs or if it’s just being used by people who are likely to get STIs. More frequent STI testing by PrEP users may also be a cause of rising diagnoses. In AURAH2, 26.8% (51/190) of men who reported using PrEP in

the previous 12 months were diagnosed with any STIs during follow-up, compared to 10.4% (76/728) of men who did not use PrEP. It is possible that the decreased rate of STI diagnosis among those not on PrEP was partly because men on PrEP tested for STIs more frequently within AURAH2. STIs in PrEP users were more common among those who reported condomless anal sex with two or more partners in the past three months (83.3% who reported both PrEP use and CLS2+ also reported any bacterial diagnoses) and the use of recreational drugs (67.4%), and those with White ethnicity – non-UK born (45.2%). The fact that bacterial STI diagnoses were more common among these specific groups, and that only slightly more than 25% of total questionnaires in which PrEP use was reported also reported any diagnoses of bacterial STI suggests the possibility of identifying a group who may benefit from frequent STI screening and other targeted interventions. STI screening is beneficial, and men are urged to do it, but they should not be required to do it in order to receive PrEP. A 2018 systematic review of observational studies found no evidence that intense screening for chlamydia and gonorrhoea lowers these infections in GBMSM (407). Furthermore, data from the American Men's Internet Survey between October 2014 and March 2015 among 6,103 GBMSM in 21 States in the US reported a positive association between STI screening intensity in GBMSM and gonococcal antimicrobial susceptibility (408). This suggests that STI screening among GBMSM may play a role in the emergence of antimicrobial resistance (408).

Although prevention efforts have already had a substantial impact in reducing the HIV epidemic, further improvements to increase HIV testing coverage across all populations at risk remain very important. To ensure early identification of HIV infection, HIV testing should be scaled-up in line with national guidelines (103), focusing on the populations and settings where testing rates must increase. Health promotion services should engage GBMSM who may never have been tested for HIV. Innovative strategies such as HIV self-testing (382) to increase testing coverage are needed. The routine offers of HIV tests to all GBMSM (and other populations) at high risk and the offer of PrEP remains key to ending HIV transmission.

9.3.2 Implications for HIV health care providers

The risk of acquiring HIV was higher among GBMSM who reported high-risk sexual behaviours (CLS with multiple or HIV positive partners, group sex, greater number of new sexual partners, versatile CLS role, and sex for drugs or money), and bacterial STI diagnoses. The information from routine inquiry and documentation of these factors that have been done in sexual health should be used to ensure that PrEP discussions are made and documented, and engagement efforts are made to ensure that whilst individuals are

going through a period of high-risk sexual behaviour, they have a good relationship with their sexual health clinics and remain engaged.

While results from this thesis showed who should be the highest priority for offering PrEP, it is vital to not restrict PrEP only to those 'eligible'. Health care providers should inform all their sexually active patients about PrEP and how it can protect them from getting HIV, and providers should prescribe PrEP to anyone who asks for it. Telling sexually active individuals about PrEP will increase the number of people aware of PrEP and may help individuals overcome embarrassment or stigma that may prevent them from seeking HIV prevention (383). It is also essential to take a sexual and substance use history, whether or not an individual asks for PrEP. This information is necessary to understand each person's risk of getting HIV, if PrEP might be right for them, and what other risk-reduction tools should be offered.

Results from Chapter 8 showed that around half of men practised condomless sex in the first three months post-baseline, and 11% were at risk of transmitting the virus to their partners at around three months following their HIV diagnosis. This suggests the need for HIV providers to emphasize the importance of knowledge of viral suppression in decision making about CLS. Successful efforts to end the HIV pandemic require a thorough understanding of HIV acquisition and transmission risks and effective implementation to support sustained viral suppression (384, 385). Serodiscordant CLS, when viral suppression is not reached, remains a risk factor for HIV transmission. Furthermore, as the acquisition of STIs usually is an indicator of condomless anal sex, safer sex through condom use interventions, irrespective of the level of individual or community viral load, should never be neglected to prevent STIs. The provision of information on U=U will hopefully encourage people to get tested, link to care, get onto treatment, appreciate that they cannot pass on their HIV infections when virally suppressed, and contribute to ending stigma. For those starting ARVs, the message to use condoms until undetectable needs to be re-inforced. The fact remains that once HIV treatment is initiated, weeks or months can pass before the drugs can suppress viral load (386). At the time of diagnosis, it is essential to counsel and support men not only about how to maintain adherence, but also about the risk of ongoing HIV transmission before viral load suppression is achieved and how long it takes for someone to become virally suppressed. The work across the clinical and professional communities to scale up the capacity for effective partner notification should also be enhanced, which will help identify people who are contacts of people with HIV, offer them HIV testing and refer them to care (if positive) or offer PrEP.

Furthermore, results from this thesis also underline the need for comprehensive interventions to prevent new HIV transmissions and reduce STIs among GBMSM using recreational drugs. There is a need for expanded availability and access to HIV harm reduction and sexual health services that are capacitated to address the psychosocial and physical needs related to chemsex. This could include offering multi-disciplinary support by accessible specialist services or recruiting drug users' community members to conduct outreach prevention services. Addressing chemsex within HIV harm reduction approaches and strategies also requires the meaningful participation of the community to ensure that materials developed are relevant and appropriate (387). Injecting drug use in the context of chemsex (slamming) is practised by small numbers of people, but they are maybe more challenging to reach without the right approach (388). Specific strategies, such as peers delivering health services that could recognize and help those in distress from their drug use (such as those available at the Dean Street clinic), need to be expanded to overcome this challenge to deliver appropriate HIV prevention messages or commodities and to facilitate the development and promotion of sex- and drug-related HIV prevention policies and procedures (387).

9.3.3 Implications for informing analysis in other studies

The methods used in this thesis to analyse transition probabilities between levels of sexual behaviour could also be applied to other diseases or other behaviours. Identifying drivers of changing behaviour, such as decreasing adherence to PrEP or ART, could be extremely helpful in identifying individuals who should be targeted for greater infection prevention strategies.

One noteworthy finding from Chapter 8 of this thesis was that men continued to engage in condomless sex despite having a detectable viral load and were at risk of transmitting HIV to their partners. However, no information was collected on whether or not their contacts or partners used PrEP. The risk of HIV transmission from an HIV-positive person to an HIV-negative person who uses PrEP and adheres to it is low (26). As a result, the actual risk of HIV acquisition among men on PrEP in this study was unknown. 'HIV risk' has been most often defined as whether or not an individual engaged in condomless sex with a serodiscordant partner within some pre-determined time frame, without considering whether individuals or their sexual partners are using any biomedical strategy and are adherent to it. The individual may be misclassified as engaging in risk behaviour in these instances. Given the diversity of an individual's risk-reduction needs based on their HIV serostatus and relationship contexts, there is no longer one gold standard to prevent HIV transmission, for example, consistent condom use or ART adherence only. Furthermore, HIV prevention

strategies are no longer static due to the continuous advance in biomedical prevention modalities, such as long-acting injectable ART and PrEP (405, 406). Thus, for future studies, it is vital to obtain information that integrates biomedical and behavioural strategies into couples-based HIV prevention research, as any singular behaviour indicator may not be appropriate.

For instance, to arrive at the composite risk HIV indicator in the context of HIV serodiscordant couples, the set of questions to consider to be included in an interview with a newly diagnosed individual would be:

1. Did the patient have condomless anal sex in the past three months (or a similar time frame)?
2. What was the HIV serostatus of his sex partner(s)? (if yes to question 1)
3. Was the patient on ART?
4. Was the patient virally suppressed? (if yes to question 3)
5. Was the patient's partner(s) on PrEP? (if the partner was HIV-negative)
    - If yes, what was the type of PrEP (daily, on-demand, or long-acting)?
    - If yes, was the partner(s) adequately adherent to it to effectively prevent HIV transmission? (if daily: have they missed any dose? ; if on-demand: were the frequency and timing of use matching the reported sexual behaviour? ; if long-acting: were they leaving a long gap between injections?)

The responses to these questions would determine patients' indicator value on the composite risk of HIV transmission to HIV-negative partner(s). This set of questions that incorporates information regarding sexual behaviour, utilization of biomedical prevention strategy, and adherence to biomedical prevention strategies may have the potential to be a comprehensive tool for standardizing measurement across heterogeneous samples, guiding interventions and thereby ultimately reducing HIV incidence among GBMSM and other priority populations.

To understand the effectiveness of PrEP and its place within broader HIV combination prevention strategies, monitoring and evaluation of PrEP delivery is critical, and this depends on the data's completeness and quality (389). Data for the current UK national monitoring and evaluation framework of routine PrEP commissioning, which is based on the WHO's implementation tool for PrEP (390), collects quarterly data from specialist sexual health services (SHSs) through the national GUMCAD STI surveillance system (389). Data items collected include behavioural, PrEP use and partner notification data. There are some limitations to the data; for example, each individual's GUMCAD records can only be linked at the same SHSs; consultations at two or more specialist SHSs by the same individuals are not linked. This might result in an overestimation of the number of people starting PrEP for

the first time (389). All data for PrEP monitoring relate to people accessing STI-related care only, including HIV and STI testing, and this might underestimate the number of people receiving PrEP (389).

Future studies that evaluate the uptake of PrEP and associated risk behaviours should collect comprehensive data on people accessing PrEP in the UK. GUMCAD provides extensive data from people accessing PrEP through SHSs; however, the limitations above are essential to consider when interpreting data. Furthermore, it is necessary to include other behavioural, lifestyle, clinical or demographic characteristics that might indicate a higher risk of subsequent HIV acquisition that are not currently captured in GUMCAD for better monitoring and evaluation. Besides using GUMCAD data to monitor PrEP uptake among people accessing SHSs, estimating PrEP need and uptake among people not accessing SHSs is also essential. As this cannot be captured through the national surveillance datasets, periodic community-based studies can provide additional data to understand the need for PrEP in the general population and complement the indicators within the national PrEP monitoring and evaluation framework. These studies could also explore other factors associated with PrEP uptake that are not captured through the national surveillance datasets. Examples of community-based surveys that could be used to understand population needs and access to PrEP include the National Survey of Sexual Attitudes and Lifestyles (Natsal) (although very few GBMSM were sampled) (391), the Gay Men's Sexual Health Survey (392) or internet-based studies among the general population that are done periodically. The use of these types of studies can complement each other and provide mutually reinforcing data on PrEP use among people accessing SHSs and the general population in the UK.

9.3.4 Implications for retaining participants in the cohort

In Chapter 4, I have demonstrated that there was a substantial proportion of men who did not continue on the study. Findings from this chapter contribute to a better understanding of factors associated with the loss to follow-up among GBMSM in the AURAH2 study. Results indicate that to prevent non-participation bias, tailoring recruitment and retaining strategies specific to the participants' demographic, behavioural, and lifestyle characteristics might be needed to increase retention in a cohort study. This could include innovative methods such as those with flexible data collection or those that emphasize the benefits of the study.

A 2018 systematic review on retention strategies in longitudinal cohort studies suggested that, for greater effectiveness, strategies that aim to reduce participant burden might be most effective in maximising cohort retention (254). Long duration and repeated assessments can increase attrition due to the significant burden on participants (393). Established retention

strategies within longitudinal cohort studies include incentives, sending a reminder to participants, or offering more methods of data collection (253). However, these strategies were effective in longitudinal cohort studies that used the traditional data collection and may not be as well suited to contemporary methods of collecting longitudinal data, such as web and mobile surveys (394), as in AURAH2. Evidence suggested that strategies that involve flexibility in data collection methods or shorter time for the completion of the questionnaire or interview may substantially affect retention (254).

Furthermore, previous data also emphasised that researchers need to strategically invest their resources to target better participant retention rather than simply increase the number of strategies applied. Open and regular protocol revision to incorporate innovations that offer greater flexibility to participants may help with systematic attrition (254). Perhaps men in AURAH2 could have been retained better if the various elements of the study had been more effectively tailored to meet their needs. For example, for participants who are chemsex users or alcohol dependents, motivational enhancement interventions may be needed by emphasising the study benefits for them (395).

9.4 Directions for future research

9.4.1 PrEP studies to enhance HIV elimination

Although no direct causal link can be established in this thesis between estimated HIV incidence trends and the various components of combination prevention, the analysis has provided a better understanding of how prevention policies have shaped HIV incidence trends in England, particularly where they have been introduced and strengthened in different ways over time. At the national level in England, expanded testing and treatment as prevention has controlled the HIV epidemic in GBMSM. The combination of HIV prevention measures, including PrEP, is needed to maintain the trajectory towards HIV elimination.

PrEP became available in the United Kingdom in 2017, but the national PrEP programme in England began in July 2020, and PrEP use is projected to rise in the future years (114, 396). As PrEP has become freely available, further research is necessary to investigate the barriers of use among GBMSM who opt-out of PrEP. The decision to take PrEP is based on an individual's recognition of potential risk, and the gap between risk perceptions and actual risk behaviours has been recognised as a major factor in persons who are at risk opting out of PrEP (232, 397). Also, given that PrEP stigma and anticipated stigma are known to be major barriers to PrEP uptake (398, 399), research on the intervention that does not stigmatise PrEP users deserves further research. As additional alternatives on PrEP have

now become accessible, it is also essential to study the acceptability of the new options and explore the potential cost-effectiveness (400). These studies can inform the public policy on their delivery methods (401, 402). End-user input on the early-stage design of new HIV prevention approaches is critical to yielding products that achieve high uptake, adherence, and acceptability of product attributes better predicted future interest. Furthermore, it is also crucial to learn about people's interests in and preferences for different PrEP modalities, not just the long-acting ones. Understanding preferences for potential products by GBMSM can help direct the further development of prevention messaging.

9.4.2 Impact of behaviour transitions or trajectories on the reduction of HIV transmission by HIV prevention interventions

While identifying transitions and trajectories in sexual behaviour is important, whether these short-term (transitions between sexual behaviour state) and long-term (trajectories of sexual behaviour over time) changes may undermine or enhance the impact of HIV prevention is still unclear. Therefore, future studies can focus on using mathematical modelling to explore how these changes affect the reduction in HIV prevalence or incidence achieved by HIV intervention programmes compared to a population with constant risk levels. For the sexual behaviour measure, it would be good to examine sexual risk behaviour not only through a single indicator (e.g., condomless anal sex with two or more partners only), but rather through the use of a potential sexual risk behaviour score for HIV infection based on a combination of variables, including the type and number of sexual partners, condom use, PrEP use, or other lifestyle characteristics.

Modelling studies have shown that PrEP and' test and treat' strategies could enormously impact the HIV epidemic among GBMSM if sexual risk behaviour does not change (3, 272). The impact of behavioural changes on intervention effectiveness has received less attention in the literature, owing to the necessity for high-quality longitudinal data to describe behaviour change among GBMSM. If there is evidence of heterogeneity in sexual behaviour within-individual among GBMSM over time, the possible impact of distinct trajectories on subsequent outcomes (for example, the cost-effectiveness of such an intervention program) is of interest. It would be informative to research or update 'static' models that do not include sexual trajectories with the addition of sexual trajectories, such as the impact of PrEP on HIV prevalence or reduction of HIV transmission by integrating sexual trajectories or transitions (such as how many men will transition in or out of high risk).

Furthermore, there is the need to build models of PrEP use that can support people alternating between periods of use and non-use, as well as switching between dose,

regimens or how the PrEP is administered as they become available and approved for use in the UK or England. This could also apply to the combination of different types of PrEP.

9.4.3 Studies on recreational drugs including chemsex-associated drugs and injection drugs

Results from analyses in this thesis indicate that recreational drug use (including chemsex associated drugs and injection drugs) remain a major factor that deserves further research as it is associated with increased risk behaviour, PrEP initiation, HIV incidence, and, in people with HIV, condomless anal sex after HIV diagnosis. The AURAH2 study is the only study from the UK to have investigated longitudinal patterns and trends in chemsex among GBMSM (305), and research with extended follow-up time (beyond three years) would help to contextualise this data and provide a better understanding of long-term patterns of recreational drugs and sexual behaviour outcomes.

Further research into the barriers to accessing HIV prevention services among GBMSM who inject drugs despite the availability of harm reduction programmes in the UK will also be useful. HIV infections and outbreaks continue to occur among PWID in the UK, although HIV prevalence in this group remains comparatively low (403). HIV prevalence in this population remained stable at 0.82% in 2019, with 100% of HIV-positive people aware of their status (404). However, missed opportunities remain, with many PWID not tested recently reporting contact with a range of clinical services. It is important that PWID at ongoing risk are offered a diagnostic test regularly. The next wave of research needs to address specific facilitators of and barriers to adherence and persistence and assess mechanisms to improve engagement. Given that PrEP is one modality within many other evidence-based prevention methods, future research should seek to understand when and how best to integrate PrEP within larger prevention programmes. Further research is required to investigate how PrEP might best complement existing combinations of evidence-based HIV preventive interventions among this population.

It would also be valuable to study individual transitions and trajectories in drug use over time. To my knowledge, such data is not available from UK prospective studies. Although such long-term changes have not been well described, individual drug use patterns are known to change over time (172). Characterising longitudinal trajectories of injection drug use, chemsex use, or other illicit drug use, as well as identifying associated characteristics or predictors of transitions, would be beneficial to determine how many men would remain at high risk throughout time and to assess the discontinuous patterns of drug use trajectories.

9.5 Final conclusion

To conclude, findings from this thesis suggest that the majority of GBMSM attending sexual health clinics in England showed minor behaviour changes over a short-term period. With HIV incidence declining among GBMSM in England and coinciding with a substantial increase in the use of PrEP, there is a clear need to focus prevention efforts on potential transmission risk. Although efforts to end the HIV epidemic are having a substantial effect, further improvements, such as increasing HIV test coverage across all populations at risk and ensuring that all have equitable access to PrEP, remain very important in the UK to reach zero new infections. GBMSM who take recreational drugs are at a greater risk of HIV infection, and this demographic should be the focus of HIV and STI testing and treatment, PrEP initiation, and drug assistance. Finally, because data reveal that GBMSM in the era of cART continue to participate in condomless sex shortly after diagnosis, it is critical to counsel men about their decision not to use condoms to prevent HIV transmission promptly after diagnosis.

9.6 Publications and presentations arising from this thesis

Throughout my PhD, I conceptualized the research questions investigated in this thesis, conducted all the literature reviews, managed the AURAH2 and the Guy's and St. Thomas' data, conducted all data analysis and interpretation, wrote and published papers with my supervisors, and presented results in conferences.

Based on the work I conducted in this PhD, I published two papers as the first author; based on results in Chapters 6 (PrEP use and associated factors) and 7 (Trends in HIV incidence), and also presented these findings at four conferences. At the time of submission of this thesis, an additional manuscript based on work in Chapter 8 (Behaviour Changes following HIV diagnosis) has also been submitted for consideration of publication and it is currently under peer-review process, and another paper based on my work in Chapter 5 (Transitions in sexual behaviour and predictors of transitions) is in preparation for submission.

Results from Chapter 6 were published in 2020 at the Lancet Public Health (346), titled *'Use of HIV pre-exposure prophylaxis among men who have sex with men in England: data from the AURAH2 prospective study'* (Appendix 19), after being previously presented at the 23rd International AIDS Conference (AIDS 2020) virtually in July 2020 as a poster presentation (Appendix 20). In November 2020, as an oral presenter, I also presented the results from Chapter 6 at the 26th Annual Conference of the British HIV Association (BHIVA) virtually (Appendix 21). In 2021, I published the results from Chapter 7 at PLOS Medicine (5), titled

'Trends in HIV incidence between 2013–2019 and association of baseline factors with subsequent incident HIV among gay, bisexual, and other men who have sex with men attending sexual health clinics in England: A prospective cohort study' (Appendix 22). Before publishing, the interim results from Chapter 7 were presented as an oral presentation at the 14th AIDS Impact International conference in London July 2019 (353) (Appendix 23), and as a poster presentation at the 25th Annual Conference of BHIVA in Bournemouth April 2019 (Appendix 24).

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Appendix 1. Summary of articles from longitudinal observational cohort studies containing data on sexual behavioural changes among HIV-Negative GBMSM at enrolment globally, 1998 – 2018

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
High-income countries						
THE NETHERLANDS						
Amsterdam Cohort Studies (ACS); Amsterdam; **An open, prospective cohort study initiated in 1984 with 6-monthly follow-up visits. Participants were recruited using convenience sampling. At each visit participants completed self-reported questionnaire on socio-demographic, sexual risk behaviour, recreational drug use, chemsex, recent PrEP use (since 2015) and tested for HIV and STIs.** • **Until 1995: HIV-negative men of all age groups who had at least two male sexual partners in the previous 6 months and lived in Amsterdam.** • **1995 – 2004: only men aged 30 or less with at least one male sexual partner in the previous 6 months. In 1996 follow-up for HIV-negative**	**1) Dukers (2001);** 1984 – 2000; To study the time trends in sexual behaviour and STIs 877 men ≤ 30 years at entry, median age 26.4 (23.8-28.5); 92.9% European nationality; 54.5% college degree.	• Rate of CLS with steady partners increased significantly from 70.1% in 1996 to 77.8% in 1999, and for casual partners from 27.5 to 33.3% • Adj. OR for CLS in 1996-2000 1.3 (95% CI 1.0-1.6) compared with 1992-1996 *(GEE models)*	**N/A**	**N/A**	• 64 seroconverted, incidence rate decreased in 1985-1988, but fluctuated afterwards, incidence rate in 1999 2/100 PY. • Incidence of gonorrhoea increased after July 1996 (non-significant), adjusted RR decreased (0.9;0.3-2.6) *(GEE Poisson)*	**N/A**
	2) Van der Bij (2005); 1984 – 2002; To compare trends in STIs and HIV among young MSM 863 men ≤30 years at entry with more than one ACS visit since 1984, mean age 25 years, 88% Dutch nationality, men entering before 1995 were older than after (27 vs. 25 year), median follow up time 4.0 years (1.5–6.6)	• % of men reporting CLS increased significantly from 1995 – 2002 (OR 1.06) with increase in risk to be more evident for CLS with steady partners (OR 1.07) • The number of sexual partners, total and casual partners, per 6-month period didn't change significantly: 11 and 10 in 1995 vs. 8 and 8 in 2002 *(GEE models)*	**N/A**	**N/A**	• HIV Incidence peaked in 1984 – 1985 (6.7/100 PY). • Between 1995 and 2002, incidence of HIV remained stable: 1.1/100 Ps in 1995 and 1.3 per 100 PYs in 2002 (yearly RR: 0.93, p=0.48), • a significant increase in syphilis (0 to 1.4/100 PY) and gonorrhoea incidence (1.1 to 6.0/100 PY) *(Poisson regression)*	**N/A**
	3) Jansen (2011); 1984 – 2009; To study trends in HIV incidence rates, sexual risk behaviour and risk factors and source for HIV seroconversion 1642 men with at least two study visits between 1984 and 2009, median age 28.8 years (24.8 – 35.9), 81% Dutch nationality, 55% had a college degree, median follow-up time 6.2 years (IQR 2.3 – 11.5).	• % of men practising CLS in the preceding 6 months decreased from 78% in 1984 to 33% in 1988, increased to 38% in 1995 and continued to increase reaching 55% in 2009. • MSM were more likely to have engaged in CLS in the time periods after the introduction of cART compared to the period just before (1992–1996), ORs 1.4 (95% CI 1.16–1.56) and 1.5 (95% CI 1.33–1.79, P<0.01) for 1996–	**N/A**	**N/A**	• 217 seroconverted during 11,123 PYs of follow-up. • Incidence rates decreased from 8.6/100 Ps in 1985 to 1.3/100 PY in 1992; remained relatively stable around 1.0/100 PY between 1992 and 1996, and slowly increased to 2.0/100 PY in 2009 (P=0.14; linear trend 1996–2009); *Poisson regression* • Men who reported more than five sexual partners (IRR 2.5, 95% CI 1.58–4.08), receptive	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
MSM aged above 35 was terminated. • **2005 – onwards: men of all age groups with at least one male sexual partners in the previous 6 months could participate again**		2003 and 2003– 2009, respectively. • Increasing trend from 1996 onwards for CLS with steady and casual partners (all P<0.01), over the whole period studied, the proportion of CLS with steady partners was higher than the proportion of CLS with casual partners (respectively 60 vs. 26% in 2009); *(Logistic regression with GEE)*			CLS (IRR 4.1, 95% CI 2.37–6.96), and a history of gonorrhoea (IRR 5.8, 95% CI 2.49–13.71), all in the preceding 6 months, were also at increased risk for HIV-1 infection. • During the study period, for 74% (134) of the seroconverters, the most likely source of infection was allocated to a casual partner, and for 26% (46) it was allocated to the steady partner *(Logistic regression)*	
	4) Heijman (2012); 1984 – 2008; To compare sexual risk behaviour pre-HIV and post-HIV seroconversion before and after the introduction of cART; 206 HIV-negative MSM at entry who seroconverted within ACS between 1984 and 2008, 125 (61%) seroconverted in the pre-cART era and 81 (39%) in the cART era. Seroconverters in the cART era were younger (mean 33.5 years) than those in the pre-cART era (mean 36.5 years). In both periods, 93% Dutch and 82% had a middle or high-level education	**N/A**	**N/A**	• The risk of having CLS 1 year after HIV diagnoses decreased significantly when compared with 1 year before diagnosis in both the pre-cART era [difference, 30%; 95% confidence interval (CI), 22–36%] and cART era (difference, 19%; 95% CI, 9–30%). • The probability of CLS in the cART era increased again to pre-seroconversion levels (61%; 95% CI, 48–74%)) 4 years after diagnosis; *(Latent class random effects logistic regression models)*	**N/A**	**N/A**
	5) Van den Boom (2014); 2007 – 2011; To investigate the prevalence and protective value of serosorting with casual partners (CPs) 445 men with CPs between 2007 and 2011, median age 33.9 years (29.7-38.8), 90% Dutch and 72% were highly educated.	• Of the 2137 follow-up visits, CLS was reported in 25%, CLS with serosorting in 11% and consistent condom use in 64%. • The proportions of visits at which MSM reported serosorting remained relatively stable over time (P=0.33), with 10.2% (20/196), 11.4% (56/485), 10.0% (48/472), 10.0% (50/492), and 13.9% (68/492),	**N/A**	**N/A**	• 31 seroconverted for HIV during a total follow-up of 1107 PYs, Overall observed HIV-incidence rate: 2.8/100PY. • MSM who practiced serosorting were less likely to seroconvert (aIRR=0.46 [95%CI]=0.13–1.59) than MSM who had CLS, but more likely to seroconvert than MSM who consistently used	**N/A**

Name of the study; Study settings; Design and method / Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives / Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
		respectively, of the visits in the years 2007-2011; *(GEE models)*			condoms (aIRR=1.32; 95%CI=0.37–4.62) MSM who consistently used condoms were less likely to seroconvert than MSM who had CLS (aIRR=0.37; 95%CI=0.18-0.77); *(Poisson regression)*	
	6) Basten (2018); 2007 – 2017; To study longitudinal trajectories of sexual risk behaviour predictive of HIV acquisition from sexual debut onwards. 815 men entered ACS in 2007 or later, mean age 35.6 years (SD 9.6). 75.6% Dutch, 75.4% highly educated, average follow-up length of 5.34 years (SD 3.26).	**N/A**	• Three trajectories of sexual risk behaviour were identified: Low risk (90.3% of the sample), Falling high risk (6.5%) and Rising high risk (3.3%). • MSM following the Falling high risk (20.5%) and Rising high risk (25.0%) trajectories were more likely to acquire HIV during follow-up. • The Falling high risk trajectory was associated with younger age at sexual debut, fewer steady partnerships and high percentages of substance use. • The Rising high-risk trajectory was associated with increasing % percentages of substance use over time; *(Latent class growth mixture modelling)*	**N/A**	**N/A**	**N/A**
	7) Coyer (2018); 2015 – 2017; To examine time trends in use of PrEP, characteristics of PrEP users, PrEP eligibility and intention to use PrEP 687 men who provided data on PrEP from mid-2015 to mid-2017. Median age 40 years (33–47) at wave 1 of the study period. 77% educated at least to college degree, 79% were born in the Netherlands. PrEP users did not differ from non-PrEP users in socio-demographic characteristics.	**N/A**	**N/A**	**N/A**	**N/A**	• Recent PrEP use: 57/687 (8%) MSM. • PrEP use increased over calendar time (P<0.001) from 2% in 2015 to 7% in 2017. • PrEP eligibility increased over time, non-significant • PrEP eligibility criteria were met by 149/460 (32%) at, of whom 21% reported PrEP • % with a high intention to use PrEP was greater among eligible than non-eligible MSM (51% vs. 24%, P<0.001); *(Logistic regression models using GEE)*

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
AUSTRALIA						
Health in Men (HIM) cohort; Sydney **A prospective cohort study of HIV-negative gay men established in 2001 with 6-monthly telephone and annual face-to-face interviews and annual testing. Participants were recruited from a wide range of community-based settings. At each interview, detailed quantitative data on sexual behaviour in the last 6 months were collected** • **18 years and older** • **reported having sex with other men within the previous 5 years** • **lived in Sydney or participated regularly in its gay community** • **tested HIV negative at baseline.**	**1) Mao (2006);** 2002 – 2005; To assess whether HIV-negative gay men engage in serosorting in casual encounters. **No data on sample demographic** Whole sample N 2002=826, N 2003=1186, N 2004=1109, N 2005 before July=645	• Decrease in the mean number of total UAIC (with casual partners, categorised as apparent serosorting) partners in the 6 months before interview (RR per year 0.92, 95% CI 0.90 – 0.94) • An increase in the mean number of UAIC partners reported to be HIV negative (RR 1.11, 95% CI 1.05 – 1.17, p<0.001). • An increase in the proportion of HIV-negative UAIC partners from 12.3% in 2002 to 24.3% in 2005 • *(GEE models)*	**N/A**	**N/A**	**N/A**	**N/A**
	2) Zablotska (2008); 2003 – 2006; To explore factors associated with having serodiscordant UAIC 1427 men who reported having casual partners in the 6 months before interview. Median age at enrolment 36 years (range 18-73)	• % of men with serodiscordant UAIC casual partners increased during 2003 – 2006 (from 3% - 4%). • Age, number of partners, seeking partners online, drug use and esoteric partices were associated with serodiscordant UAIC.	**N/A**	**N/A**	**N/A**	**N/A**
	3) Jin (2009); 2001 – 2007; To assess the extent of any reduction in HIV risk associated with risk reduction behaviours; 1427 men, median age at enrolment 35 years (18 – 75), 95.2 % gay or homosexual, 87% attended at least 1 follow-up.	• In 88% of follow-up periods in which CLS was reported, it occurred in the context of consistent risk reduction behaviours. • Serosorting outside negotiated safety associated with an intermediate rate of HIV (hazard ratio=3.11, 95% CI 1.09-8.88). Withdrawal associated with a higher risk than no CLS (hazard ratio=5, 95% CI 1.94-12.92) *(Cox regression)*	**N/A**	**N/A**	• 53 seroconverted HIV incidence of 0.78/100 PY (95% CI 0.59 – 1.02). • The median age at HIV seroconversion was 37 years (22-63). • The total follow-up time for risk factor analysis was 5161 person-years, and the median was 3.9 years per participant. • Overall, men who reported any risk reduction behaviour were about three times more likely to seroconvert to HIV than men who reported no CLS (hazard ratio=3.01, 95% CI 1.31 – 6.92)	**N/A**
	4) Jin (2010); 2001 – 2007;	• Over time 228,056 episodes of UAI was reported by 1136 men	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
	To estimate per-contact probability of HIV transmission due to UAI in the era of HAART; 1427 men with median age at enrolment of 35 years (18 – 75), 92.5% gay, No data on education or ethnicity. The estimation of per-contact risk was based on 1136 who had at least one follow-up interview and reported at least one episode of UAI during the study.	(56.1% UAI insertive vs 43.9% UAI receptive), 87% were with partners reported to be HIV-negative. • The estimated per-contact probability of HIV transmission for receptive UAI was 1.43% (95% CI 0.48% - 2.85%) if ejaculation to ejaculation was involved. • The estimated transmission rate for insertive UAI in participants who were circumcised was 0.11% (95% CI 0.02%-0.24%), and it was 0.62% (95% CI 0.07%-1.68%) in uncircumcised men.				
	5) Prestage (2011); 2004 – 2007; To assess how well gay men know their sex partners and how familiarity between casual sex partners affect the likelihood of condom use; 1157 men completed 3345 interviews between 2004 and 2007, 95% men identified as homosexual	• Total interviews = 3345, among whom 1007 men reported sex with a total of 50,959 casual partners. Of these, 9.4% were reported as being HIV negative, 2.5% were reported as being HIV-positive, 88.1% casual partners were men whose HIV serostatus they did not know. • Nonetheless, with casual partners with whom they engaged in UAIC respondents indicated that they knew 'well' 28.9% of the HIV negative partners and 26.2% of HIV-positive partners, but only 7.6% of the HIV status unknown partners. • Respondents were more likely to have engaged in UAIC with partners they knew well (McNemar p<0.001)	**N/A**	**N/A**	**N/A**	**N/A**
	6) Jin (2012) 2001 – 2007; To examine the associations between serosorting, strategic positioning and the incidence of a range of STI;	**N/A**	**N/A**	**N/A**	• serosorting was associated with an increased risk of urethral (HR=1.97, 95% CI 1.43–2.72) and anal (HR=1.62, 95% CI 1.11–2.36) chlamydia. • Compared with men who reported UAI with HIV	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
	1427 men with median age at enrolment of 35 years (18 – 75), 92.5% gay, No data on education or ethnicity.				nonconcordant partners, men who practised serosorting had significantly lower risk of incident syphilis (HR=0.21, 95% CI 0.05–0.81) and urethral gonorrhoea (HR=0.61, 95% CI 0.39–0.96). Compared with men who reported no UAI, strategic positioning was associated with an increased risk of urethral gonorrhoea (HR=1.72, 95% CI 1.05–2.83) and chlamydia (HR=2.22, 95% CI 1.55–3.18). • Compared with men who reported receptive UAI, the incidence of anal gonorrhoea (HR=0.38, 0.20–0.74) and chlamydia (HR= 0.44, 95% CI 0.27–0.69) was significantly lower in those who practised strategic positioning.	
	7) Jin (2015); 2001 – 2007; To address whether summary measures such as any CLAI accurately measure HIV sexual risk behaviour; Sample characteristics: the same as above (Jin, 2012). The overall follow-up time was 5,160 person-years contributed by 1,381 (96.8%) men who completed at least one follow-up interview, with a median of 3.9 years per participant.	• A total of 228,064 episodes of CLAI were reported, mean of 44 episodes per year per participant (median: 14). • The great majority of CLAI episodes were with a regular partner, most of them with HIV-negative regular partners (84.8%). Participants were more likely to engage in insertive CLAI with casual than with regular partners (66.7 vs. 55.3% of all acts of CLAI with each partner type,p <0.001). • Men were more likely to report CLAI in the receptive position with HIV-negative and HIV status unknown partners than with HIV-positive partners (p <0.001 for both regular and casual partners) *(Logistic regression)*	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
CANADA						
The Vanguard Project; Vancouver **A prospective cohort study of young gay and bisexual men with 6-monthly follow-up. Participants completed annual self-administered questionnaires at baseline and follow-up and provided blood samples for HIV testing annually.** **Participants were recruited through posters, advertising and word-of-mouth, began in 1995 and ended in 2002;** • **Aged 18-30 years** • **lived in the greater Vancouver region** • **had not previously tested HIV positive** • **identified themselves as gay.**	**1) Strathdee (2000);** 1995 – 1998; To identify trends in HIV infection rates and associated risk behaviours; 681 men who completed a baseline questionnaire and HIV testing as of May 1998. Median age 25.8 years (23.1 – 28.6), 80.6% homosexual, 58% completed high school, 69.8% employed and 72.1% white ethnicity. Median duration between baseline and first follow-up visit was 14 months.	• Of the 285 men reported regular partners at baseline, 196 (68.8%) having had protected insertive and 185 (64.9%) protected receptive anal sex. • At follow-up, 26.5% of the 196 subjects and 29.7% of the 185 had unprotected insertive anal sex.	**N/A**	**N/A**	The prevalence and incidence of HIV seropositivity were 1.8% (95% confidence interval [CI] 0.8%–2.8%) and 1.7 per 100 person-years [95% CI 0.7–2.7], respectively. Compared with subjects who remained HIV-negative, those who became seropositive were younger and more likely to report high-risk behaviours.	**N/A**
	2) Piaseczna (2001); 1995 – 2000; To characterize longitudinal patterns of sexual behaviour in a cohort of gay and bisexual men 130 participants that had completed a baseline questionnaire and HIV test between 1995 and 1996 and four annual follow-up questionnaire. Median age at baseline 26 years (24 – 28), 79% of white ethnicity, 85% had completed high school, 82% currently employed, 95% lived in a stable housing.	**N/A**	• Over 5 years of study >70% of study subjects reported having >= 1 regular male sexual partners in the previous years. • During each of the five successive 1-year periods, between 34% and 40% of respondents reported having had receptive CLS. Between 29%-39% reported having had insertive CLS with regular partners, between 13% and 25% insertive CLS with casual sex partners, and between 9% and 18% receptive CLS with casual sex partners.	**N/A**	**N/A**	**N/A**
	3) Rusch (2004); 1997 – 2002; To identify determinants of the association of specific drugs and CLS; 261 men who attended the study visits at least once in each 2 year period: 1997 – 1998, 1999 – 2000, 2001 – 2002, and without history of injection drug use. Media age 27 (range 24-30), 77% white ethnicity, 58% college graduate, 90% employed, 99% in a stable housing.	CLS significantly associated with: • sexual situation specific use of marijuana (OR 1.43), • crystal methamphetamine (OR, 1.75), • ecstasy (OR, 1.88), • and ketamine (OR, 2.17);	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
The Omega Cohort Study; Montreal; **A longitudinal cohort study with 6-monthly follow-ups. Participants completed a self-administered questionnaire, a structured interview, and HIV testing and counselling as well as syphilis testing at each visit. Participants were recruited through bilingual promotion in the general gay and gay communities;** • **Self-identified HIV-negative** • **MSM aged 16 years or older** • **lived in Montreal, Quebec**	**1) George (2006);** 1997 – 2003; To determine temporal trends in CLS; 1587 men with at least two follow-up visits. 53% older than 30 years, 70.4% had a college degree or more, 56% born in Quebec. For trend analysis by visit number, data was based on men who had completed 8 follow-up visits / based on individual level data (n=579)	From 1997 – 2003: Significant increases in CLS with seroconcordant partners from 21.4% to 28.9% (OR = 1.04, 95% CI: 1.02 to 1.05; P<0.0001), with any type of partner from 34.1% to 43.9% (OR 1.03, 95% CI: 1.02 to 1.04; P <0.0001), with casual partners from 8.2% to 12.2% (OR = 1.03, 95% CI: 1.00 to 1.05; P = 0.01) and with any type of partner except a seroconcordant partner from 15.7% to 18.8% (OR = 1.02, 95% CI: 1.00 to 1.04; P = 0.02). *(GEE models)*	From the first follow-up visit – last follow-up: Important increases in UAI with seroconcordant partners, from 21.3% to 31.1% at the last visit (OR = 1.06, 95% confidence interval [CI]: 1.04 to 1.09; P< 0.0001), with any type of partner (from 31.8% to 43.9%; OR = 1.05, 95% CI 1.03 to 1.07; P< 0.0001), with casual partners (from 7.3% to 9.6%; OR = 1.05, 95% CI: 1.01 to 1.09; P = 0.01).	**N/A**	**N/A**	**N/A**
	2) Lavoie (2008); 1996 – 2003; To estimate HIV incidence and associated risk factors; 1587 men with ≥1 six-month follow-up visit. The mean and median age at study 32.0 (SD 9.9) and 30 years (range: 24–38), 75% being single, 20% employed, 67% had more than a high-school degree.	**N/A**	**N/A**	**N/A**	HIV incidence 0.62 per 100 person-years (95% CI: 0.41–0.84). compared with subjects not reporting any anal sex with serodiscordant or casual partners, those reporting anal sex with such partners (all P values <0.05), whether consistently protected [hazard ratio (HR) 3.4], or unprotected exclusively receptive (HR 12.0), exclusively insertive (HR 4.7), or both receptive and insertive (HR 8.3), were at increased risk of seroconversion; *(Cox Regression)*	**N/A**
Polaris HIV Seroconversion Study; Ontario; **A longitudinal study of recent HIV infection using a retrospective case-control design with 6-monthly follow-up of cases and controls. Participants were interviewed using standardized questionnaires and completed**	**Calzavarra (2012);** 1998 – 2007; To investigate the hypothesis that gay and bisexual men experiencing stressful life events 207 HIV negative and 155 HIV positive men with at least two follow-up interviews; among the HIV-negative men, Mean age 37.7 years (10), 91% gay, 86% from Toronto, 85% White	• At any given interview, among the negative men,13% reported CLS and 55% reported one or more stressful life events. • Odds of CLS increased by 1.15 for each additional stressful event (95%CI 1.06-1.24).	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
a paper questionnaire on sexual behaviours and stressful life events at follow-up and annual HIV test; • **Men and women aged 18 years and older with documented recent HIV infection (seroconverters)** • **Two HIV-negative controls per case were enrolled.**	ethnicity, 66% had college university, and 66% employed full time.					
Momentum Health Study; Vancouver; **A longitudinal cohort of of sexually active gay, bisexual and other men who have sex with men with 6-monthly follow-ups.** **Participants completed a behavioural questionnaire and HIV and other STI testing, up to seven visits.** **Participants were recruited by respondent-driven sampling, a form of peer-to-peer recruitment;** • **Gender self-identified men (including trans men)** • **aged ≥ 16 years** • **lived in Metro Vancouver** • **reported sex with a man in the past 6 months** • **able to complete a questionnaire written in English.**	**1) Card (2017);** 2012 – 2015 To identify the social factors predicting even-level CLS between online met partners; 774 participants of which 71.8% HIV negative. Median follow-up time 1.98 years. Median age was 34 years; 75.6% White ethnicity, 85.6% identified as gay, 9.4% bisexual.	• CLS was reported during 32.4% (n = 1,015/3,133) of men's events. • CLS were more likely among men with incomes between $30,000 and $59,999 (compared with those who made < $30,000), OR 1.31 (95% CI 1.01 – 1.69), and those who reported knowing more MSM well, OR 1.05 (95% CI 1.00 – 1.05); *(GEE models)*	**N/A**	**N/A**	**N/A**	**N/A**
	2) Moore (2017); 2012 – 2015 To examine trends in attitude regarding the benefits of ART and risky sex over a 3-year period while TasP policy was actively implemented across British Columbia **Inclusion and exclusion criteria: the same as above (Card, 2017)**	• The HIV treatment Optimism-Skepticism Scale (HOSS) increased from 24 (20–26) to 26 (24–29) in Periods 1–6 (p<0.001), as did TasP statement agreement (20%–36%, Periods 1–6; p<0.001) • However, proportions of men reporting risky sex were unchanged (30% in Period 1, 27% in Period 6; p=0.104). • HOSS scores were associated with risky sex (aOR=1.03; 95%CI 1.00–1.06). *(mixed-effect modelling);*	**N/A**	**N/A**	**N/A**	**N/A**
	3) Mosley (2018); 2012 – 2016;	**N/A**	**N/A**	**N/A**	**N/A**	• Awareness of PrEP increased significantly from 18 to 80% • PrEP awareness was associated with greater

Name of the study; Study settings; Design and method / Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives / Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
	To examine trends in awareness of PrEP and factors associated with PrEP awareness; 732 participants of which 72% HIV-negative. The median age was 34 years (range 26-47), 61.8% reported an annual income of less than $30,000, 75.7% white ethnicity, 84.3% being gay, 77.9% reported some formal education beyond high school.					annual income (> $60,000 vs < $30,000: aOR = 2.24; 95%CI 1.52, 3.29), education level greater than high school (aOR = 2.10; 95%CI 1.41, 3.15), practicing viral load sorting (aOR = 2.61; 95%CI 1.72, 3.94), being between 29 and 40 years old versus 18-28 years old (aOR = 1.65; 95%CI 1.20, 2.26), having used ecstasy in the previous 6 months (aOR = 1.45; 95%CI 1.07, 1.95), and reporting higher sexual sensation seeking scale scores (aOR = 1.04 per point increase; 95%CI 1.001, 1.07); *(Glimmix Analyses)*
THE U.S						
Multicenter AIDS Cohort Study (MACS); Baltimore, Pittsburgh, Chicago, and Los Angeles; **Ongoing prospective study since 1984 that includes over 7000 MSM with and without HIV infection with 6-monthly follow-up visits; Participants are tested for HIV (if HIV-negative), provide a blood sample, undergo a physical exam, and complete study questionnaires through ACASI on demographic, behavioural, medical history, psychosocial, and health services at baseline and follow-up visits.**	**1) Ostrow (2008);** 1998 – 2003; 501 active MACS participants had anal sex in the last 12 months (1324 person-visits), 238 HIV-negative. Mean age 48 years (SD 7.7), 83% White ethnicity, no data on education	• A higher Unprotected anal sex partnerships (UASP) since the last semi-annual visit at 12 months of 21.5% (95% CI 1.6 – 41.4 %) was associated with safer sex fatigue among seronegative men (*GEE models*);	**N/A**	**N/A**	**N/A**	**N/A**
	2) Lim (2012); 2003 – 2008; 2389 stimulant drug use MACS participants had at least one male sex partner (17,222 person-visits), 1207 HIV-negative. Mean age 47 years (SD 10), 64% Caucasian, 52% had a college/post graduate degree	**N/A**	Drug use trajectories (*group-based trajectory analyses*), changes in number of unprotected insertive anal sex partners (NUAII) and number of unprotected receptive anal sex partners (NUARI) (*individual growth curve modelling*); Three trajectories were identified: consistent users of stimulant drugs over time (9.8% of the cohort, N=234), men whose use increase over time (5.4% N=129), men whose use declined over time (6.9%	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **HIV negative, or** • **HIV positive and no history or current use of highly active antiretroviral therapy (HAART), or** • **HIV positive HAART recipient with documentation of HAART initiation, no AIDS diagnosis prior to HAART initiation, and a CD4 cell count and HIV-1 RNA measurement within 6 months prior to first HAART use.** • **Sexual intercourse with men or at least 5 male or female partners in the 5 years prior to enrollment.**			N=165) and a group of abstinent or rarely-using men (77.9% N=1861), Men in the decreasing group reported a reduction in NUARI over time compared to the men who were not using drugs (reduction of 0.24 partner, t = 4.93, P < 0.001), and men in the increasing group reported greater NUARI over time compared to those who did not men who did not (t = 2.49, P = 0.013).			
	3) Pines (2014); 2003 – 2011; study objectives: To inform the development of targeted PrEP delivery guidelines, we characterized sexual risk trajectories among HIV-negative MSM. 419 MACS participants that were HIV-negative at enrolment (4,834 person-visits). Mean age 38.3 years (SD 9.8), diverse ethnicity (38.4% White; 42.2% Black; 15.0% Hispanic), 43% had a college degree	**N/A**	Sexual risk behaviour trajectories (*Nagin's group based trajectory modelling based on sexual risk behaviour score over time*); Three sexual risk trajectory groups were identified: low risk (N=264 63%), moderate risk (N=96 23%) and high risk (N=59 14%). Compared to low risk group, high risk group was associated with younger age AOR 0.9, 95% CI 0.88–0.96), being White (AOR 3.7, 95% CI 1.5–9.1), depression (AOR 2.36, 95% CI 1.1–4.9), and substance use (AOR 2.0, 95% CI 1.01–3.9).	**N/A**	Over the course of follow-up, 3% (8/264), 10.4% (10/96), 32.2% (19/59) of participants seroconverted from the low, moderate, and high risk groups, respectively.	**N/A**
	4) Swartz (2017); 1985 – 2008; 1044 MACS participants composed of 348 seroconverting, 348 seronegative, and 348 seroprevalent that matched on demographics, recruitment cohort, and study visits (participants averaged 24 visits, SD 15.3). Averaged 33 years of age at enrolment, 83.5% White, 87.3% had a college degree.	**N/A**	**N/A**	Effects of sero-status, recruitment cohort, and time on self-reported stimulant/nitrite use, numbers of male sex partners, and number of unprotected receptive anal intercourse (URAI) partners (*mixed effects regressions*); MACS participants who seroconverted had the highest odds of stimulant/inhaled nitrite use (AOR 10.3, 95% CI 4.8–22), incident rates of intercourse (IRR 1.6, 95% CI 1.3–2.1), and URAI partners (IRR 5.1, 95% CI 3.5–7.3).	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
	5) Zhu (2018); 1985 – 2008; 558 MACS participants who seroconverted during observation, not missing seroconversion dates, and were not administratively censored (13,018 person-visits). Mean age 31 years (SD 11), 85% non-Hispanic White, 49% had a college degree.	**N/A**	**N/A**	Changes in time-varying risk behaviours following HIV seroconversion with and without exposure to HIV treatment (*fixed effects regressions*); HIV seroconversion was associated with reduced odds of subsequent engagement in sex with ≥2 partners (AOR 0.4, 95% CI 0.26-0.52), reduced odds of insertive anal sex with ≥2 partners (AOR 0.36, 95% CI 0.22-0.59), and reduced odds of heavy drinking (AOR 0.7, 95% CI 0.51-0·98). Seroconversion after 1996 was associated with further reduced odds of insertive anal sex with ≥2 partners (AOR 0.22, 95% CI 0.12-0.4), compared to before 1996 (AOR 0.41, 95% CI 0.24-0.7).	**N/A**	**N/A**
Centers for Disease Control and Prevention Collaborative Seroincidence Study (CSS); Chicago, Denver, San Francisco; **Prospective cohort study with 6 monthly follow-up visits among susceptible gay men; Participants were interviewed about sexual behaviour in the previous six months for up to 4 interviews. Information collected include: total number and types of sexual contacts, anal acts, oral acts, protected sex, unprotected sex, sex with a partner of unknown HIV status, and sex with a partner believed to be**	**1) Romero-Severson (2012),** **2) Romero-Severson (2015);** 1992 – 1995; study objectives 882 CSS participants that were observed for all 4 periods of the study (from full dataset of 1883 men). No data on demographic	**N/A**	Trends overtime in number of contacts per individual, contact heterogeneity (*Poisson and Negative Binomial Models using gamma random variable as the rate of process*), dynamic variation in individual sexual contact rates (*iterated filtering model*); A decreasing trend in the average number of contacts (a decrease of 35% from 1.97 contacts of any type per month per susceptible individual in the first observational period to 1.29 in the final period), The total number of sexual contacts made over the course of the study (mean 1.55 per month) were highly variable between individuals (SD 9.8 per month), The average duration of time for which an individual has a constant average contact rate is	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
HIV-positive. The exact time at which each sexual contact occurred in an observational period is unknown. **Inclusion and exclusion criteria**			approximately 2 years (μR = 0.04 contacts/month).			
In the Pipeline; Los Angeles **Microbicide Clinical Trials that followed participants for one year, 50% from total participant were HIV-negative; Participants completed self-interviews through ACASI on socio-demographics, substance use, and sexual behaviours at baseline, 3-months, and 12-months visits.**	**Pines (2016);** 2007 – 2010; study objectives 163 low-income, HIV-negative *In the Pipeline* participants. Mean age 35.8 years (SD 11), diverse ethnicity (38% White, 24% African American; 27% Hispanic/Latino), 87% had a high school education	**N/A**	Individual-level, partnership-level, and sexual event-level factors associated with condom use during receptive anal intercourse (RAI) (logistic generalized linear mixed models); Condom use during RAI was negatively associated with reporting ≥ high school education (AOR 0.32, 95% CI 0.11-0.96) and methamphetamine use with non-main partners (AOR 0.20, 95% CI 0.07 - 0.53) and those that included lubricant use (AOR 0.20, 95% CI: 0.08 - 0.53).	**N/A**	**N/A**	**N/A**
Project Q2; Chicago **A longitudinal study of LGBT youth for 6-monthly follow-ups focused on the sexual and mental health. Participants completed measures using ACASI on characteristics and sexual behaviours. Participants were recruited through a combination of venue sampling (38%) and incentivized snowball sampling (62%).**	**1) Newcomb (2010);** 2007 – 2010; To describe the moderating effect of sensation seeking on the association between alcohol / drug use and risky sex by simultaneously modelling within-person's variability in substance use prior to sexual encounters; 144 young men, mean age at baseline 18.53 (SD = 1.21), 23.0% were under age 18, 48.4% Black African American, 65.6% identified as gay, 23% bisexual	**N/A**	Sensation seeking was a significant moderator of the relationship between frequency of alcohol use prior to sex and frequency of unprotected sex (Event Rate Ratio, ERR = 1.40, P<0.001 *(Hierarchical Linear Modeling (HLM) statistical software and procedures outlined by Raudenbush and Bryk)*	**N/A**	**N/A**	**N/A**
	2) Mustanski (2011); 2007 – 2010; To use longitudinal partnership-level data to explore the effects of partner and relationship characteristics on the frequency of CLS within young MSM relationship;	**N/A**	• On average, participants had 5.74 episodes of CLS in each partnership; ICC indicated that 29% of the variance was across participants and 71% across partnerships.	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **Youth LGBT aged 16-20 at baseline** • **Lived in metropolitan area in the Midwest** • **Only male participants who reported anal sexual intercourse with males were included in this sample** • **Eligibility screening included a question asking, "Project Q2 is a study for lesbian, gay, bisexual, transgender and other youth who do not use these terms but have same sex attractions. Does this include you?**	122 young men, mean age at the baseline 18.53 (range = 16-20; SD = 1.21) and 23.0% were under age 18, 48.4% African American, 65.6% were gay, participants reported their socioeconomic status as 10.9% "upper," 71.4% "middle," and 17.6% "lower		• CLS was significantly associated with considering relationship with partners to be serious (ERR 7.82, 95% CI 5.6-10.92, p<0.001), older partners (ERR 1.20), drug use prior to sex (ERR 1.45), physical violence (ERR 1.88), forced sex (ERR 5.46), and partnership lasting more than 6 months (ERR 1.62) *(Hierarchical Linear Modeling (HLM) statistical software and procedures outlined by Raudenbush and Bryk)*			
	3) Beidas (2012); 2007 – 2010; To explore the main effects of psychiatric disorders and psychological distress on total male partners and total CLS acts; 119 men, mean age at baseline 18.51 (SD=1.22), 54.6% African-American (including multiracial African-Americans) and 45.4% non-African-American, 77.3% identified as homosexual/gay, 90.8% identified as males, and 9.2% transgendered	**N/A**	• Over 24 months, participants reported an average of 1.37 – 2.47 CLS acts and an average of 1.25 – 1.36 male partners per wave (6 months). • Ethnicity significantly related to number of total male partners (ERR=0.67, p=0.01); African-American participants had 34% fewer partners than non-African American and to number of unprotected anal sex acts (ERR=0.50, p<0.01); African-American participants had 50% fewer unprotected sex acts than non-African-American participants. • The moderating effect of PTSD on the relationship between psychological distress and CLS acts (ERR=0.03, p<0.001) was significant. • A main effect of MDD was significantly related to the number of unprotected anal sex acts (ERR = 0.51, p = 0.05); participants with MDD at baseline had 49% anal sex acts than did participants without MDD at baseline.	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
			(Hierarchical Linear Modeling (HLM) statistical software)			
	4) Newcomb (2016) 2007 – 2010; To examine the developmental changes in the influence of sexual partner and relationship characteristics on sexual behaviour in the same longitudinal sample of YMSM; 118 young men, Mean age of the sample at baseline was 18.53 (SD = 1.21) and 23.0% were under age 18. 48.4% Black/African-American (48.4%), 65.6% identified as gay, 23.0% bisexual	Significant change over time in the association between relationship status and CLS (ERR = 0.8, p < .001); the difference in rate of CLS with serious compared to casual partner's decrease over time. The positive association between having older partners and CLS increased significantly over time (ERR = 1.07, p < .01). A similar pattern was found for the change over time in the effects of meeting partners online (ERR = 1.27, p <.001), physical IPV (ERR = 1.17, p = .061), and sexual IPV (ERR = 1.56, p < .001) on CLS. *(Hierarchical Linear Modeling (HLM) statistical software)*	The strongest longitudinal correlate of CLS was relationship status (ERR = 12.50, p < .001), such that serious sexual partnerships were associated with an approximate 12-fold increase in rate of CLS relative to casual partnerships. The odds of CLS with a serious partner was about 4 times higher than casual partners (OR = 3.86, p < .001). In fact, the odds of CAI with a serious partner remained more than twice as high (OR = 2.44, p < .001) even after controlling for the total number of anal sex acts, which itself was a significant predictor of CLS (OR = 1.04, p < .01). Sexual IPV was the next strongest effect (ERR = 2.04, p < .001), and the rate of CLS was approximately twice as high in partnerships in which sexual IPV had occurred. Additionally, physical IPV (ERR = 1.88, p < .05) and larger partner age differences (ERR = 1.18, p < .001) were each associated with a higher rate of CLS. *(Hierarchical Linear Modeling (HLM) statistical software)*	**N/A**	**N/A**	**N/A**
P18 Cohort Study; New York City **A prospective cohort study of YMSM to understand syndemic condition in a new generation of racially/ethnically and socioeconomically diverse YMSM with 6-monthly follow-ups. Participants completed an ACASI based assessment on**	**1) Halkitis (2015);** 2009 – 2013 To examine the extent to which the constructs of drug use, CLS, and mental health burden remained consistent over an 18-month period. 592 young men with available data on baseline, 6, 12, and 18-month follow-up aged 18-19 at enrolment, 38% Latino, 29% White non-Hispanic, 15% Black non-Hispanic, 13% mixed or other race/ethnicity, and 5% Asian/Pacific Islander), 86% enrolled in school (86%), 29.5% perceived their	Unprotected oral receptive intercourse (UROI) increased from an average of 1.85 episodes per month at baseline to an average of 2.60 episodes per month by the 18month follow-up visit. Both unprotected insertive anal intercourse (UIAI) and unprotected receptive anal intercourse (URAI) increased, overall, from baseline to the 18-month follow-up visit, UIAI from 0.4 to 0.63 and URAI from 0.52 and 0.65, but there was considerable variability in reports of	The factor loading for UIAI was β = .400 (p < .001) at baseline, it declined to β = .171 by the 6-month visit (p < .01) but then its relative contribution increased at both the 12- (β = .359, p < .001) and 18-month follow-up visits (β = .630, p < . 001). In a somewhat similar fashion, factor loadings for URAI declined across the first three time points but then increased at the 18-month follow-up visit, again suggesting somewhat less stability in the	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
sociodemographic characteristics, mental health, and social factors at baseline and follow-ups. Data on recent (past 30 day) sexual and drug use behaviours were ascertained via an interviewer-administered. Participants also received HIV pre-test counselling, provided an oral swab sample for HIV antibody testing and received their results as well as post-test counselling. Participants were recruited using both active and passive recruitment modalities. • **Between 18-19 years-old** • **biologically male** • **reporting sex with another man in the past six months** • **self-reporting an HIV negative serostatus** • **provided written, informed consent to take part in P18.**	socioeconomic status to be upper class, 37.1% middle and 33.5% lower class	these two sexual behaviours both within and across time.	unprotected sexual activity latent construct. *(Structural equation / latent class modelling,* *Unconstrained models)*			
	2) Kapadia (2015); 2009 – 2013 To describe changes in oral and anal, disaggregated as receptive and insertive, sexual activity without condoms **Sample characteristics: the same as above (Halkitis, 2015)**	**N/A**	There was engagement in receptive oral sex (b0 = 2.58, p<0.001) as well as insertive anal sex ((b0 = 0.63, p<0.001 and receptive anal sex (b0 = 0.65, p<0.001) at the 18-month follow-up visit, also statistically significant positive growth in the number of reported episodes of receptive oral sex as indicated by the significant slope (b1 = 0.04, p<0.001). Black, Hispanic/Latino, APIYMSM and those self-identifying as some other race reported engaging in significantly fewer episodes of oral receptive sex without a condom at the 18-month follow-up relative to White sexual minority youth (intercepts, b0 ranging from -0.81 to -2.23 with accompanying p's raging from <0.05 to<0.001). Importantly, compared to White YMSM, receptive oral sexual activity without a condom for Black YMSM actually declined over time ((b1 =-0.08, p\0.05). *(Latent growth curve modelling)*	**N/A**	**N/A**	**N/A**
	3) Halkitis (2017); 2009 – 2014 To model changes in drug use, sexual risk behaviours, and their association over time, while controlling for differences in race/ethnicity and SES, and to examine the pattern that emerges for YMSM and whether drug use and sexual risk behaviours are related over time. 598 young men, 430 had data for up to 36-month follow-up, on average	Participants reported increases in condomless ROI across time, from 1.83 episodes per month to just under 3 episodes per month.	• Drug use across over time (baseline – 36 month): Days of alcohol to intoxication (β =.023,p < .001), marijuana use (β =.091,p < .001), and inhalant use (β = .003, p < .05) all increased over time. • Condomless sexual activity across time: condomless ROI (β =.029,p<.001), condomless IAI (β =.011,p<.01), and condomless RAI (β = .009, p < .05) all increased over time.	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
	participants were 18 years old at baseline (M = 18.23, SD = 0.43, MD = 18). For those completing the assessment at 36-month in person, age was 21 years old (M =21.27, SD=0.48, Md = 21). 14.9% African American, 38.3% Hispanic, and 28.9% White. 33.5% low SES, while 37.1% and 29.5% identified as middle and upper SES respectively.		• Predicting condomless sex from drug use across time: Alcohol use to intoxication at the 36-month follow-up visit was positively associated with both condomless ROI (B= .197, p < .001) and condomless RAI (B = .054, p < .05) • Days of marijuana use at the 36-month follow-up visit was also positively related to instances of condomless ROI at the 36-month follow-up visit (B = .048, p < .01). *(Latent growth curve modelling)*		
	4) Cook (2018); 2009 – 2014; To examine how romantic relationship cognitions are associated with changes of CLS **Sample characteristics:** **The same as above (Halkitis, 2017)** with additional data on sexual orientation: 84% homosexual, 11.7% equally heterosexual and homosexual, and 4.4% predominantly heterosexual.	**N/A**	• YGBM's insertive CLS episodes increased over the emerging adulthood period (b=32, p<0.001). • The number of initial insertive condomless anal sex episodes differed significantly across YGBM (b = 5.71, p < .001) • receptive CLS increases over the emerging adulthood period among YGBM (b=.30, p<0.001). • There was significant variability in initial levels of receptive CLS (b = 6.87, p < .001) *(Zero-inflated Poisson (ZIP) growth modeling technique)*	**N/A**	**N/A**	**N/A**
HIV Seroadaptive Behaviours Study; **San Francisco** **A longitudinal study of seroadaptive behaviours with 6-monthly follow-ups. Participants completed a computer-based, self-administered questionnaire on demographics and detailed sexual history at baseline, and**	**1) McFarland (2011);** 2007 – 2009; To measure the individual level stability of seroadaptive behaviours, to gauge the role of chance in the prevalence of these strategies and to explicitly link prior intentions for seroadaptation to individuals' future behaviour. 732 (61%) of 1207 men enrolled at baseline who completed and provided sufficient information of which 79% HIV negative. 35% were between 25-	• HIV-negative men did not increase or decrease their level of risk by 12-month follow-up (paired t-test, t = 0.42, p = 0.67). • substantial men changed their behavioral pattern from baseline to 12 months. Behaviours least adhered to were condom serosorting (1%), condom seropositioning (7%) and oral sex serosorting (14%). • 100% condom use was intended by 71% of men at baseline, adhered to by 30% of these men	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
on patterns of sexual behaviour at the 6-month and 12-month follow-up interview. Participants were recruited by location time-sampling (TLS) methods • **Men aged ≥18 years** • **Resident of ten Bay Area counties**	34 years, 53% white ethnicity, 38% had a college graduate, 62% employed full time, 91% gay and 77% resided in the city and county of SF	at 12 months, non-significantly higher than among men who did not have the intention of always using condoms (18%, v2 1.6, p = 0.21).				
	2) Chen (2012); 2007 – 2009 To characterize MSM with intention to serosort and to identify factors associated with subsequent failure, defined as potentially discordant unprotected anal intercourse (PDUAI) events; 609 men who were HIV negative at baseline and 6 months, 50.2% were over 35 years of age, 56.4% White, 67.5% were employed full time, 64.1% had a college degree education,	• 363 (60%) men expressed intention to serosort at baseline. • Predictors for failing to serosort: College educated men (IRR = 5.18; 95% CI [1.18, 22.64]), frequent alcohol users (IRR = 9.93; 95% CI [1.82, 54.08]), frequent methamphetamine users (IRR = 40.13; 95% CI [5.27, 305.66]), and frequent "downers" users (IRR = 7.38; 95% CI [1.65, 32.91]) • Blacks were estimated to have fewer episodes of PDUAI compared to Whites (IRR = 0.03; 95% CI [0.00, 0.29]), and men with "other" employment status were estimated to have fewer episodes of PDUAI compared to those with full-time employment (IRR = 0.08; 95% CI [0.01, 0.73]). • *(Poisson-family generalized linear models with design-based standard errors).*	**N/A**	**N/A**	**N/A**	**N/A**
	3) Truong (2017) 2007 – 2009; To examine whether beliefs about ART efficacy and re-infection prospectively predicted subsequent CLS 773 men who completed both the baseline and 6-month behavioural surveys including 630 men HIV-negative. Median age 37 (range 28-46), 72.3% white, 60% had a college degree,	• Men who said they were less worried about getting HIV infection because treatment taken after exposure, i.e., PEP, could prevent infection were subsequently more likely to engage in DRCAI (sero-discordant receptive condomless anal intercourse) at follow-up (aOR 1.48 per scale point increase in agreement, 95% CI [1.16, 1.89]). • Being less worried about becoming HIV infected at baseline because of availability of treatment predicted DRCAI at	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
		follow-up (aOR 1.38 per point, 95% CI [1.12, 1.69]). These beliefs did not predict CCAI *(Bivariate and multivariate logistic regression models)*				
The 'Young Men's Survey'; Phoenix, Albuquerque, Austin; **A longitudinal study to test the effectiveness of a community-based HIV-prevention intervention with 18-monthly follow-ups, Data collected at three points in time.** **Participants were recruited independently by peers who sought out eligible men through venues, organizations, and social networks** • **Between the ages of 18 and 30** • **not in a monogamous relationship** • **HIV-negative or untested, men who failed to report their HIV testing status were excluded**	**Huebner (2004);** 1998 – 2001 To determine whether optimism about HAART is associated with sexual risk 538 men with available data for at least 18 months (wave 2, from total 3 waves) Mean age 27 years, 51% had high school education, 48.8% had a college education, 66.8% European American, 91.4% gay	• Wave 2 risk behavior significantly predicted Wave 3 treatment optimism (B = 0.18, SE B = 0.08, β = 0.11, p < .05). • Wave 2 treatment optimism was also associated with Wave 3 treatment optimism (B = 0.36, SE B = 0.04, β = 0.41, p < .001). *(Ordinary least squares / OLS regression analysis)*	**N/A**	**N/A**	**N/A**	**N/A**
Young Men Study; Los Angeles; **A cohort of emerging adult YMSM over the course of 2 years, at 6-months intervals. Semi-annual surveys were administered in English and Spanish using ACASI. Participants reported sexual**	**Wong (2012);** 2005 – 2009 To examine transitions in HIV-related risk behaviours 526 men recruited, 487 remained in the study at wave 5, overall retention rate of 93%. By final wave, the mean age of participants was 22.15 years	The maximum change in the proportion of participants engaging in monogamous seroconcordant CLS between wave 1 and wave 5 of the study was 7%.	The movement across different stages of behavioral risk-taking over time: • Between 35 and 52 % of individuals who practiced protected anal intercourse at any one wave were predicted to transition to a different risk group by the next wave.	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
behaviours, alcohol use and illicit drug use at each interview. **Participants were recruited at public venues using the stratified probability sampling design** • **young men aged 18–24** • **self-identified as gay, bisexual, or uncertain about their sexual orientation and/or reported having had sex with a man** • **resident of Los Angeles County and anticipated living in Los Angeles for at least 6 months** • **self-identified as Caucasian, African American, or Latino of Mexican descent.**	old; the sample was 24 % African American, 40 % Latino of Mexican descent, and 36 % White; 42 % of participants lived with their families; 83 % were employed; 35 % were enrolled in post-secondary education; and 52 % reported involvement in a primary partner relationship		• Similarly, between 46 and 53 % of individuals at highest risk were predicted to transition out of that group by the next wave *(Hidden Markov Models)*			
The impact of relationship dynamics longitudinal study; San Francisco; **A longitudinal study of gay male couples with a total of six times survey over a period of 3 years. The second survey was conducted 1 year after baseline, while the third through sixth surveys were conducted every 6 months thereafter.** **Participants were recruited through both active and**	**Darbes (2013);** 2005 – 2010 To investigate relationship dynamics and psychosocial predictors of unprotected anal intercourse with outside partners of serodiscordant or unknown HIV serostatus (UAIOUT) over time as well as UAI with primary partner in serodiscordant couples (UAIPP). 556 gay couples of which 56% were seroconcordant negative, 18% seroconcordant positive, and 26% were serodiscordant. The sample was ethnically diverse, with the largest proportions of	**N/A**	Seroconcordant couples: For every one unit increase in a couple's grand mean score on HIV-specific social support, there was an 18% greater odds that neither partner reported UAIOUT (AOR: 1.18; 95% CI: 1.10, 1.26). Similarly, couples with greater levels of relationship satisfaction had 36% higher odds of neither partner engaging in UAIOUT (AOR: 1.36; 95% CI: 1.16, 1.60). Over the course of the study, within-couple increases in trust were associated with higher odds of neither partner	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
passive recruitment strategies. **Participants reported their age, race/ethnicity, and relationship length during the baseline interview, and reported the result of their most recent HIV test, their primary partner's HIV-status, and the number of times they engaged in specific sexual behaviors in the past three months at each visit.** • **Men at least 18 years old,** • **be in their relationship at least 3 months** • **know their own and their partner's HIV-status** • **identify as gay/bisexual.** • **Couples were eligible to participate if both partners met all of the eligibility criteria.** • **Over the course of data collection, couple had to continue to meet all baseline eligibility requirements.** • **couples who broke up, couples in which one partner passed away, and couples who moved away from the San Francisco Bay area were ineligible for future visits.**	couples being interracial (47%) or White (45%). At baseline, the median age was 42 years (18 – 83). individual incomes were less than $60,000 annually for most men and, in 49% of couples, both partners were employed.		engaging in UAIOUT (AOR: 1.10; 95% CI: 1.05, 1.15). Serodiscordant couple: For every one unit increase in a couples grand mean score, there was a 19% higher odds of neither partner reporting UAIOUT (AOR: 1.19; 95% CI: 1.04, 1.36). On average, over the course of the study, within-couple increases in commitment were associated with higher odds of neither partner engaging in UAIOUT, such that for every increase in a couples' commitment over time there was an 11% greater odds of neither partner reporting UAIOUT (AOR: 1.11; 95% CI: 1.03, 1.19). Specifically, a one-unit increase in a couple's grand mean level of attachment across time was associated with 12% higher odds of engaging in UAIPP (AOR: 1.12; 95% CI: 1.000, 1.26). Conversely, a one unit increase in a couple's grand mean level of HIV-specific social support across time was associated with 16% lower odds of engaging in UAIPP (AOR: 0.84; 95% CI: 0.74, 0.95). A one unit increase in a couple's grand mean level of intimacy across time was associated with 6% higher odds of engaging in UAIPP (AOR: 1.06; 95%b CI: 1.01, 1.12). *(random coefficient models/multilevel models)*			

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
Metromates Cohort Study; Los Angeles **A cohort study followed MSM seeking testing for HIV for one year with quarterly follow-up visits. Participants completed self-interview through CASI on sexual behaviour, alcohol and drug use, and use of ART for treatment. All baseline data was collected after a known diagnosis but refer to behaviour that occurred before or at the time of infection or negative result.** • **Men at least 18 years of age** • **reporting sex with a man in the past 12 months** • **sought HIV testing at the Los Angeles LGBT center**	**Gorbach (2018);** 2009 – 2013; To examine the effect of an HIV diagnosis on subsequent sexual behaviour behaviour of men who have sex with men 328 men enrolled of which 216 HIV positive; 125 recently infected, 91 not recently infected and 113 HIV negative. 55% from total participants completed any follow-up after enrolment. 59% less than 30 years, 51% Hispanic, 15% African American, and 27% White Most participants were interviewed within a month of their diagnosis (median 15 days, range 7–31).	**N/A**	**N/A**	• Median number of partners reported in past year dropped significantly over time among recently infected MSM (10 at baseline to 5 at 12 month follow-up) and HIV negative men (5 to 3), p<0.001, but not for not recently HIV infected. • No changes comparing baseline to follow-up were noted in reports of CAI within each HIV-group. • after HIV testing recently HIV infected and not recently HIV infected men practiced more CLS within serodiscordant partnerships than HIV negative MSM: more CRAI than the HIV negatives (AOR= 4.90; 95% CI 1.80–13.29 and AOR =5.01; 95% CI 1.77–14.16 among recently infected and not recently infected, respectively) but only more CIAI among not recently infected (AOR 3.48; 95% CI 1.31–9.24) when compared to HIV negatives. *(GEE models)*	**N/A**	**N/A**
RADAR Study; Chicago; **An ongoing longitudinal cohort study of HIV-negative and HIV-positive with 6-monthly follow-up assessments and a total of 18-month reporting windows. Participants reported data on demographics at baseline and sexual risk behaviour, PrEP and HIV status at each visit**	**Newcomb (2018);** 2015 – 2017; To examine whether PrEP use and PrEP adherence were associated with change in sexual risk behaviours among YMSM reporting on multiple sexual partnerships over time 953 participants reported male sexual partners, Mean age 21.5 (3.5); 71.1 % gay; 25.6% White, 34% Black / African American, 29.4% Hispanic / Latino; 86% HIV negative.	**N/A**	**N/A**	**N/A**	**N/A**	• PrEP use was more likely for HIV-negative YMSM in serodiscordant partnerships than seroconcordant partnerships (OR= 4.96, P<0.01), • Among HIV-negative cohort members with partners perceived HIV-negative or unknown status, PrEP use was associated with a significantly higher rate of receptive anal sex (IRR = 1.27, P , 0.05) and receptive CAS acts (IRR = 1.49, P , 0.05).

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
through a computerized self-administered interview. Participants were recruited using multiple recruitment methods • **male sex assigned at birth** • **previous sexual encounter with a male** • **identification as gay or bisexual, or same-sex attracted** • **English speaking**						• PrEP adherence was associated with total CAS (IRR = 1.62, P , 0.05) and receptive CAS acts (IRR = 1.79, P , 0.05) *('glmmTMB' package / count data models)*
Seroconversion Cohort Study; Seattle; **A retrospective cohort of MSM attending an STD clinic who tested HIV positive but had a negative HIV test <2 years before diagnosis. 1000 HIV-negative who were frequency-matched to the seroconversion cohort based on HIV diagnosis were selected were randomly selected. Sexual behaviour, drug use, and HIV testing information was collected through face-to-face interviews or computer-assisted self-interview, including partner HIV status, in the past 12 months at each visit as part of routine clinical care.**	**Khosropur (2016);** 2001 – 2013; To describe patterns in sexual behaviour before and after HIV diagnosis and to compare that pattern of behaviour to that observed in MSM who remained HIV uninfected. 186 HIV positive (with 1000 HIV-negative controls), Mean age 32 years; 63.4% were white non-Hispanic, 10.2% were black non-Hispanic, 15.1% were Hispanic, 11.3% were other non-Hispanic. 41.9% were diagnosed between 2006 – 2009, 37.1% between 2010 and 2013.	**N/A**	**N/A**	• The proportion (of the 186) reporting CLS with HIV-negative partners declined from 73% at diagnosis to 12% after diagnosis (P<0.001), whereas CLS with HIV-positive partners increased (11%–67%; P <0.001). • The proportion who serosorted did not change before or after diagnosis (34%–40%; P = 0.65), and remained stable for up to 4 years after diagnosis. • Among HIV negative controls, serosorting and CLS with HIV-positive and HIV-negative partners was constant.	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• MSM tested positive between 2001 and 2013 and had a negative HIV test <2 years before diagnosis • Made ≥2 visits • Had complete sexual behaviour data available						
The Public Health Seattle & King County (PHSKC) Cohort Study; Seattle **A cohort of MSM who initiated PrEP through an STD clinic with quarterly clinical follow-up and mentoring. Participants completed a behavioural questionnaire by CASI, tested for HIV and STIs at initiation and quarterly visits.** **Transgender persons who have sex with men and MSM who report any of the following risk factors in the past 12 months:** • **diagnosis of rectal gonorrhea or early syphilis, use of methamphetamine or amyl nitrites (poppers), or exchanging sex for money or drugs.** • **PrEP patients were included in this analysis if they initiated PrEP during the study period, and**	**Montano (2018);** 2014 – 2017 To examine changes in sexual behaviour and STIs prevalence among men initiating PrEP 183 patients with complete behavioural data at their initial visit and at least one follow-up visit from 196 patients initiated PrEP. The mean age was 31.2 years (SD 8.9). Half the patients were White, non-Hispanic, almost 60% were on private insurance.	• Reporting never using condoms in the prior 30 days increased (adjusted relative risk = 1.46; 95% confidence interval 1.13, 1.88) at 12 months after PrEP initiation compared to the initial PrEP visit. • Reporting unknown status partners in the prior 30 days decreased at 12 months compared to the initial PrEP visit, but there was no change in number of sexual partners or reporting HIV-positive or HIV-negative partners. *(GEE models)*	**N/A**	**N/A**	The percentage of patients diagnosed with any STI while using PrEP (49.2%) was higher than the percentage diagnosed in the 12 months prior to PrEP use (35.0%)	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
completed a questionnaire during their initial visit and at least one follow-up visit.						
Rhode Island PrEP Programme Cohort **Rhode Island** **A cohort study of MSM initiating PrEP in a clinical PrEP programme with quarterly follow-ups. Data were collected at baseline, 3, and 6 months following PrEP initiation including total number of anal sex partners and condom use. Demographic information was collected at the baseline Visit, sexual behaviours were collected at baseline and each follow-up visit via clinician interview.** **The analysis was restricted to individuals who:** • **reported having sex with another man** • **had two clinical follow-up visits for PrEP (e.g., those who had been on PrEP for at least 6 months and who had been retained in care) as of May 2016.**	**Oldenburg (2017);** 2013 – 2016; To explore sexual behaviour changes following PrEP initiation by describing immediate changes in sexual behaviours over a 6-month period following PrEP initiation. 61 patients who were retained in care for at least 6 months and had clinical follow-up visits. Median age 31 years (range: 26 - 46). 73.8% had a college education or above, 24.6% Hispanic / Latino, and 4.9% African American.	**N/A**	There was a significant increase in mean number of CLS partners at 6 months compared to baseline (mean increase 1.31 partners, 95% CI 0.09–2.53, P=0.035), with association stronger in an analysis restricted only to individuals who reported multiple partners in the previous 3 months at a given time point (n=55). *(Mixed effect models)*	**N/A**	**N/A**	**N/A**
Non high-income countries						
Bangkok MSM Cohort Study; Bangkok, Thailand **A prospective cohort study with 4-monthly follow-up**	**1) Holtz (2015);** 2006 – 2012 To determine changes in three HIV-risk behaviors: CLS, recreational drug use, and multiple sexual partners, and	At 36-month follow-up: • any UAI decreased from 56% at baseline to 19%	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
visits; Men were tested HIV at every visit and STIs at baseline. Demographic and behavioural data collected through ACASI at baseline and at regular visits. Clients were screened during VCT for the presence of HIV antibodies in blood with three consecutive rapid tests for the virus. Participants were recruited from HIV testing providers, entertainment venues, the internet, and by word of mouth • **Men aged 18 years or older** • **Thai Nationals** • **Resided in the Bangkok metropolitan area** • **had male-to-male penetrative anal intercourse or oral sex in the past 6 months** • **were available for follow-up visits every 4 months for up to 3 years, which was later extended to 5 years.**	factors associated with each one separately 1569 MSM recruited from venues patronized by MSM. Median age 26 (18–56); 96% homosexual, gay or bisexual; 96% employed / studying.	• having had more than four sexual partners decreased from 49% at baseline to 23% • recreational drug use decreased from 16% to 7% • Odds of the three HIV-risk behaviours significantly decreased with each one-unit increase in number of subsequent follow-up study visits (2% for CLS, 1% for recreational drug use, and 1% for multiple sexual partners) in multivariate analyses.				
	2) Van Griensven (2015); 2006 – 2013; To assess the temporal trends in HIV incidence and key behavioural risk factors by comparing data of BMCS with data obtained from clients using anonymous VCT clinical services 1259 men with more than one follow-up test from the 1744 BMCS participants, median age 26 years (22–30 years). Median age of participants in the VCT cohort at first registration was 27 years (IQR 23–33) and 11% were non-Thai nationals (26% east Asians, 68% from western countries, and 6% other nationalities); The age distributions at enrolment between the cohorts were significantly different (p<0·0001).	• Overall in BMCS and VCT cohorts, 100% condom use (p<0.0001), drug use (p=0·03), drug use to enhance sex (p=0·0006), use of drugs for erectile dysfunction (p<0·0001) increased over time, whereas the proportion of individuals reporting receptive anal intercourse decreased (p=0·004). • Overall, for receptive anal intercourse, there was a linear reduction from above 60% in 2006 to about 50% in 2012–13 (p=0·02), and individuals aged 21 years and younger were more likely to report receptive anal intercourse than were older people (p<0·0001) *(GEE models)*	**N/A**	**N/A**	• VCT cohort: 235 (12%) from 8176 individuals seroconverted. The overall HIV incidence was 5·5 per 100 person-years (95% CI 4·8–6·3), with an increasing trend (adjusted p=0·02). • BMCS cohort: 238 (17%) of 1259 seroconverted. The overall HIV-1 incidence was 5·3 per 100 person-years (95% CI 4·7–6·1), with an increase and then a decline (inverted U-shaped curve, p=0·0001). • Individuals aged 21 years and younger were at significantly higher risk of HIV infection than were those aged 30 years and older in the in the VCT (rate ratio 2·29, 95% CI 1·88–2·78, p<0·0001) and BMCS cohorts (1·99, 1·50–2·65, p<0·0001). *(Poisson regression)*	**N/A**
Beijing VCT Study; Beijing, China;	**Lau (2015);** 2009 – 2012 To investigate potential positive or negative consequences of taking up	• 18 % of the participants interviewed at month 21 self-reported increased in CLS and other risk behaviours, comparing	**N/A**	**N/A**	At month 21: 65 HIV cases detected, The overall HIV incidence from baseline to month 21 was 7.13	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
A 21-month prospective cohort study with 6-monthly follow-ups. Participants were invited to take up VCT repeatedly at baseline and every 6 months afterwards and reported socio-demographic data and HIV-related information (months 6, month 12 and month 18). Levels of HIV-related risk behaviours were assessed. Participants were recruited from multiple sources, including: (1) outreaching at gay venues, (2) placing a recruitment advertisement on a website which disseminated HIV prevention information and (3) referrals made by participants • **Had anal intercourse with man in the last 6 months** • **age 18 years old or above** • **Exclusion criteria were intention to leave Beijing within the next 3 months and HIV positive diagnosis.** • **All participants who visited the clinic at month 18 were invited to join the extension study at month 21.**	multiple times of VCT, including those related to potential changes in HIV incidence and level of risk behaviours 228 participants who joined an extended study at month 21 from 809 men present at baseline. 68.8 % ≤35 years old, 24.6 % were currently married to women; 75.9 % were not registered Beijing residents; 82.5 % had attended a college or a university; 49.5 % had had personal monthly income of B3000 RMB (460 USD). There was no statistical difference in socio-demographic characteristics assessed at baseline between those who participated in the month 21 survey and those did not (n = 581), 66.7% had a homosexual orientation, or had recruited most of their male sex partners via the internet (64.5 %).	recent and pre-baseline experiences. • Despite multiple rounds of VCT received, 64.5 % of the participants self-reported having had multiple male sex partners in the last 3 months (18.0 % had had [1 RP and 50.4 % had had [1 NRP) and the prevalence of CLS in the last episode of anal sex with any male sex partner and UAI in the last 3 months with any male sex partner was 77.1 and 57.1 %, respectively, while perceived likelihood of having UAI in the next 3 months was 42.6 % RP: regular male sex partners, NRP: non-regular male sex partners			per 100-person year (95 % CI 5.50–8.76). HIV prevalence at months 0, 6, 12, 18 and 21 ranged from 2.5 to 6.3 %; HIV incidences for the four intervals between the five visits ranged from 5.00 to 14.28 per 100-person year The HIV incidences for the periods from baseline to month 6, from month 6 to12, from month 12 to 18 and from 18 to 21 was very high: 5.00 (95 % CI 3.46–6.54), 8.81 (95 % CI 6.67–10.95), 6.57 (95 % CI 4.45–8.69) and 14.28 (95 % CI 10.16–18.40) per 100-person years, respectively.	

Appendix 2. Summary of articles from longitudinal interventional studies containing data on sexual behavioural changes among HIV-Negative GBMSM at enrolment globally, 1998 – 2018

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
BIOMEDICAL INTERVENTION						
High-income countries						
ANRS IPERGAY Trial; France and Canada **A double-blind, randomized combined prevention trial with 2-arms providing sexual activity-based PrEP with 2-monthly follow-up visits;** **TDF-FTC vs. Placebo, all participants received risk reduction counselling, condoms, tested for HIV and STIs. Men completed an online questionnaire on socio-demographic, alcohol and recreational drug use, sexual behaviour, and PrEP adherence during recent episode of sexual intercourse (using CASIs).** • **HIV-negative male or transgender women who have sex with men** • **aged ≥18 years** • **at high risk of HIV acquisition that is reporting anal sex with at least two different partners over the previous 6 months.** • **Exclusion criteria included positive results on testing for hepatitis B surface antigen, chronic infection with hepatitis C virus, a creatinine clearance of**	**1) Molina (2015);** 2012 – 2014; To assess the efficacy and safety of sexual activity–dependent PrEP among high risk MSM on the basis of the rate adherence (and thus efficacy) might be higher than that with a daily regimen. 400 men enrolled (from 414 randomized), 199 in the TDF-FTC group and 201 in the placebo group). Median age 34.9 (29–43) years; 72.3% had a high school or higher educational level; and 84.6% were in active employment. median follow-up time 9.3 months (4.9 – 20.6)	• a significant decrease in the number of sexual partners within the past 2 months in the placebo group as compared with the TDF-FTC group (7.5 and 8, respectively; P=0.001). • no significant between group differences in the total number of episodes of sexual intercourse in the 4 weeks before visits (P=0.07), in the proportion of episodes of receptive CLS (P=0.4), or in the proportion of episodes of CLS during the most recent sexual intercourse (P=0.9). *(mixed models and binomial mixed models)*	**N/A**	**N/A**	• 16 HIV occurred during follow-up, 2 in the TDF-FTC group (incidence, 0.91 per 100 person-years) and 14 in the placebo group (incidence, 6.60 per 100 person-years) • a relative reduction in the TDF-FTC group of 86% (95% CI 40 – 98, p=0.002) • new STIs during follow-up similar in both groups (41% vs. 33%, p=0.1) *(Kaplan-Meier method and log rank test)*	• median number of 15 pills taken monthly (11-21) in the TDF-FTC group vs. 15 (9-21) in the placebo group (p=0.57) • Individual patterns of pill use showed large interpatient and intrapatient variability over time.
	2) Sagaon-Teyssier (2016); 2012 – 2014 To analyse PrEP adherence and sexual risk behaviour trends over 24 months of follow-up. **Sample characteristics: the same as above (Molina, 2015)**	**N/A**	• on average 29% (22.9–35.6%) reported both PrEP and condom use; 11.7% (7.2–18.9%) reported condom-use only, and 16.7% (10.8–29.6%) reported no PrEP or condom use with no significant change during the study. • Overall, 70.3% (65.3– 79.4%) and 69.3% (58.3–75.4%) of participants reported, respectively, CLS and receptive CLS during their most recent sexual encounter without significant change during follow-up. • Overall, on average 83.3% (min: 70.4–max: 89.2%) of participants	**N/A**	**N/A**	• on average, 42.6% (min: 32.1–max: 45.8%) reported PrEP use only during their most recent episode of sexual intercourse; • Scheduled (i.e., correct) PrEP use was reported on average by 59.0% (47.2–68.5%) of those reporting PrEP use during their most recent sexual intercourse *(Mixed models)*

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
less than 60 ml per minute, an alanine aminotransferase level of more than 2.5 times the upper limit of the normal range, and glycosuria or proteinuria of more than 1+ on urine dipstick testing			protected themselves by PrEP intake or condom use or both during the trial, and no increase in at risk sexual practices was observed. *(Mixed models)*			
ANRS IPERGAY OLE; France and Canada **The open-label extension of the randomised placebo-controlled ANRS IPERGAY trial, with on-demand TDF-FTC to be taken before and after sexual intercourse, 2-monthly follow-up visits;** **intervention: the same as ANRS IPERGAY**	**1) Molina (2017);** 2014 – 2016; To assess the efficacy, safety, and effect on sexual behaviour of on-demand PrEP 361 men enrolled (from 400 who started randomised placebo-controlled phase). Median age 37 years (30-44), 91% white, 98% had a post-secondary level education, 78% not in a couple. Median follow-up 18·4 months (17.7–19.1).	A significant increase in the proportion of participants reporting receptive CLS from 77% (136 of 176 participants) at baseline to 86% (66 of 77 participants) at 18 months' follow-up (p for trend=0.0004) *(Linear regression)*	**N/A**	**N/A**	• HIV incidence 0.19/per 100 PY (95% CI 0.01–1.08), compared with 6.60/100 PY (3.60–11·05) in the placebo group of the randomised study, indicating a relative reduction of 97% (95% CI 81–100) in the incidence with on demand PrEP. *(mid-p exact test)* • Bacterial STIs incidence did not change significantly compared with the randomised phase (59 *vs* 49.1 per 100 p-y, respectively; p=0·11).	Median number of 18 pills taken monthly (11-25)
Inclusion and exclusion criteria: the same as ANRS IPERGAY	**2) Sagaon-Teyssier (2018);** 2012 – 2015; To identify behavioral trajectories over time for PrEP and condom use, and to investigate the link between these trajectories. 332 men participating in both the double-blind and OLE phases; Median age 36 years (29–43), 73.9% had a high-school diploma or higher, 84.6% employed, 93.3% financially comfortable, 23.2% experienced stress related to PrEP side effects	**N/A**	• Two condom trajectories were identified: 53% (n = 176) of the 332 participants were ''low-level users'' of condoms, and 47% were ''high-level users.'' • Among the low-level trajectories, 24.4% also belonged to the ''low adherence to PrEP'' group. This most-at-risk group represented 13% of all the participants. *(Group-based trajectory modelling using logistic specification)*	**N/A**	**N/A**	• Four distinct group trajectories were identified: 49.7% of the participants had ''systematic adherence to PrEP,'' 19%had ''high adherence to PrEP, 15.3% had ''declining adherence to PrEP,'' and 16%had ''low adherence to PrEP.'' *(Group-based trajectory modelling using logistic specification)*
Saint Louis Hospital Paris Cohort Study; Paris, France	**Noret (2018);** 2015 – 2017; To assess the incidence of HIV infection among PrEP users and the safety and	• a significant increase in the rate of last CLS from 53.3% at baseline to 79% at month 12 (P<0.0001)	**N/A**	**N/A**	• 4 HIV occurred over 486 p-y in non-adherent patients (HIV incidence 0.82/100 p-y) • a significant increase in bacterial STI rates 14.6% at	The proportion of participants opting for on-demand PrEP remained unchanged during follow-up (75.6% at

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
A single-center, open-label, prospective cohort study enrolling participants to start PrEP with daily or on demand TDF-FTC with quarterly follow-up visits; **At baseline and follow-ups, patients were tested for HIV and creatinine plasma levels, and provided data on demographics, sexual behaviour, STIs, through an electronic database.** • **Adults with a negative HIV test** • **Had a high risk of sexual acquisition of HIV (MSM with CLS with at least two different partners over the past 6 months, or having a STI over the past 12 months, or multiple courses of PEP within the prior 12 months, and/or use of chemsex.**	the impact of PrEP on sexual behaviour and STIs. 1049 participants started (from 1069 attended first visit), 99.4% (1043) were MSM; Median age 36 years, MSM had a median number of partners of 10, 75.6% opted for on demand PrEP, 87% French citizenship, 84.4% had a post-secondary education, and 82.7% had a professional activity.	• a significant increase in the number of CLS in the prior 4weeks before the visit from a mean of 3.4 at baseline to 8.5 at month 12 (P<0.0001). • The use of chemsex at last sexual intercourse remained unchanged (27.5% at baseline and 28.3% at month 12; P=0.06). *(Logistic regression models)*			baseline vs. 19.2% at month 12; P<0.0001).	baseline vs. 72.0% at month 12; p=0.40).
PROUD Study; England, The UK **An open-label randomised trial done at 13 sexual health clinics in England;** **Participants were randomly assigned to receive daily combined tenofovir disoproxil fumarate (245 mg) and emtricitabine (200 mg) either immediately or after a deferral period of 1 year. Randomisation was done via web-based access to a central computer-generated list with variable block sizes (stratified by clinical site). Follow-up was quarterly.**	**McCormack (2015);** 2012 – 2014; To assess the net effect of efficacy, adherence, and any change in sexual behaviour as a result of PrEP Questionnaires about sexual behaviour in the previous 90 days were completed and returned by 534 participants at baseline (271 in the immediate group *vs* 263 in the deferred group) and by 406 participants at 1 year (212 *vs* 194) from total 540 participants in the trial; Median age 35 years (29–43), 61%) university graduates, 40% were born outside of the UK, and 30% were living with a partner.	• Total number of different anal sex partners varied widely at the two timepoints • no significant difference between groups at 1 year (p=0·57) • However, a larger proportion of participants allocated to immediate PrEP than allocated to deferred PrEP reported receptive anal sex with ten or more partners without a condom (21% *vs* 12%; p=0·03, test for trend).	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **HIV-negative gay and other men who have sex with men who had had anal intercourse without a condom in the previous 90 days**						
The San Francisco PEP Study; San Francisco, the U.S **A 1-year study of non-randomized trial of adults with high-risk sexual or drug-use exposures within the prior 72 h with 6-monthly follow-up visits; Antiretroviral medication for 4 weeks and five counselling sessions, Participants were followed for repeat request for PEP and for changes compared with pre-enrollment in overall high-risk behavior and the acquisition STIs and HIV. Participants were assessed by a structured interview, at study entry and at 6 and 12 months following entry, regarding their sexual behavior and recreational drug use in the previous 3 months, and for aspects of their mental health.** • **HIV-negative age ⩾13 years** • **Able to give informed consent** • **Reporting a potential exposure to HIV in the prior 72 h**	**Martin (2004);** 1997 – 2000; To evaluate the concern that the availability of PEP for sexual or drug-use exposures might result in behavioural disinhibition. 397 participants (of 401 eligible), 85% (334) were MSM; Median age 32 years (17-72), 69% white, 59% college educated, 83% employed, 6% reported homeless, 94% residents or lived within 50 miles of San Francisco	**N/A**	at 6 months following receipt of PEP, 77% of MSM reported a decrease compared with baseline in the number of times they had performed any high-risk act with a high-risk partner, 15% reported no change and only 8% reported an increase (P<0.001, comparing the number reporting a decrease with those reporting an increase). At 12 months, 76% reported a decrease, 11% no change, and 13% an increase (P<0.001).	**N/A**	• 3 MSM seroconverted; HIV incidence rate 1.2/100 P-y • 85% participants had no change in the incidence of STD; 8.5% had a decrease and 6.8% an increase	After 12 months following receipt of PEP, the majority of participants (83%) did not request a repeat course of PEP *(Kaplan-Meier methods)*
The VISION / VAX004 Study; the U.S, Canada, and the Netherlands; **A randomized, double-blind,**	**Bartholow (2005);** 1998 – 2002; To evaluate HIV sexual risk behaviour among MSM and women over 36 months of vaccine trial	The proportion of men remaining uninfected who reported CLS decreased from the baseline to the 6-month visit (OR = 0.75, 95% CI = 0.70–0.81), increased slightly from the 6- to 30-month visits (OR (30 vs. 6 mo) = 1.15, 95% CI = 1.07–	**N/A**	Among men who became infected: • fewer reported engaging in CLS at the 6-month visit than at baseline (OR = 0.69, 95% CI = 0.54–0.89); however, this behavior returned to the baseline level at 12 months and	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
placebo-controlled efficacy trial of a bivalent rgp120 vaccine semi-annually follow-up visits; **Two-thirds of participants were randomly assigned to the vaccine arm and one-third to the placebo arm of the trial.** **Sexual behaviour data were provided through face-to-face structured interview.** • **HIV seronegative, 18–60 years** • **having engaged in anal sex with a male partner during the previous 12 months** • **MSM were excluded if they had been involved in a monogamous relationship with an HIV-seronegative partner for >12 months or reported a history of injection drug use any time during the 3 years prior to the baseline visit.**	5095 MSM and 308 women enrolled, men were more likely to be white (86%), college educated (42%), and younger than women (median age 36 years).	1.23), and then returned to the 6-month level at 36 months (OR (36 vs. 6 mo) = 1.05, 95% CI = 0.98–1.13) *(GEE models)*		did not significantly differ from baseline for the remainder of the trial. • a decrease in CLS with HIV-seropositive partners from the baseline to the 6-month visit (OR = 0.75, 95% CI = 0.59–0.95) and then reported increases from the 6- to 36-month visits (OR = 1.67, 95% CI = 1.13–2.47).		
The US CDC Safety Study; San Francisco, Atlanta, Boston, the U.S; **A Phase 2 Randomized, double-blind, placebo-controlled extended safety of TFD trial with quarterly follow-up visits over a 2-year period;** **Participants were randomized 1:1:1:1 to receive one of 4 arms: 1) daily tenofovir disoproxil fumarate beginning at enrollment; 2) daily placebo beginning at enrollment; 3) daily TDF beginning 9 months after enrollment; 4) daily placebo beginning 9 months after**	**Liu (2013);** 2005 – 2009; To evaluate changes in sexual behaviours associated with daily pill-use in a PrEP trial. 400 men, demographics and the proportion of men reporting alcohol/drug use were similar between the immediate (n=200) vs. delayed arms (n=200). median age 38 (18-60) vs. 38.5 (18-59); white 72% vs 75%; Hispanic 10% vs. 8%; college graduate 56% vs.56%, for immediate vs. delayed arms respectively	• Mean numbers of sex partners (per subject, in the past 3 months) decreased significantly from 7.25 at baseline to 6.02 during months 3–9 and 5.71 during months 12–24 (p<0.001). These declines were similar between the immediate vs. delayed arms during months 3–9 (p for interaction=0.67) • At baseline, over half (57%) of men reported engaging in any UAS in the past 3 months. These proportions were similar between the immediate vs. delayed arm (p = 0.29). • Overall, the proportion of men engaging in UAS decreased from baseline (57%) to months 3–9 (48%, p=0.001) and months 12–	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
enrolment and followed for 24 months. • **being male at birth** • **18–60 years-old** • **HIV-1 negative, healthy (no serious or life-threatening diseases or conditions and adequate hematologic, biochemical, hepatic, and pancreatic function by laboratory testing)** • **able to understand English and provide written informed consent at screening** • **reporting any anal sex with or without a condom with a man in the last 12 months (including main or casual partners).** • **Men in a mutually monogamous relationship for _ 1 year with a known HIV-negative partner were excluded.** • **Transgender women who met eligibility criteria were included in the study.**		24 (52%, p=0.03). The change in proportion of men reporting UAS from baseline to months 3–9 was similar between the immediate vs. delayed arms (p for interaction = 0.15) • The proportion of men reporting UAS did not change significantly after initiation of study drug in the delayed arm (p=0.41) but may have increased slightly with continuation of drug in the immediate arm (IRR 1.17, 95% CI 0.98– 1.39, p=0.09). *(logistic and negative-binomial regression fitted with GEE)*				
PrELUDE Study; Sydney, Australia; **An open-label, single-arm, multi-centre study tested participants for HIV/STI and collected behavioural information three-monthly; All participants were prescribed daily TDF/FTC as PrEP. At 1 and 3 months and then three-monthly, participants were assessed for ongoing PrEP eligibility and willingness to continue taking**	**Zablotska (2018);** 2014 – 2016; To report trends over 18 months in medication adherence, side-effects, HIV/STI incidence and behaviour 320 GBM, 4 women and 3 transgender participants, followed on average 461 days (406 – 532); Median age 35 years (29–43). 71.9% European origin, 78.0% were employed full- or part-time, 65.6% had attained a University degree	• 31.5% men reported having CLAI with regular partners, and this did not change over time. • a significant increase in the mean number of HIV-positive partners (Wald z = 2.53, p = 0.011). • At enrolment, 23.8, 58.1 and 41.3% of respondents reported having had CLAI in the preceding 3 months with other regular partners of HIV-positive, negative and unknown HIV status, respectively. At Month 3, these proportions were lower	**N/A**	**N/A**	• No HIV infections were observed; HIV incidence was 0 (95% CI 0–0.93/100 p-y). • STI incidence was high and stable, while gonorrhoea infections declined from 100.0 to 25.8/100 person-years between 6 and 15 months (p < 0.001). • The incidence of chlamydia was 82.6/100 PY (95% CI 65.0–105.0/100 PY) in the first 3 months on PrEP, with no statistically significant change over the study period	Participants reported taking seven pills/weel on 1591 (88.5%) occasions and 4-6 pills/week on 153 (8.5%) occasions.

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PrEP, tested for HIV, STIs, renal and liver function, and were assessed for adverse events and PrEP adherence (self-report). Following each study visit, all patients were invited to complete online surveys about attitudes, behaviours and adherence to PrEP. Electronic data capture and management system OpenClinica (OpenClinica, LLC, developed by Isovera, Inc.) was used to gather information from clinical assessments, including all results of HIV, STI, renal and liver function tests, safety events, and information about PrEP use and adherence to the study medication. • **MSM reported at least one of the four risk factors: (a) being a regular partner of an HIV-positive man, (b) having condomless anal intercourse (CLAI) with casual partners, (c) reporting a recent anal STI diagnosis, or (d) methamphetamine use** • **aged 18 years or older** • **HIV negative at enrolment** • **lived or visited NSW with sufficient frequency for participation** • **were Medicare-eligible** • **proficient in written and spoken English.**		(18.2, 33.8 and 22.6%, respectively). • The levels of CLAI increased again with HIV-positive and negative other regular sex partners (p-trend: 0.007 and 0.008, respectively), but not with those of unknown HIV status. • The mean number of HIV-positive casual partners increased over time (Wald z = 13.41, p < 0.001), while the mean number of HIV negative or unknown status casual partners did not change. • At baseline, 79.2, 78.9 and 78.9% of the male participants who had HIV-positive, negative and unknown serostatus casual partners reported having had CLAI with these partners in the previous 3 months. These proportions significantly increased over time, regardless of the HIV status of casual partners *(Cox regression)*			*(Kaplan-Meier methods)*	
Amsterdam PrEP Project; Amsterdam, The Netherlands	**Hornenborg (2018);** 2015 – 2016;	• The number of receptive and insertive condomless anal sex acts (CASa) increased (baseline:	**N/A**	**N/A**	The prevalence of any STI (chlamydia, gonorrhoea, or	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
A prospective, open-label demonstration PrEP study with quarterly follow-up visits; Participants completed self-administered questionnaire about sexual behaviour in the preceding 3 months, and were tested for STI and HIV. Participants were given a choice of daily PrEP or event-driven PrEP regimens. Participants were seen every 3 months for HIV and STI testing. • **HIV-negative MSM** • **had one or more risk factors for HIV infection in the 6 months preceding the screening visits: CLS with casual partners, at least one bacterial STI, use of PEP after a sexual risk incident, or an HIV-positive sexual partner with detectable viral load.**	To examine changes in sexual behaviour between baseline and 6 months after PrEP initiation 328 MSM and 2 TGW who completed sexual behaviour questions at baseline and 6 months after starting PrEP included (from 376 AmPrEP participants); Median age 40.5 years (33 – 49), 86% white, 61% were living in Amsterdam, 77% highly educated, 78% employed	median 11, range 4-23; 6 months: median 14, range 6-26, P < 0.001), whereas the number of anal sex partners (P = 0.2) and anal sex acts (P = 0.8) remained unchanged. *(Wilcoxon signed rank tests)* • older age, PEP use in the 6 months prior to baseline (aOR 3.09, 95% CI 1.24–7.71), engaging in chemsex with casual partners in the 3 months prior to baseline (aOR 1.72, 95% CI 1.07–2.77) and PrEP regimen choice (daily vs. event-driven, aOR 2.48, 95% CI 1.38–4.47) at baseline were factors associated with increased rCASa with casual partners at 6 months *(Logistic regression)*			recent syphilis) was 17% (56/328) at baseline and 17% (56/329) at 6 months (no changes).	
Non-high income countries						
PrEP Brasil; Rio de Janeiro and Sao Paulo, Brasil **A 48-week prospective, multicentre, open-label demonstration project assessing PrEP delivery; Participants were seen at weeks 4, 12, 24, 36, and 48 for PrEP provision, clinical and laboratory evaluation, and HIV testing. Computer-assisted self-interviews were also done at study visits 12, 24, 36, and 48, and**	**Grinsztejn (2018);** 2014 – 2017; To test the week 48 PrEP retention, engagement, and adherence, trends in sexual behaviour, and incidence of HIV and STIs 450 participants initiated PrEP, 375 retained at 48 weeks, participants were mostly in the age category of 25-34 years (47%), have been schooling for more than 12 years (74.4%), White (54%), Male (94.4%, the rest were transgender women)	• receptive anal sex with the last three partners increased from 45% at enrolment to 49% at week 48 (p=0·17) • the mean number of sexual partners in the previous 3 months decreased from 11.4 (SD 28.94) at enrolment to 8.3 (19.55) at week 48 (p<0·0013).	**N/A**	**N/A**	Two individuals seroconverted; HIV incidence 0.51/100 p-y, 95% CI 0·13–2·06)	At week 48, 277 (74%) of 375 participants had protective drug concentrations consistent with at least four doses per week

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		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
assessed sexual behaviour and drug use • **HIV-negative MSM/transgender women, aged at least 18 years** • **resident in Rio de Janeiro or Sao Paulo** • **reported one or more sexual risk criteria in the previous 12 months (CLS with two or more partners, two or more episodes of anal sex with an HIV-infected partner, or history of STI diagnosis)**						
BEHAVIOURAL INTERVENTION						
THE U.S (High-income country)						
EXPLORE Study; Boston, Chicago, Denver, New York, San Francisco, Seattle; **A Phase IIB RCT with 2 arms and twice-yearly follow-up visits included HIV testing and assessment of behavioural outcomes through ACASI. Recruitment strategies varied included advertising, outreach, referrals and through internet sites;** **Ten on-on-one counselling sessions every 3 months vs. standard twice yearly counselling.** • **HIV-uninfected men aged 16 years or older** • **Reported anal sex with another man during the past year** • **Men were excluded if they reported that they had been**	**1) Koblin (2004);** 1999 – 2003; To test the efficacy of a behavioural intervention in preventing HIV infection among 4295 men who have sex with men 4295 MSM Mean age 34 (SD 9.4); 72.5% white; 64.2% college degree.	- Overall rate of HIV infection 2.1 per 100 PY, OR for the intervention group 0.82 (95% CI 0.64 – 1.05) relative to the standard group (proportional hazard model). - The estimated ORs of reporting serodiscordant URAI, serodiscordant UAI, and any UAI were 0.80 (0.71 to 0.89), 0.85 (0.78 to 0.94), and 0.86 (0.79 to 0.94) in the intervention group relative to the standard group (GEE logistic regression).	**N/A**	**N/A**	**N/A**	**N/A**
	2) Colfax (2005); 1999 – 2003; To document longitudinal patterns of use of methamphetamines, poppers, and sniffed cocaine and to assess predictors of baseline use and changes in use of these drugs and to examine whether increased use is associated with increases in sexual risk behaviour.	**N/A**	386 of the 736 men reported serodiscordant unprotected anal sex (SDUA) during at least one follow-up, lower risk behaviour at another, and variability in drug use or depression across visits. Within-person changes on the influence of drug-use patterns on risk behaviour analysis was based on these men: Participants were significantly more likely to report SDUA during 6-month reporting periods	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
involved in a mutually monogamous relationship for 2 or more years with a male partner known to be HIV-negative or known to be HIV positive, or not fluent in English.	The analysis limited to 736 San Francisco EXPLORE participants, 42% between 26 – 35 years, 69% white, non-Latino, 37% had a college degree, 69% reported an annual income of $30,000/year or more.		characterized by higher composite drug-use scores, after controlling for current depression levels. However, a nonlinear response was apparent, with nominally lower odds ratio point estimates for scores of 3 (OR 2.8, 95% CI 1.6 – 4.9, p=0.002) and ≥4 (OR 2.2, 95% CI 1.5 – 3.4, p=0.002) than for a score of 2 (OR 3.2, 95% CI 2.2 – 4.7, p<0.0001). *(conditional logistic regression)* interpretation: *This within-person analysis found that compared with periods of no drug use, periods of both light drug use (less than weekly use of drugs) and heavier drug use (at least weekly use of at least one drug) were significantly associated with increased risk of engaging in unprotected anal sex with an HIV-positive or unknown-status partner.*			
	3) Donnel (2010); 1999 – 2003 To assess the perceptions and use of nPEP over 4 years in six cities across the United States **Sample characteristics:** **The same as above (Koblin, 2004)**	• Those reporting 10 or more partners had almost triple adjusted odds of nPEP use (aOR: 2.9, [95%CI: 1.9, 4.4]) relative to those reporting 0 / 1. • Highest odds of nPEP use were found with highest risk behaviors (URA with HIV, OR = 6.8 [95%CI: 5.0, 9.2], UIA with HIV? OR = 3.6 [95%CI: 2.7, 4.9]); increased odds of nPEP were found with partners of unknown HIV status (URA with HIV-unk, OR = 3.5 [95%CI: 2.7, 4.5]; UIA with HIV-unk, OR = 1.4 [95%CI: 1.0, 1.8]). • Any non-injection drug use was associated with 50% increase in adjusted odds ratio (aOR) of nPEP use (aOR: 1.5, 95%CI [1.1, 1.9]).	**N/A**	**N/A**	3 seroconversions occurred in the 384 visits where nPEP courses were reported, with no effect of nPEP on risk of HIV acquisition in this cohort (hazard ratio= 0.91, 95% CI [0.29, 2.86]).	Overall, 1.9% of MSM reported use of nPEP prior to enrollment, and 6.3% at least once during the trial. Awareness of nPEP was reported by 47.5%, with higher awareness in two sites with funded nPEP programs (Boston and San Francisco).

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		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
		• Men reporting injection drug use had significantly higher odds of reporting nPEP use (aOR: 2.44, [95%CI: 1.69, 3.51]). Alcohol use, reflecting drinking frequency behavior, was not associated with higher odds of nPEP use. • In men who used nPEP at the prior visit, there were elevated odds of reporting SDUA compared to those who didn't previously use nPEP (aOR: 1.6, [95%CI: 1.2, 2.1] *(GEE models)*				
	4) Bedoya (2011); 1999 – 2003 To examine data on Latino and non-Latino white MSM who participated across six cities in a 2-year randomized behavioural intervention study **Sample characteristics:** **The same as above (Koblin, 2004)** Latinos were more likely to: be younger (32.1% under 25 vs. 15%), have lower educational attainment (college 32.7% vs 37.5%), report lower annual household income, and be unemployed (13.8% vs. 8.8%) than white non-Latinos.	Among Latino only: • predictors of an increased odds of engaging in SDUA over study follow-up included: heavy alcohol use (AOR = 1.56; 95% CI: 1.03–2.36), marijuana use (AOR = 1.32; 95% CI: 1.04–1.68), popper use (AOR = 1.91; 95% CI: 1.50–2.44), amphetamine use (AOR = 1.98; 95% CI: 1.44–2.73), lower self-efficacy for adopting safer sexual behaviors (AOR = 1.80; 95% CI: 1.27–2.55), poorer communication skills regarding safer sex practices (AOR = 1.88; 95% CI: 1.49–2.36), weaker safe-sex norms (AOR = 1.39; 95% CI: 1.05–1.86), and more perceived enjoyment of risky sex (AOR = 2.17; 95% CI: 1.66–2.83). • Intervention effects did not significantly differ between Latino and non-Latinos. *(Logistic regression and replicated using GEE models)*	**N/A**	**N/A**	• 259 seroconverted; overall rate of 2.1/100 PY • 8.0% of Latinos (52/652) and 5.5% of non-Latino whites (171/3112) tested positive for HIV. Latinos had an overall rate of 2.99/100 PY (95% CI: 2.23–3.92), whereas non-Latino whites had an overall rate of 1.90/100 PY (95% CI: 1.63–2.21) • Latino MSM had a significantly higher overall rate of HIV infection over study follow-up than their non-Latino white peers (AHR = 1.44; 95% CI:1.05–1.99). • Significant independent predictors of becoming infected with HIV over study follow-up among Latino participants included: popper use (AHR = 1.97; 95% CI: 1.08–3.59) and engaging sexually in SDUA (AHR = 1.94; 95% CI: 1.02–3.66). *(Cox regression)*	**N/A**
Project MIX; **Chicago, Los Angeles, New York City, San Francisco**	**1) Mansergh (2010);** 2004 – 2008; To test the efficacy of a group-based, cognitive-behavioral	The sample reported high-risk behaviour during the past 3 mo prior to their baseline visit: 67% reported unprotected anal sex, and	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
A randomized group-based, cognitive-behavioural intervention with follow-up assessments at 3,6, and 12-months post session collecting information on demographic, alcohol and other substance use and sexual risk behavior during the prior 3 months, and on current psychosocial and mental health measures through an audio computer–administered self-interview. **Participants were recruited using a variety of recruitment strategies including outreach, advertisements, and word of mouth;** **2-hours group sessions focused on reducing substance use and sexual behaviour vs. six 2-hours group sessions of attention-control group vs. a nonrandomized standard HIV-testing group.** • **Men in the prior 6 months reported (1) being drunk or "buzzed" on alcohol 2+ times and/or high on non-injection drugs at least once during or 2 hours before anal sex; and (2) having at least 1 unprotected anal sex episode with a male partner whose HIV serostatus was unknown or different from their own.** • **Men were ineligible if they reported only marijuana use or use of erectile dysfunction medications (without any other**	intervention to reduce risk behavior of substance-using MSM, compared to a randomized attention-control group and a nonrandomized standard HIV-testing group. 1686 men were enrolled: 1206 randomly assigned to the intervention and attention-control groups; 480 standard group. Intervention vs attention control vs standard: Mostly 35 – 44: 40% vs, 44% vs. 35% White ethnicity: 38% vs. 40% vs. 45% College degree or higher: 35% vs. 33% vs. 40% Gay: 84% vs. 84% vs.85%	77% reported substance use during their most recent anal sex encounter with a non-primary partner. The three groups significantly (p,0.05) reduced risk behavior (e.g., unprotected anal sex reduced by 32% at 12-mo follow-up), but were not different (p.0.05) from each other at 3-, 6-, and 12-mo follow-up. Outcomes for the 2-arm comparisons were not significantly different at 12-mo follow-up (e.g., unprotected anal sex, odds ratio=1.14, confidence interval=0.86–1.51), nor at earlier time points. Similar results were found for each outcome variable in both 2and 3-arm comparisons.				
	2) Koblin (2011); 2004 – 2008; To examine condom-use making in the context of hypothetical PrEP efficacy among men who have sex with men who use alcohol and other substances during sex. 645 men with complete data on PrEP use and completed the 3-month visit. These participants ranged from 18 to 67 years old; 51.8% were less than 35 years of age, 19.1% black, 19.4% Latino, 49.8% white, and 11.7% mixed race or another group. 79.2%) had at least some college education and 86.0% self-identified as gay. About half (54.1%) had private health insurance.	**N/A**	Among the 605 men who never used PrEP and had completed data for PrEP efficacy with receptive and insertive UAI, 353 (58.4%) did not differentiate PrEP efficacy based on UAI role, 211 (34.9%) indicated a higher PrEP efficacy for receptive UAI compared with insertive UAI, and 41 (6.8%) indicated a lower PrEP efficacy for receptive UAI compared with insertive UAI. *(by calculating the difference between the PrEP efficacies indicated for receptive and insertive CLS)*	**N/A**	**N/A**	• Of the 645 HIV-negative men with complete data on PrEP use, 630 men had never used PrEP. • Among 630, 15.2% of men were in the mid-range efficacy group for receptive UAI and 12.3% were in the low efficacy group. • The largest proportion (72.5%) of men was in the high efficacy group for receptive CLS.

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		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
substance use) soon before or during anal sex in the past 6 months; reported injecting drugs other than steroids, hormones, prescribed medications, or methamphetamines in the past 6 months; had known for less than 6 months that they were HIV infected						
HPTN 061 Study; Atlanta, Boston, Los Angeles, New York City, San Francisco, and Washington **A community-level, multi-component intervention for Black MSM with 6-monthly follow-ups for 1-year period of intervention. Participants were recruited using community recruitment methods; At baseline and follow-ups, participants were asked about demographic and sexual behaviour through ACASI, offered HIV and STIs testing, as well as an opportunity to work with a 'peer health navigator' to assist them in getting connected to resources.** • **Self-identification as Black, African American, Caribbean Black or multi-ethnic Black MSM** • **At least one self-reported instance of CLS with a man in the past 6 months**	**Levy (2017);** 2009 – 2012; To assess correlates of treatment optimism and its association with subsequent risk behaviours for HIV acquisition or transmission. 1515 BMSM with a non-missing HIV status, 1167 HIV-negative, median age 40 years; range 27–47; range 18–68), 46% had a college degree or higher	• The prevalence of treatment optimism decreased from 12% at baseline to 7% at month 12 (p<0.001). • There was a non-significant association between treatment optimism and CAS with at least one male partner of positive or unknown HIV status in the next six months (aOR = 1.21 [95% CI: 0.81–1.81]) *(GEE logistic models)*	**N/A**	**N/A**	**N/A**	**N/A**
SF repeat testers study; San Francisco; **A randomized, controlled, counselling intervention trial.**	**Dilley (2002);** 1997 – 2000 To study whether one counselling intervention session focusing on self-justifications (thoughts,	A novel counseling intervention focusing on self-justifications significantly decreased the proportion of participants reporting UAI with nonprimary partners of unknown or discordant	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
Two intervention groups received standard HIV test counseling plus a cognitive-behavioral intervention, and two control groups received only standard HIV test counseling. Follow-up evaluation was at 6 and 12 months. Interview was measured via self-report during face-to-face interview • **MSM aged 18-49 years** • **history of at least one previous negative HIV test result and self-reported UAI (receptive or insertive) in the previous 12 months with partners of unknown or discordant HIV status.**	attitudes, or beliefs that allow the participant to engage in high-risk sexual behaviors) at most recent unprotected anal intercourse (UAI) is effective in reducing future high-risk behaviors among HIV-negative men. 248 MSM were enrolled and randomized into one of the four study arms. Mean age 32.6 years, 76% white, 42% held a college degree	HIV status at 6 and 12 months (from 66% to 21% at 6 months and to 26% at 12 months, p =.002; p <.001) as compared with a control group when added to standard client-centered HIV counseling and testing.				
New York Motivational Interviewing Trial Study; New York City; **A randomized trial with follow-up occurred at quarterly intervals for 1 year.** **Participants were recruited using both direct outreach and advertising;** **Participants were assessed and randomly assigned to 4 sessions of motivational interviewing (MI) or an educational control intervention.** • **Male ages 18–65** • **reported at least 5 occasions of club drug use in the prior 90 days**	**Morgenstern (2009);** 2004 – 2007 To examine the effectiveness of 4 sessions of motivational interviewing (MI) on club drug use and risky sex men in non-treatment-seeking MSM 150 men, mean age (37.8, SD: 8.8), 56.2% unemployed or not currently working, 77% had some college or more education, 36.3% White ethnicity. Briefly, both conditions did not differ significantly on select demographic, substance use, and risky sex measures at baseline except those in the MI condition reported greater marijuana use M = 26.9 (SD = 32.1) compared to those in the control condition M = 13.3 (SD = 21.9).	• MI did not result in a significant reduction in risky sex relative to education. There were no significant changes in the number of unsafe sex acts across the study period. • For the primary sex outcome analyses, the following covariates were significant in the model: baseline unsafe sex acts (B = .048; z = 5.44, p < .001) and drug dependence severity (B = −.055; z = −2.19, p < .03). These findings indicate that individuals who engage in greater number of unsafe sex acts at baseline were more likely to engage in unsafe sex acts during follow-up. In addition, greater drug dependence severity at baseline was associated with less unsafe sex during follow-up. *(GEE models)*	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **reported sexual contact with a non-primary male partner in the past 90 days** • **not enrolled in drug treatment in the prior month** • **reported that club drug use was at least as significant a problem as alcohol or opiate use**						
HOLA en Grupos; **North Carolina** **A 2-group, randomized, intervention–comparison group designed to increase condom use and HIV testing among Hispanic/Latino GBMSM. Follow-up assessments occurred 6 months after sessions completion. Participants were recruited by distributing information at gay bars, through media, and by word of mouth;** **4 interactive modules HOLA en Grupos intervention vs. general health education** • **Men who self-identified as a Hispanic/Latino male or transgender person** • **were aged 18 years or older** • **spoke fluent Spanish** • **reported male to-male sexual contact since 18 years** • **provided written informed consent.** • **Persons who had participated in any other HIV prevention intervention in the past 12 months were ineligible.**	**Rhodes (2017);** 2012 – 2015; To test whether participants randomized to HOLA en Grupos increased consistent consistent condom use and HIV testing compared with participants randomized to general health education comparison intervention 304 men (152 Hola en Grupos intervention vs. 152 general health education), the average age of the 304 study participants was 30 years (SD=8.9 years; range=18–55years); 45% had less than a high school education or general equivalency diploma equivalent; and 74% were employed year round. Most participants were foreign born (90%), Most participants (66%) self-identified as gay, 23% as bisexual, 5% as heterosexual, and 6% as male-to-female-transgender. Most participants—75% (n=114) of HOLA en Grupos participants and 67% (n=102) of comparison participants— completed all 4 of their assigned intervention sessions. Overall retention for 6-month follow-up assessments was 100%.	At follow-up, relative to comparison participants, HOLA en Grupos participants reported increased consistent condom use during the past 3 months (adjusted odds ratio, AOR 4.1; 95% confidence interval [CI]=2.2, 7.9; P<.001) and HIV testing during the past 6 months (AOR 13.8; 95%CI=7.6,25.3;P<.001). Participants also reported inceased knowledge skill of HIV (p<0.001) and STI (p<0.001), condom use skills (p<0.001), self-efficacy (p<0.001), expectancies (p<0.001), sexual communication skills (p<0.01). *(multivariable random effects logistic regression)*				

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
Men's INTernet Study (MINTS-II) **A randomized controlled trial with 2-arms to test an internet-based sexual health promotion intervention (Sexpulse). Participants completed the study during a 3-week period with 3-, 6-, 9- and 12-month follow-up surveys.** **Participants were recruited through banner advertisements placed on two of the nation's largest gay websites and emails to participants from previous research connected MISM to the study webpage;** **Participants were randomly assigned to receive 'sexpulse'; an internet-based sexual health promotion intervention vs. null control condition** • **Male 18 years or older** • **US resident** • **Had recent history of engaging in CLS with at least one other man** • **Would need to be comfortable viewing sexually explicit materials online and be prepared to complete all online activities** • **Be willing to provide an email address and phone number to maintain contact**	**Rosser (2010);** 2007 – 2009 To test whether an Internet-based sexual health promotion intervention for MISM can reduce their unprotected anal intercourse. 650 men who use Internet to seek sex with man (MISM), retention over the 12-month ranged between 76% and 99%. 34.5% were 26 – 35 years, 68.2% were White Caucasian, 35.2% were Graduate / professional school, 29% were business profession.	• Unprotected Anal Sex (UAIMP): 20% of participants in both experimental conditions did not report any risk change at the 3-month follow-up. Unfortunately, 12% of the control arm, compared to 10% in the treatment arm, reported more than one additional UAIMP at follow-up. • Sexpulse program reduced short-term risk by an estimated 16.8% (95% CI: 0.69, 1.00; p=0.05) in the unadjusted and by 15.6% (95% CI: 0.704, 1.013; p=0.068) in the adjusted full sample models. • Similar effects are observed in those who reported some baseline risk. By 12-month follow-up, no meaningful differences between treatment and control conditions are observed. *(Negative binomial regression)*	**N/A**	**N/A**	**N/A**	**N/A**
Many Men, Many Voices (3MV) Project;	**Wilton (2009);** 2005	• 3MV intervention participants reported significantly greater reductions in the total number	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
New York City **A small RCT addresses behavioural and social determinants of HIV for Black MSM with follow-ups at 3 and 6 months following baseline assessment.** **participants completed behavioural risk assessment through ACASI that assessed demographics, drug use, and sexual risk behaviours.** **Participants were recruited through active and passive recruitment methods included street outreach, displays at gay festival, referrals, ;** **Participants were randomly assigned to the 3MV intervention condition (n = 164) or wait-list comparison condition (n = 174), scheduled to receive the 3MV intervention 6 months following baseline.** • **self-identify as a Black MSM** • **be 18 years of age or older** • **willing to attend and participate in an HIV/STI prevention intervention retreat delivered outside New York City** • **could not have previously participated in the 3MV intervention.**	To evaluate the efficacy of a small group intervention developed HIV/STI prevention developed by Black MSM-serving community-based organizations and a university-based HIV/STI prevention and training program. 338 Black MSM, 99.1% male, 0.9% transgendered, Mean age 29.6 years (SD = 9.3; range 18–72). 67.6% African American, 41.7% had attended college, 29.9% had a college degree, 71.8% gay / homosexual	of UAI episodes at the 6-month assessment (RR = 0.34, 95% CI = 0.14–0.83, P = 0.012). • a significant intervention effect on reductions in insertive UAI episodes with casual male sex partners at the 6-month assessment (RR = 0.24, 95% CI = 0.09–0.65, P = 0.005). • Examination of linear trends across the entire study period indicated that 3MV participants reported a 51% greater reduction than comparison participants in the total number of insertive UAI episodes with casual sex partners (RR = 0.49, 95% CI = 0.28–0.87, P = 0.015 • At the 3-month assessment, 3MV participants reported a 25% greater reduction in the number of main or casual male sex partners during the past 3 months than comparison participants (RR = 0.75, 95% CI = 0.57–0.98, P = 0.04 • 3MV participants reported a trend for greater consistent condom use during receptive anal intercourse with casual partners across the entire study period than comparison participants (OR = 1.55, 95% CI = 0.99–2.43, P = 0.056). • at the 6-month follow-up 3MV participants had an 81% greater odds of testing for HIV than comparison participants (OR = 1.81, 95% CI = 1.08–3.01, P = 0.023) *(GEE models)*				
Get Real Evaluation Project Philadelphia and Baltimore	**Lauby (2017);** 2007 – 2010; To evaluate the Get REAL community level-intervention	• Philadelphia sample started with a significantly higher average anal risk score at baseline than did the Baltimore sample (66.04 vs. 34.23; p < .05), and ended up	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
A community-level intervention focused on two racial/ethnic groups; Black or African YMSM and White YMSM over 36 months in a sample of YMSM in Philadelphia (intervention site) and Baltimore (comparison site) and Baltimore (comparison site). **Three annual follow-up interviews was conducted, with the last interview at 36-months post baseline.** **Respondent-driven sampling was implemented;** • **Black or White male between the ages of 15 and 29** • **having had sex (oral, anal, or mutual masturbation with or without condoms) with a man in the past 12 months** • **reporting the use of illegal drugs and/or binge drinking alcohol in the past 3 months.**	Philadelphia sample n=175 Age, mean (SD)=21.82 69% Black, 31% White 95% HIV negative 55% employed 15% housing instability Baltimore sample n=98 Age, mean (SD)=23.62 85% Black, 15% White 81% HIV negative 65.31% employed 19% housing instability	with a slightly lower score (45.01 vs. 48.79; p ≥ .05). • number of partners in the past 6 months and number of non-main anal sex partners in the past 3 months, did not differ significantly by city at either baseline or 36-month follow-up. • While the anal sex risk score decreased over time in Philadelphia and increased in Baltimore for both subpopulations, the city × time × race interaction term was significant (F = 412.04, p < .001) only for those who did not use drugs other than marijuana. *(ANOVA)*				
Keep It Up! **Atlanta, Chicago, New York** **A two-group, double-blinded, interactive online RCT with 1-year follow-up.** **Participants were recruited through advertising and from HIV testing sites and outreach;** **After completing baseline surveys and sexually transmitted infection testing, participants were randomized by an eHealth platform to the intervention (HIV knowledge and motivate safer**	**Mustanski (2018);** 2013 – 2017; To determine if online intervention reduce condomless anal sex and STI compared with an HIV knowledge condition 901 participants, 445 randomized to the intervention arm and 456 to the control. 63% from ethnic minorities, 53% between 18 – 24 years, 64% between 25 – 29 years, 47% had a college education, and 86% gay.	Both arms showed reductions over time with 44% of control and 37% of intervention participants reporting CLS at month 12 (from 69% and 68% at baseline, prevalence ratio=0.83, 95% CI=0.70, 0.99, p=0.04). *(Unconditional generalized estimated equation logistic regression model)*	**N/A**	**N/A**	Sexually transmitted infections at Month 12 was 40% lower for intervention participants (risk ratio=0.60, 95% CI=0.38, 0.95, p=0.01). The rate of self-reported incident HIV diagnoses was 2.1% (17/793 person years PY, 95% CI=1.25, 3.43), with no difference between control (8/410 PY, rate=2.0%, 95% CI=0.84, 3.85) and KIU! arms (9/384 PY, rate=2.3%, 95% CI=1.07, 4.45).	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
behaviours) or control condition (existing online HIV information). • **HIV-negative Male between the ages of 18 and 29 years** • **reporting at least one act of CAS with a male partner in the prior 6 months** • **not being in a monogamous relationship for >6 months** • **able to read English at an 8th grade level** • **having an e-mail address**						
NON HIGH-INCOME COUNTRIES						
MSM Internet RCT Hongkong; Hongkong, China **A randomized controlled trial to evaluate an internet-based HIV behavioural intervention. Participants were interviewed anonymously at the baseline and after six months. Participants were recruited directly via the internet or from venues;** **Periodic HIV information dissemination, monitoring of risk behaviours and interactive feedback, online peer counselling and provision of a hotline, vs. control group that only received some educational materials.** • **Hong Kong Chinese men aged ≥18 years** • **having engaged in oral or anal MSM behaviours in the last six months** • **self-reported to be regular internet users**	**Lau (2008);** 2005; To investigate the efficacy of an internet-based behavioural intervention program that combines periodic HIV-related information dissemination, monitoring of behaviours with interactive feedback and online peer counselling, targeting MSM who are internet users. 280 participants completed baseline and the 6-month evaluation questionnaire, 140 belonged to the intervention group and 140 to the control group. 53.6% were of age 21 – 30, around 60% had received some tertiary education, only 3.6% and 2.1% of the members of the intervention group and the control group were currently married, both groups did not differ significantly in these characteristics, 99% Chinese ethnicity.	No statistically significant between-group differences in background characteristics, HIV risk behaviours and perceptions were observed both at the baseline and after the 6-month period (consistent condom use when having anal sex with non-commercial non-regular MSM partner in the intervention group: 63% at baseline, 60% at post-program; in the control group: 49.1% at baseline, 61.1% post-program) *(Chi square test)*	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **able to read Chinese** • **residents of age 18 and above and able to read Chinese.**						
Nanjing HIV Risk Reduction Counselling; **Nanjing, China** **A risk reduction counselling and HIV testing intervention with follow-ups occurred at 6, 12 and 18 months after baseline. Participants were interviewed anonymously. Participants were recruited using respondent-driven-sampling methods;** **HIV risk reduction counselling and testing was implemented for each participant at each round** • **having an oral or anal sex with a man in the past 12 months** • **currently living in Nanjing** • **at least 18 years-old**	**Huan (2013);** 2008 – 2010 To evaluate the role of HIV risk reduction counselling and testing in China 430 participants, 70.2% between 21 – 35 years, 28.9% students, 18.8% married, 67% had a higher education	• Self-reported CLS decreased from 60.9% to 42.9% during the study period. • % of participants who had one or no partner significantly increased from 40.9% to 48.0%. • some risk behaviors decreased between baseline and 12 months, followed by a slight increase between 12 and 18 months.	**N/A**	**N/A**	At baseline, HIV prevalence was 4.7%, whereas HIV incidence was 5.2 per 100 person-years. The incidence was 3.8 during six to 12 months, and 1.1 during 12 to 18 months. with an HIV incidence rate at each round of 5.2 (95% CI: 2.1–10.1), 3.8 (95% CI: 1.2–8.8), 1.1 (95% CI: 0.03–6.1) per 100 person-years, respectively, while overall HIV incidence was 3.6 (95% CI: 1.9–6.2) per 100 person years.	**N/A**
Pilot RCT Chennai; **Chennai, India** **A 2-arm pilot randomized controlled trial (N = 96) with 1:1 allocation ratio of a behavioral intervention (4 group and 4 individual sessions) integrating risk reduction counseling with counseling to foster self-acceptance in MSM in India compared to enhanced standard of care (ESOC). Both conditions involved HIV and STI testing and counseling at baseline and 6-months, and assessments of condomless sex at baseline, 3-, and**	**Safren (2014);** 2013; To test an integrating risk reduction counselling in decreasing the incident of STIs 96 men randomized, 81.3 % completed a 3-month assessment, 87.5% completed a 6-month assessment. Mean age 29.0 (SD = 7.5), 93% were never married, 92% had no children 77 %) were Hindu, 64 % had completed secondary school or less), 62 % reported being employed full-time	• There was a significant condition by time interaction, suggesting a difference in the rate of change in number of condomless sex acts in the intervention versus the comparison condition (F = 45.55, 2/68 df, p< 0.0001). More specifically, between baseline and 3-month follow up, the intervention group had a significantly larger decline in condomless anal sex acts as compared to the control group (Est. =-0.95, 95 % CI -1.47, -0.44, t =-3.62, 68 df, p = 0.0006); *(PROC GLIMMIX / mixed-effects model specifying a Poisson distribution and log link with a random intercept and slope for month of follow up)*	**N/A**	**N/A**	The incidence of bacterial STIs wa at follow-up was 17.5 % in the intervention condition and a 28.6 % in ESOC (non-significant). No incident of HIV infections throughout the course of the study among those who tested at their 6 month visit.	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
6-months. Participants reported their sexual risk via structured interview with an interviewer • **had CLS (insertive or receptive) with another man in the 3 months prior to screening** • **identifying as Kothi (in India Kothi are MSM who typically display more effeminate characteristics and are likely to take the receptive role in sex) or Double-Decker (in India DoubleDecker are MSM who do not necessarily display effeminate characteristics and may have sex with either men or women, and may be either insertive and/or receptive during anal sex)** • **a resident of Tamil Nadu.** • **Exclusion criteria were being under the age of 18, being unable to complete or understand consent procedures, or identifying as a Panthi, transgendered individuals**						
Coastal Kenya Cohort Study; Mtwapa, Kenya; **A prospective cohort study of MSM receiving risk reduction counselling intervention with quarterly follow-up visits.** **Participants were identified and recruited by a team of trained peer mobilizers who approached individuals via personal networks and at venues where they met with their partners and clients;**	**Moller (2015);** 2005 – 2011; To describe changes in sexual risk behavior among Kenyan MSM who received regular risk reduction counseling (RRC) 561 MSM had at least one follow-up visit and were included in this study, of which 92 (16%) were HIV-1-positive and 469 (84%) were HIV-1-negative. The median number of follow-up visits per participant was 9 [interquartile range (IQR) 4–16] for HIV-1negative and 8 (IQR 4–14)	• HIV-1-negative and HIV-1-positive men showed a similar decrease in number of regular sex partners (P interaction = 0.72), but the time trend itself was only significant for HIV-negative men, most likely due to the differences in sample size (P < 0.001 for HIV-1-negative men and P = 0.14 for HIV-1positive men • There was a borderline significant difference in trend between HIV-1-negative and HIV-1-positive men for number	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
At each scheduled follow-up visit, brief RRC was conducted for all participants. These sessions lasted 20 minutes on average and included assessment of HIV-1 knowledge, risk behavior, and substance use; identification of what supports and hinders use of condoms and other strategies to reduce risk, and negotiation of a realistic and incremental plan for reducing risk of HIV-1 and other STIs. • **HIV-1-negative adults aged 18 to 49** • **reported transactional sex, recent STI, multiple sexual partners, anal sex, or regular sex with an HIV-1-infected partner in the previous 3 months** • **Men who reported no sex during the past week on all of their study visits were excluded.**	for HIV-1-positive men. The median follow-up time was 1.2 years (IQR 0.5–2.3), with a median of 1.1 years for HIV-1-negative and 1.8 years for HIV-1-positive men. 54% of the 561 had none or only primary education, 45% not employed, 82% never married	of casual sex partners (P = 0.09). The number of casual partners seemed to decrease earlier in follow-up for HIV-1-positive men, but the trend itself was not significant (P = 0.36), whereas it was significant for HIV-1negative men (P < 0.001 • Both HIV-1-negative and HIV-1-positive men showed a significant decrease in UAI over follow-up years (P = 0.05 for HIV-1-negative men and P = 0.01 for HIV-1-positive men) with the largest change observed in the first 12 months. In accordance, the odds of engaging in UAI were higher at baseline compared to 1 year of follow-up for both HIV-1-negative and HIV-1-positive men (aOR 2.07, 95% CI 1.19–3.61 and aOR 2.63, 95% CI 1.12–6.20, respectively), (Random effects logistic and Poisson regression models)				
The CNRIST/TAR of Bangui; Bangui, Central African Republic; **A cohort study of MSM attend regularly the STI clinic for HIV and STI screening and care, to receive specific treatment, HIV counselling with 2-years period of follow-up; at inclusion and follow-ups, a standardized form was used to collect data on demographic, sexual behaviors and STIs/HIV test result at inclusion and at the of the 2-years period of follow up.**	**Marcel (2018);** No data on when data collection began and stopped To assess the effect of 2 years of HIV testing and counseling on risk-taking and HIV and STI incidences 99 MSM included in analysis, mean age 24 years (14-39) 84.8% single, 33% unemployed, 23.9% students, 80% living in only 4 (out of 10) neighbouring district of Bangui.	• A significant decrease in Insertive anal intercourse from 54% at inclusion to 46% after 2 years of follow up (P < 0.001). • A slight increase in receptive anal intercourse (60% versus 66%) and oral sex (70% versus 74%), non-significant • A decrease in the mean number of sexual partners 4.0 ± 3.0 per month at inclusion to 3.0 ± 3.1 after 2 years, non-significant • a slight decrease in condom use with the last sexual partner during the study follow up (68% versus 60%), without significant difference.	**N/A**	**N/A**	The prevalence of HIV, syphilis and hepatitis B infection increased between the study period from 29% to 41%, 12% to 21% and 14% to 23%, respectively (P < 0.001).	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• having sex with men by his peers • to accept to be followed over a period of at least 2 years • to have a fully informed medical record						
Romanian mHealth Study; Bucharest, Romania **A pilot mHealth HIV prevention among YGBM with 3-monthly follow-ups.** **Participants were recruited through ads posted on GBM-specific Facebook sites and groups and social sexual networking apps, word of mouth, and fliers;** **each participant received eight 60-minute text-based counseling sessions grounded in motivational interviewing and cognitive behavioral skills training with trained counselors on a private study mobile platform.** **Participants completed the same survey approximately 3 months postbaseline, as an immediate postintervention follow-up assessment (given that participants took between 2 and 3 months to complete their 8 weekly intervention sessions)** • between 16 and 29 years • self-report an HIV-negative or unknown status • have had at least one CLS act with a male partner in the past 3 months;	**Weinberger (2018);** 2015 – 2016; To adapt and pilot test, in Romania, a preliminarily efficacious mobile health (mHealth) HIV-prevention intervention, created in the United States, to reduce HIV risk among YGBM. 43 YGBM mean age 23.2 (SD 3.6) years, the majority (35/43, 81%) were aged ≤24 years (mean 23.39 years, SD 3.6; range 17-29 years) and gay (30/43, 70%). Nearly half of the participants had at least a college degree (18/43, 42%) and were working full time (20/43, 47%). Nearly one-quarter (10/43, 23%) were students. The majority (26/43, 60%) of the sample indicated being single.	From baseline to follow-up, participants reported significant (1) increases in HIV-related knowledge (mean 4.6 vs mean 4.8; *P*=.001) and recent HIV testing (mean 2.8 vs mean 3.3; *P*=.05); (2) reductions in the number of days of heavy alcohol consumption (mean 12.8 vs mean 6.9; *P*=.005), and (3) increases in the self-efficacy of condom use (mean 3.3 vs mean 4.0; *P*=.01). Participants reported significant reductions in anxiety (mean 1.4 vs mean 1.0; *P*=.02) and depression (mean 1.5 vs mean 1.0; *P*=.003). The intervention yielded high acceptability and feasibility: 86% (38/44) of participants who began the intervention completed the minimum dose of 5 sessions, with an average of 7.1 sessions completed Participants' number of sex acts without a condom decreased (mean 15.3, SD 13.8 vs mean 14.9, SD 17.4, *P*=.90) and number of sex acts with a condom increased (mean 6.3, SD 7.3 vs mean 8.6, SD 9.8, *P*=.12) from baseline to follow-up, although not significantly.	**N/A**	**N/A**	**N/A**	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
• **have either at least 5 heavy drinking days (at least 5 standard drinks on one occasion) or at least one condomless anal sex act under the influence of alcohol in the past 3 months.**						
Russia and Hungary Prevention Intervention Trial; St. Petersburg and Budapest; **A 2-arm randomized trial with 18 sociocentric networks of MSM randomized to the social network intervention or standard HIV/STD testing/counselling;** **Intervention: Empirically-identified network leaders were trained and guided to convey HIV prevention advice to other network members. The intervention guided network leaders in giving personal HIV risk reduction advice to their friends. Intervention facilitators were centrally trained and followed a manual. The intervention was delivered in 5 weekly 3-hour group sessions attended by 5 to 11 leaders, followed by 4 booster sessions spaced over the next 3 months.**	**Amirkhanian (2015);** 2007 – 2012; To test a novel social network HIV risk reduction intervention for MSM in Russia and Hungary Participants in both countries were typically in their 20s, most were single, employed, and well-educated or attending school. Over 61% of men had multiple partners in the past 3 months. More than 23% ever exchanged sex for money. N total = 314 intervention vs 272 comparison Age: 29 (6.7) intervention vs. 26.9 (6.6) comparison Single: 85% vs. 93% Employed: 74% vs. 69% Student: 28% vs. 32% All no-differences.	Changes in sexual behavior from baseline to 3- and 12-month follow-up: • a significant reduction in the intervention versus comparison arm for proportion of men engaging in any UAI (P=.04); UAI with a nonmain partner (P=.04); and UAI with multiple partners (P=.002). The mean percentage of unprotected AI acts significantly declined (P=.001), as well as the mean number of UAI acts among men who initially had multiple partners (P=.05). • % of intervention condition men who engaged in any UAI during the past 3 months declined from 54% at baseline to 38% at 3-month follow-up and 43% at 12-month followup while the proportion of comparison men was largely unchanged over time (P=. 036). • % proportion of men who engaged in UAI with a non-main sexual partner declined significantly more in intervention condition networks than comparison networks (18% to 8% to 9% versus 23% to 21% to 21%, P=.042), as well as the proportion reporting UAI with multiple partners (14% to 2% to 5% versus 19% to 17% to 13%,	**N/A**	**N/A**	composite HIV/STD incidence measured at 12-months: Biological HIV/STD incidence was 15% in comparison condition networks and 9% in intervention condition networks 3% (n=8) of men in intervention networks relative to 5% (n=11) of comparison participants contracted HIV infection during the 12-month followup period. 5% (n=21) of intervention-arm participants were diagnosed. with syphilis, gonorrhea, or chlamydia at followup relative to 8% (n=28) in the comparison group. 9% (n=28) of intervention and 15% (n=37) of comparison men had an incident HIV or STD infection on the aggregate biological measure.	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
		P=.002). There was a trend for greater decline in mean number of UAI acts reported by men in intervention condition networks (12 to 7 to 10 versus 12 to 13 to 11, P=.07). *(Mixed-effects multiple regression analyses (for linear, logistic, and Poisson distributions)*				
POOLED DATA						
HIV North American MSM Study (pooled data from 4 longitudinal HIV prevention studies: VPS, VAX004, STEP, and project Explore); **The U.S** **The HIVNET Vaccine Preparedness Study (VPS) (1995–1998), was an observational study of HIV risk behaviors and seroincidence; VAX004 (1998–2001) was an RCT of an HIV vaccine; EXPLORE (1999–2003), was an RCT of a behavioral intervention; and STEP (2004–2007), was an RCT of another HIV vaccine;** **All four studies followed participants every six months for 18–48 months. Sexual behavior over the last six months was assessed at each visit. VPS, VAX004, and STEP used face-to-face interviews, while EXPLORE used ACASI. HIV antibody testing was conducted at the time of each interview.** • **all of the studies sought to enroll men who reported, at the**	**Vallabhaneni (2012);** 1995 – 2007; To assess the association of seroadaptive practices with HIV acquisition 12,277 HIV-negative MSM from North America were included in the analysis. The median age was 34, and more than three-quarters were White. Participants were similar across cohorts, with exceptions: VAX004 participants were more likely to be White (85.9% vs. 76% VPS, 74% Explore, and 72% STEP)	12,277 participants contributed to 60,162 six-month intervals, • No UAI was reported in 47.4% of intervals, UAI with some seroadaptive practices in 31.8%, and UAI with no seroadaptive practices in 20.4%. • compared to no UAI, serosorting carried twice the risk (HR=2.03, 95%CI:1.51–2.73), whereas seropositioning was similar in risk (HR=0.85, 95%CI:0.50–1.44), and UAI with a single negative partner and as an exclusive top were both associated with a lower risk (HR=0.56, 95%CI:0.32–0.96 and HR=0.55, 95%CI:0.36–0.84, respectively). • Using no seroadaptive behavior as the reference category, there was a substantial, statistically significant adjusted reductions in risk of HIV acquisition in intervals in which any of the four seroadaptive practices were reported (Table 2). Specifically, we observed a 38% reduction (HR: 0.62, 95% CI: 0.47–0.82) with pure serosorting, a 74% reduction (HR: 0.26, 95% CI: 0.15–0.43) with pure seropositioning, and 83% reductions with both single negative partner (HR: 0.17, 95% CI: 0.10–0.30) and exclusive top	**N/A**	**N/A**	663 HIV seroconversions occurred in total 60,162 six-months interval	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
very least, anal sex with one or more men in the past 12 months • **VPS, VAX004 and STEP also enrolled participants from other continents or risk groups, however in this analysis, we include only North American MSM**		(HR: 0.17, 95% CI: 0.11–0.25) categories. Adjusted risk was also 69% lower (HR: 0.31, 95% CI: 0.25–0.37) in intervals where no UAI was reported. • Using no UAI as the reference category, pure serosorting was associated with a doubling of risk (HR: 2.03, 95% CI: 1.51–2.73). In addition, UAI with a single negative partner (HR: 0.56, 95% CI: 0.32–0.96) and UAI as an exclusive top (HR: 0.55, 95% CI: 0.36–0.84) were both associated with significantly lower risk. *(Cox regression models)*				
The JumpStart, VPS, VAX004 and Project Explore; The U.S **The four prospective longitudinal HIV prevention studies, the CDC Collaborative HIV Seroincidence Study (Jump-Start, 1993–1994), the HIVNET Vaccine Preparedness Study (VPS, 1995–1997), the rpg120 Vaccine Study (VAX004, 1998–2002), and Project Explore (1999–2003), shared several key characteristics that facilitated combined analysis: each study tested and enrolled HIV-negative MSM who reported anal intercourse with at least one male partner in the preceding 12 months. Every 6 months, participants were tested for HIV and interviewed concerning sexual behavior up to a specified duration or until infection. The intended duration for each study was**	**Johnson (2018);** 1993 – 2003; To estimate condom effectiveness per partner in four cohorts of MSM during 1993-2003 The sample of men who reported oral or anal sex with an HIV-positive male partner during the 6 months before their final study visit constituted 3262 participants. Of these, 335 were from JumpStart (10%), 605 from VPS (19%), 1540 from VAX004 (47%), and 782 from Project Explore (24%). Most (2712) were non-Hispanic white (83%); 262 were Hispanic/Latino (8%), 140 non-Hispanic African American (4%), and 148 Asian or other race or ethnicity (4%). Nearly a third (987; 30%) were ages 18–30, 775 (24%) were ages 31–35, and 1500 (46%) were age 36 or older. One-fifth (658; 20%) had a high school degree or less, 1741 (53%) had a college degree or	• The excess odds of HIV infection per HIV-positive partner were 83% for URAI and 7% for PRAI. The resulting failure rate (9%) indicated per-partner condom effectiveness of 91% (95% confidence interval 69–101) • Odds ratios per partner for RAI with whom condoms were always used (PRAI) ranged from 1.01 to 1.11, indicating a 1–11% increase in odds, with a pooled odds ratio of 1.07, thus a 7% increase (95% CI 1% decrease to 16% increase). *(Logistic regression)*	**N/A**	**N/A**	• Across the four studies, odds ratios per HIV-positive partner for URAI ranged from 1.40 to 3.48, reflecting an increase in odds of acquiring HIV infection ranging from 40 to 248% per partner • In the pooled analysis, the overall odds ratio (1.83) indicates an increase in odds of new HIV infection of 83% per URAI partner [95% confidence interval (CI) 59–111	**N/A**

Name of the study; Study settings; Design and method Inclusion and exclusion criteria	First author (year); Years of data collection; Study objectives Sample characteristics	Main findings *(statistical analysis)*				
		Sexual behaviour changes / factors			HIV and STI incidence	PrEP use
		over time	within-person	post-HIV diagnoses		
at least 18 months (36 months for VAX004, and 48 months for Project Explore). Sexual risk behavior data were collected in all four studies via self-report, and included numbers of occasions and partners, by serostatus, for insertive or receptive oral or anal sex with and without condoms during the preceding 6 months. In all four studies, HIV status of participants was based on clinical results of HIV testing by the standard procedures of the time	some college, and 862 (26%) had a graduate or professional degree or some training beyond a bachelor's degree. Data were collected from 1993 through 2003.					

Appendix 3. AURAH2 study Protocol

AURAH2 Protocol

A prospective study of sexual behaviour and risk of HIV acquisition in HIV-negative men who have sex with men.

Attitudes to and Understanding of Risk of Acquisition of HIV over Time:

AURAH2 Study

REC ref: 14/LO/1881

V 1

AURAH2 Study Group

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Sponsor: University College London

1. BACKGROUND AND RATIONALE

During 2012, 6360 people were newly diagnosed with HIV in the UK, and the estimated number of people living with HIV in the UK was 91,500 by the end of that year [1]. Although the annual number of new diagnoses has not risen since 2005 in the UK population overall, this figure is increasing among men who have sex with men (MSM) [2] and, in 2012 reached an all-time high of 3,250 new diagnoses in the year for this risk group [1].

Evidence of on-going or increasing HIV transmission among MSM [1-4] is consistent with evidence of ongoing sexual risk behaviour in this group. Studies of MSM in the UK [3, 5-11] and elsewhere [12-16] have found increases in the prevalence of condomless anal intercourse among MSM coincident with the widespread introduction and use of successful combination antiretroviral treatment for HIV in developed countries during the late 1990's and in to the early 2000's. There have also been increases in diagnoses of other sexually transmitted infections over this period [17, 18]. This increase in risk behaviour that became apparent in the late 90's has now reportedly stabilised, recent data from the Natsal-3 survey shows that over the last decade there has been no change in sexual risk behaviour or risk perception in MSM although HIV testing has increased among this group [19].Despite this report, and other research demonstrating that sexual risk behaviour has plateaued over the last decade [19, 20] the HIV incidence in MSM has increased and this is not completely justified by changes in HIV testing [21].

Sexual transmission risk arises as a result of the negotiation of sex practices, or lack thereof, between HIV positive and HIV negative individual. It involves the perceptions and behaviours of both individuals which often differ according to sero-status. Hence strategies aimed at reduction of HIV transmission need to address differences in both HIV positive and negative individuals' perceptions, choices and behaviours [22]. This is particularly relevant when considering how the 2008 Swiss statement [23] (which stated that HIV-positive individuals on effective ART with undetectable VL for at least six months and without sexually STIs are sexually non-infectious) and also the HPTN 052 study [24] (which demonstrated a reduction of heterosexual transmission in the immediate ART treatment arm of 96%), might have reached and influenced HIV negative persons in different ways to their HIV positive counterparts. The PARTNER study recently presented interim transmission estimates of zero in heterosexuals and MSM for condomless sex where the positive partner was on suppressive ART, albeit with a high upper confidence limit in MSM [25], and this kind of data may also influence HIV negative persons in their understanding and perception of HIV transmission. Reports from outside Europe suggest (even before the Swiss Statement was released) that HIV negative MSM perceive a number of sexual practices with HIV positive MSM on ARVs as less risky than with HIV positive MSM not on ARVs [22]. More recently, it has been noted that there is an increased likelihood in HIV negative MSM to engage in risky sexual practices (e.g. unprotected anal sex) in sero-discordant relationships where their partner reports an undetectable viral load [26]. Evidence from Australia demonstrates that the behavioral response of MSM to the risk of HIV transmission has evolved considerably over time and that 'risk reduction' strategies such as sero-sorting, strategic positioning, negotiated safety and withdrawal are now commonly used to reduce the risk of transmitting or acquiring HIV while engaging in condomless anal intercourse (UAI) [27-29]. In another Australian study in HIV negative MSM, strategic positioning was not associated with a significantly increased risk of acquiring HIV compared to those who reported no condomless anal intercourse [30].

HIV prevention approaches have mainly focused on condom use. This remains critically important but additional approaches are needed, not least because while condom use is common, strategies other than exclusive condom use are emerging in MSM communities [11]. Other approaches include pre-exposure prophylaxis, although at present this is not widely used by UK MSM as it is not generally available. Frequency of HIV testing among MSM in the UK also remains low (estimated 30% never tested, 75% not in past year) [2]. Approximately 25% of HIV positive MSM are unaware of their HIV infection and disproportionately contribute to onward transmission (60% to 80% of new HIV transmissions come from people not diagnosed) [31] as well as presenting late with consequent increased risk of death. There are likely to be many different ways to have an HIV test in the near future including self-testing where you take the sample and do the test yourself, which takes about 5 minutes. Increased HIV testing may also be likely to have prevention benefits as people diagnosed with HIV may be more likely to use condoms though this data is currently lacking for UK MSM.

Current data from the UK which inform on these themes from the perspective of HIV negative MSM are limited. It is important to understand in particular attitudes to unprotected sex with individuals of unknown HIV status and describe this risk behaviour in the context of mental/general health features, STI history, alcohol and drug use (and similarities/differences with counterpart data from HIV positive MSM).

The AURAH study (REC ref: 13/LO/0246, referred to here as AURAH1) used a cross sectional questionnaire to assess knowledge of, and attitudes to HIV transmission risks and the role of ART, and to assess the prevalence of medical and psychological symptoms (e.g. hepatitis C, depression and anxiety), quality of life, lifestyle factors (e.g. drug and alcohol use) and their possible links to sexual risk behaviours, in a large sample of HIV-negative patients attending Genito-Urinary Medicine (GUM) clinics in the UK, and among key demographic subgroups (MSM; Black African men and women). The AURAH2 study builds on the work of AURAH1 by providing further longitudinal data on HIV transmission risk in a group of initially HIV negative MSM.

It is important to study longitudinally the incidence and predictors of new infections among this group at particular risk of HIV infection, and to assess changes over time of the risk behaviour within individuals. Since there is no evidence that HIV incidence is decreasing among MSM in the UK, there is clearly a need for research among this group. In particular, little is known regarding changes in sexual behaviour during crucial periods such as primary HIV-infection and immediately following an HIV-diagnosis nor on variability in sexual risk behaviour over time at an individual level (including on the duration of periods of very high risk). Although there are cohort studies of MSM that provide some limited information on these issues [32-34] there have been no studies among individuals at risk of HIV infection in the UK. The longitudinal component of this study will be highly relevant to HIV prevention efforts among MSM, and help to inform national policies aimed at reducing HIV incidence in the UK and to increase HIV testing in the UK.

AURAH 2 will also provide data for the cost effectiveness component of the programme grant PG (RP-PG-1212-20006) which aims to assess the cost-effectiveness of strategies for preventing HIV in MSM. Areas of uncertainty for which definitive UK data are needed for the

cost-effectiveness analysis are on longitudinal patterns of condom-less sex around the time of infection and as a result of diagnosis. Such information is needed to inform the key parameters of the simulation model which will assess the cost effectiveness of HIV prevention strategies, including HIV testing interventions, to determine the cost-effectiveness (from an NHS perspective with outcomes as Quality-Adjusted Life-Years) of strategies for preventing HIV transmission, alone and in combination.

Impact of the research

The high level of on-going transmission of HIV in the UK, among MSM in particular, means that HIV prevention is a priority research area. Although people newly diagnosed with HIV in the UK can now expect a near-normal life expectancy, due to current combination antiretroviral treatments [35,36], living with HIV and taking lifelong treatment may nevertheless have considerable and lasting impact on an individual's physical and mental health, as well as their social circumstances. On-going HIV transmission in the UK is also associated with substantial cost to the NHS [37]. This project will provide a unique dataset combining socioeconomic, health and lifestyle information with detailed information on sexual activity, prevention approaches and preferences, HIV testing behaviours and HIV risk, among MSM who as a group are particularly affected by HIV in the UK. Therefore the results will contribute to understanding the social, psychological and health-related factors that are linked to high risk sexual and HIV-testing behaviours, and therefore to on-going transmission of HIV. The results will also provide important information on the acceptability of pre-exposure prophylaxis for HIV (PrEP), a possible prevention strategy under consideration in pilot studies among high-risk MSM in the UK.

AURAH 2 will also underpin our economic assessment of prevention approaches by providing information about longitudinal changes in risk behaviour. Insights from the AURAH2 study will be highly relevant to HIV prevention efforts among MSM , and help to inform national policies aimed at reducing HIV incidence in the UK. In particular, results should provide information useful in developing and targeting potential interventions to reduce high risk sexual behaviour and to increase HIV testing in the UK.

2 STUDY AIMS AND OBJECTIVES

a. Aims

The aim of the AURAH2 study is to study the incidence and predictors of new infections among HIV negative MSM at risk of acquiring HIV, and to assess changes over time in risk behaviour and testing practices within individuals

b. Objectives

1. Provide longitudinal assessment of:
    i. changes over time in high risk sexual behaviours including numbers of condomless sex partners, sex with casual partners and partners of unknown HIV-status, numbers of new partners, specific high risk sexual activities, and low self-efficacy for ensuring or discussing condom use,
    ii. number of condom-less sex partners before, during and after the estimated period of primary HIV-infection, and time of HIV diagnosis.
    iii. frequency of HIV testing over time

iv. type of HIV testing accessed over time; provided by GUM service, self-testing, GP surgery, hospital, other health care provider

2. Assess the extent to which baseline demographic, socio-economic, health and lifestyle- factors, and attitudes to HIV are predictive of subsequent levels of condomless sex, incident HIV infection and HIV-testing behaviours
3. Assess the relationship of attitudes to HIV transmission, disclosure, treatment and prognosis, with high-risk sexual behaviours and acquisition of HIV
4. Assess factors which are linked to HIV-testing practices among MSM at high risk of HIV
5. Assess the associations of participant characteristics, sexual behaviour and attitudes with reported use of, and willingness to consider use of, post exposure prophylaxis (PEP), PrEP. In particular attitudes to PrEP will be evaluated among those who are at very high risk of HIV-infection.

3. METHODS

3.1 Study Design

Prospective study of UK MSM at high risk of HIV infection. Information collected on each participant through the AURAH1 baseline questionnaire (REC ref: 13/LO/0246) on demographics, ethnicity, psychological health and well-being, knowledge and understanding of HIV and antiretroviral treatment will be supplemented by a shorter risk assessment completed online by participants no more frequently than every 3-4 months over a 3 year follow up period.

3.2 Study population and recruitment

HIV negative MSM adults that attend sexual health clinics at three sites in the UK for STI screening or HIV testing at: Mortimer Market Clinic, London, Chelsea and Westminster Hospital Foundation Trust, London and Brighton Sexual Health Centre, Brighton, will be approached to take part in the study. Two groups of participants will be recruited to the AURAH2 longitudinal study through different recruitment routes:

Recruitment route 1. This group will consist of HIV undiagnosed MSM who were enrolled in the AURAH1 cross sectional study (REC ref: 13/LO/0246) from the clinics detailed above during 2013 to 2014 who reported condomless anal sex with positive or unknown HIV status partner(s) in the 3 months prior to completing the baseline questionnaire and who consented to be contacted for longitudinal follow. These participants will be contacted by the UCL AURAH1 study team and will be sent information about the AURAH2 study and given the opportunity to enrol in the longitudinal component. If they agree, they will be consented to take part in AURAH2 (see below for details of consent procedures).

Recruitment route 2. This group will consist of HIV undiagnosed MSM who will be prospectively recruited in person through the 3 clinic sites until the target of 1000 MSM are recruited to the study. This group will be asked to complete the baseline AURAH1 paper questionnaire on site as part of their enrolment.

<u>Inclusion criteria:</u>

HIV negative (or HIV positive but undiagnosed i.e. men who may have become positive since their last test and men who have never had an HIV test) MSM subjects aged >= 18 years, attending or who have previously attended for routine sexually transmitted infection (STI) or HIV testing in the study clinics, willing to be contacted for longitudinal follow-up for up to a 3 year period.

Exclusion criteria: Unable to complete questionnaire in English due to language difficulties; already diagnosed as HIV positive; not willing to participate in future follow-up; under 18; not self-defining as MSM

3.3 Consent

Consent for the study will be gained through two different mechanisms, according to the recruitment route. Initial contact for consent will be made by a study nurse or doctors who are members of the clinical care team.

Recruitment route 1) Subjects who participated in AURAH1 and consented to being contacted in the future about further research by UCL will be sent information about the study, using the email address or phone number that they provided at the time of their consent for AURAH1. They will be emailed or texted (depending on which form of contact details they provided) a maximum of 3 times over a 6 week period. If there is no response after 3 attempts at contact, the participant will not be contacted further for the study. If the participant agrees to take part in AURAH2, the email will direct them to a secure website where they will be asked to view an information page and then complete an online consent form. As part of the consent process they will be asked to enter their full name and date of birth. They will also be asked to agree that the data from the original AURAH1 study (including logged information, test results and questionnaire data) can be included in the AURAH2 study.

Recruitment route 2) Participants recruited in person in clinic to AURAH 2 will be given a patient information sheet by the recruiter and given the opportunity to ask any questions about the study. If they consent to join the study they will complete the baseline AURAH paper questionnaire on site. They will also be notified that the results of any HIV test taken on the day of questionnaire completion will be included as part of the study data.

Recruitment time will be as long as the participant needs to decide whether they would like to enrol in the study but this will be limited to the time that they spend in the clinic for their appointment as they will not be expected to return at a later date to complete consent. This consent process was used in the AURAH study and had a good response rate.

For both recruitment routes the consent process will have the following common elements:

- Participants will be made aware participation means they are expected to complete a brief online questionnaire about sexual behaviour and HIV testing on a regular basis over a 3 year period
- Participants will be asked to provide their email address and mobile phone number and consent to receive reminders to complete the online questionnaires via email and/or text message – but also told that there will be a maximum of two reminders by email followed by 1 text message if they do not respond

- Participants will also be asked to provide their full name and date of birth and made aware that this information will be used to find out if there is matching data in UK national clinical databases (see section 3.9.5)
- Participants will be made aware that the study researchers will be securely storing all personal information securely and separately from the main study questionnaire data
- Participants will be made aware that they can withdraw from the study at any point and ask for their personal data to be deleted and that this would not affect their care at their GUM clinic.
- Participants will be advised that should they wish to withdraw from the study they should send an email to a specified contact address to make this request
- During the consenting process, it will be reiterated that the study is recruiting HIV undiagnosed individuals only.

3.4 Data collection

Baseline data collection and measurements

Baseline data: The AURAH1 baseline study questionnaire (REC ref: 13/LO/0246) is self-administered and will be completed for all participants either as part of their participation in AURAH1 (if recruited through route 1) or at the time of enrolment for AURAH2 in clinic (if recruited through route 2).

Extensive baseline data is collected through the AURAH1 baseline questionnaire (including demographic, social, lifestyle, physical and psychological symptoms, attitudes to HIV transmission, disclosure, treatment, use of PEP and PreP, attitudes to PreP, HIV-testing preferences and recent sexual behaviour).

Participants entering the study through route 2 will be invited to complete the paper based questionnaire while waiting for their GUM appointments, or directly following their appointment, whichever is most convenient for the patient and/or appropriate for each particular clinical centre. Each questionnaire will have a study number pre-completed on the first page. Participants will be given a questionnaire, pen and envelope. A private area within the clinic will be available for completion of questionnaires, if desired. Once completed, the questionnaires can be placed in a sealed envelope and put in a box in the clinic. Participants are asked to complete the questionnaire on the same day, in the clinic. The questionnaire will not be available in any languages other than English.

3.5 Participant online questionnaires

Regular data collection will consist of a brief online questionnaire to be completed approximately 4 monthly to assess risk behaviour and testing experience and history in the preceding months. A more detailed questionnaire will also be undertaken no more frequently than annually

Individuals will initially be sent an email or text message with an individualised link to register an account on the secure website. Use of this link to access the questionnaire pages will enable the researchers to ensure that only known participants recruited in clinic can register. Once registered, users will login to complete the first brief online questionnaire and will then

be reminded to return subsequently and login as required to complete questionnaires in future.

The online questionnaires will collect information on sexual behaviour and any HIV tests undertaken (see section 3.9.3 for details), but they will not ask users to enter any personally identifying details. If a participant reports that they have tested positive for HIV, they will be directed to questions specific to newly infected individuals. Participants who become HIV positive will also be reminded that they can continue to participate in the AURAH2 study for its full duration. The importance of remaining in the study after a positive HIV test result will be reiterated at the baseline consent by the research nurse to ensure the longitudinal data collection on patterns of condom-less sex around the time of infection and as a result of diagnosis.

3.6 Sample size:

Sample size calculation is based on objective 1ii) *assessing within-person changes in sexual behaviour after receiving an HIV diagnosis* which, along with predictors of incident HIV is more constrained by power than other objectives because it relies on comparisons within the group who are infected with HIV during follow-up . Considering sexual behaviour classified as whether or not a man reports > 3 condom-less sex partners in the past 3 months, 85 new HIV diagnoses would be needed to detect, with 80% power and 5% significance level, the following changes: 17 (20%) of men newly diagnosed switching from >3 to ≤3 condom-less sex partners pre to post- diagnosis, and 4 (5%) of men newly diagnosed switching from ≤3 to >3 condom-less sex partners pre to post- diagnosis. With 1000 HIV-negative men initially enrolled in the study sample, assuming an annual HIV incidence of 4% (as reported in high risk MSM) and a drop-out rate of 15% per year, 96 new HIV infections would be expected to accrue over a three year period. This sample size should provide adequate power for the other objectives.

3.7 Analysis plan:

Standard statistical approaches for analysis of cohort data with time updated covariates. In addition, we will estimate the change after HIV diagnosis in men who report 3 or more condom-less sex partners in the past 3 months. Predictors of having 3 or more condom-less sex partners in the past 3 months will be assessed using random effects models that include the number of condom-less partners in the previous 3 month period. These results will all be compared with similar analyses conducted on the model simulated population in order to inform model calibration.

3.8 Role of clinic based study staff

The study nurse or research assistant in each clinic will have a major role in recruiting to the study via recruitment route 2, including consenting particpants, collecting contact details and administering the baseline questionnaire

3.8.1 Documents held by study nurse/research assistant

- Information sheets
- Consent forms

- Study log (including clinic numbers, study numbers, full name, date of birth and email addresses)
- Numbered paper questionnaires (and pens)
- Pre-paid envelopes addressed to research team

3.8.2 study nurse/research assistant tasks

In each centre, the study nurse/research assistant will undertake the following tasks:

- Together with the clinical and research team, deciding on clinics/days to recruit to the study
- Together with the clinical and research team, deciding on how best to organise study recruitment and completion of questionnaires
- Inviting subjects to participate and distributing the study information sheet
- Obtaining subjects written informed consent to participate including longitudinal follow up
- Discussion/ demonstration of study website and how to log-in as a participant (can be done on mobile or laptop)
- Completing the study log (see section 3.9.1)
- Distributing paper questionnaires to participants
- Identifying a suitable private space for participants to complete the paper questionnaire, if desired
- Entering the study number and date on paper questionnaires
- Ensuring completed questionnaires in sealed envelopes are placed in the box provided
- Encouraging questionnaire completion in the clinic
- Returning a copy of the study log to the coordinating centre each week
- Having paper questionnaires available for collection by courier or other means (monthly)
- Communicating with the core group regarding study progress and any problems identified
- Storing the study log and consent forms securely in the clinic

3.9 Measurements

3.9.1 Study log

At each clinic at which recruitment takes place, the study nurse/research assistant will complete a study log containing the following information for each subject approached:

- Date and clinic (am/pm)
- Whether the subject is eligible for the study and,
- Whether the subject refuses to participate and, if supplied, the reason for refusal

For each participating subject, the nurse will record:

- Consent status of the participant

- Relevant identifying details - clinic number, study number, full name, date of birth, email address and mobile phone number
- The final result of any HIV test taken at the study visit

3.9.2 Baseline questionnaire

The AURAH1 questionnaire includes the following sections completed already or to be completed by newparticipants:

Demographic/social factors, Psychological and physical symptoms (using a modified version of the Memorial Symptom Assessment Scale Short-Form [38,39]), Depression (using the PHQ-9 [40]) and anxiety (GAD-7 anxiety score scale) [41], Health-related quality of life (using the EuroQoL 5D [42]), Social support (using a modified version of the Duke–UNC Functional Social Support Questionnaire - FSSQ) [43], Detecting alcoholism (CAGE questionnaire) [44]Relevant medical history, Transmission risk beliefs (in relation to ART and risk of transmission from HIV positive individuals), Lifestyle factors and Sexual activity.

MSM who have had anal sex in past 3 months will be asked whether this was with a regular or short term partner; number of partners; type of sex; had sex using condom; had condomless penetrative anal sex (receptive/insertive) with HIV positive partner or unknown status partners; number of times condomless penetrative sex; reasons for not using condom with last partner of positive or unknown status; extent to which they discuss HIV status with partners; if the partner was assumed HIV negative did they know when partner has last tested; had oral sex without condom; number of partners; undertook fisting, group sex or other high risk sexual activities;

For all participants: self-efficacy regarding condom use; discussion of HIV-status of partner with new partners; discussion of condom use; whether used internet to find sexual partner; whether participated in group sex; whether received money for sex; whether had taken PrEP / PEP (antiretroviral drugs before or after sex to prevent HIV transmission)

3.9.3 Online questionnaires

The regular secure online questionnaire will comprise a limited number of questions about sexual behaviour and HIV testing:

Participants will be asked to report their last HIV test result (if ever tested) and to describe the number of sexual partners, number of new partners; type of sex; had sex using condom; had condomless penetrative anal sex (receptive/insertive) with HIV positive partner or unknown status partners; number of times condomless penetrative sex.

If a participant reports a positive HIV test result during the course of the study, the questionnaire will ask whether they have been linked to care as well as similar risk behaviour questions to the above.

Participants will be asked to complete a more extensive questionnaire no more frequently than annually, which will take a maximum of 15 minutes to complete. The annual questionnaire will include the HIV risk assessment questions as well as questions on social factors, physical symptoms, Depression (using the PHQ-9 [37]), Health-related quality of life (using the EuroQoL 5D [39]).

3.9.4 Clinic data

The result of any HIV test taken at the same time as the baseline questionnaire completion will be stored as part of the study records. No other clinical data will be recorded.

3.9.5 *Linkage with national clinical databases*

At the end of and during the study period, the participants' full name, date of birth and sexual health clinic number will be used (in collaboration with Public Health England) to check for corresponding records and data in national clinical databases such as HARS (HIV diagnoses), GUMCAD (sexual health) and ONS (mortality).

3.10 Data analysis

3.10.1 Transfer of clinic data to the coordinating centre

Route 2 consent: Questionnaires will be sealed in envelopes and transferred from each clinical centre to the coordinating centre approximately every month. The study log will also be sent to the coordinating centre each week using secure NHS.net email addresses. Clinic numbers will be removed from the study log prior to transfer to the coordinating centre. However the study logs will contain full names, dates of birth, mobile phone numbers and email addresses (see section 4.4 for safeguarding of this information). The core group will also request additional data from the clinical centres including the total number of eligible, approached individuals seen over the study period in each centre.

3.10.2 Data entry and download

Data from paper questionnaires will be double entered into an appropriate data entry package. Personal details supplied as part of the online consent process and questionnaire data will be regularly and securely downloaded from the secure website and copies stored at the study centre. Once downloaded any personal details will then be deleted from the secure website.

3.10.3 Statistical methods

Logistic regression analyses will be used to investigate associations of sexual risk behaviour and transmission risk beliefs and other factors. Study clinic will be considered as a stratification factor. Analyses will be conducted in the study population as a whole.

4. ETHICAL CONSIDERATIONS

4.1 Ethics review

Prior to the initiation of the AURAH2 study, the protocol, patient information sheet, informed consent form, and study questionnaire will be submitted for ethical review. Any future amendments to the study protocol will also be submitted.

4.2 Patient information

The information sheet for clinic based recruitment (route 2) clearly states that the baseline questionnaire and follow-up risk assessment questionnaire will include personal questions on sexual lifestyle. It states that if the questionnaire raises any issues or concerns,

participants can ask the recruiter to arrange for them to speak to an appropriate professional. It also specifies that participants are free to withdraw consent for the study at any time, including after completing the baseline questionnaire or at any point during the follow up period.

Appropriate study information web pages will be made available online providing all the information available in the patient information sheet. The information will be context specific and accessible to users when consenting via recruitment route 1 and when returning to complete the brief, regular online follow-up questionnaires. The information will include access to general HIV related resources (the Terrence Higgins Trust website and helpline) and specific contact details if there are queries about participating or withdrawing from the AURAH2 study.

4.3 Confidentiality

Private areas in the clinic will be available for completion of paper questionnaires, if preferred. The questionnaires themselves will contain a study number only, with no identifying information. The patient's name and clinic number will not be recorded on the questionnaire. Participants will be able to place their completed paper questionnaires in a sealed envelope in a box in the clinic. Participants will be informed that their questionnaire responses will not be seen by clinical staff or recorded in their clinical notes. In the clinics the study log will be the only document linking study number with clinic number and/or names. Clinic numbers will be removed from the study log before these data are transferred to the coordinating centre.

The online questionnaire pages will be made available on a secure public website exclusively via an individual user account whose password will be known only to the person invited to participate. For recruitment route 1 (previous participants in AURAH1) there will be an initial consent form to fill in that will ask the participant to enter full name and date of birth as part of the consenting process. However for all other subsequent questionnaire pages, the information collected will not include any data items that would allow a person to be individually identified.

At the coordinating centre, information will be treated as completely confidential. The personal identifiable information (names, dates of birth, mobile numbers and email addresses) collected during the consent process will only be used for the consented purposes. The data from the questionnaires will be kept separately from the study log and from the personal information and will be linked by study number only. No individual subject will be able to be identified in any results that are presented or published from the study.

4.4 Data security

The online questionnaire web pages will be hosted on a secure web server. All procedures and processes for online data collection and storage will be assessed against the requirements of the NHS Information Governance Toolkit and any recommendations will be acted on.

The study result datasets will be held on IT facilities at University College London and will be securely stored on centrally managed servers or on encrypted PC and laptop drives. Paper forms (including questionaires and copies of the study log) will be stored securely in locked

cabinets. Any participant personal identifable details will be securely stored in encrypted form or within a secure environment for handling personally identifiable data in a manner compliant with the Data Protection Act and only used for the consented purposes . Once the personally identifiable information has been used for the consented purposes, and after the period of 6 months as indicated on the consent form has expired, the personal details will be permanently deleted.

4.5 Data transfer (handling, processing and storage)

In the study, the full name, date of birth and contact details (email address and telephone number) will be collected from consented participants in accordance with the patient consent form, patient information sheet and sections 3.3, 3.4 and 3.5 of this protocol.

These personally identifiable details will be handled appropriately and securely by study staff acting on behalf of the Department of Infection and Population Health, Royal Free Hospital, Rowland Hill Street, London, NW3 2PF. In particular the study Data Manager and Study Coordinator will process, store and dispose of personal identifiable information in accordance with all applicable legal and regulatory requirements, including the Data Protection Act 1998 and any amendments thereto.

5. STUDY MANAGEMENT

The study will be managed by the core group at the research department. The protocol and all study material will be reviewed and approved by all members of the AURAH2 study group.

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

5.1 Setting up study procedures

At the start of the AURAH2 study, members of the core group will visit each clinical centre in order to discuss study procedures and recruitment with the study nurse/s and the clinical team. As the AURAH2 study follows a similar procedure for recruitment and will be taking place in 3 sites that are familiar with the AURAH study, the protocol, patient information sheet and changes to the consent process can also be discussed over email or telephone with the clinic research team.

5.2 Funding for the study in each centre

As per the AURAH1 study, the 3 clinics will continue to be paid £40 per each completed baseline questionnaire from a study participant that reaches the UCL study group. The study has been funded by an NIHR programme grant.

Neither the Chief Investigator nor any other investigator/collaborator has any direct personal involvement (e.g. financial, shareholding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest.

5.3 Incentives for participants

The study burden for participants is minimal (15-20 minutes to complete the baseline questionnaire and 5 minutes on an approximately 3 monthly basis for follow-up, with an annual 15 minute questionnaire). However in order to improve recruitment, subjects will be notified that as participants they will entered into an annual prize draw for the chance to win up to £1000 each year for the duration of the study.

5.4 Monitoring of recruitment

Online and clinic based recrutment will be monitored and information will be provided to the clinical centres on recruitment and response rates.

5.5 Data monitoring

Throughout the recruitment period, regular audits of study data will be performed to check data completeness and data quality. The data manager will undertake data checks and data cleaning prior to statistical analysis.

5.6 Data analysis and publications

Statistical analyses will be performed at the coordinating centre by the core group. All material submitted for publication or presentation will be circulated to all members of the AURAH2 study group for comments. The primary publications from the study will be authored by the 'AURAH 2 study group' (including all site members).

6.0 Insurance

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

7.0 TIMETABLE

AURAH2

October 2014: Ethics approval

March 2015: 3 study sites switch from AURAH1 to AURAH2 protocol and recuit to AURAH2 only. Previous AURAH participants that consented to be contacted for future follow up by the UCL AURAH study team will be contacted and consented to take part in AURAH2

August 2015: Recruitment ends for baseline AURAH 2 participants

December 2014-December 2017: Ongoing follow-up of participants via email.

December 2017: Data analysis; dissemination of findings for AURAH 2

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Appendix 4. AURAH2 online Patient Information Sheet and Consent

Thank you for registering to join the AURAH2 study, which will help us to inform improvements in health care for gay men and other men who have sex with men.

Before proceeding we need to make sure that you understand what is involved in the study and that you are comfortable with participating.

Please take a minute to read through the information sheet and complete the consent form at the bottom so that you can proceed to your questionnaire.

Online Participant Information Sheet AURAH2 - version 0.6

18/11/2014

REC ref: 14/LO/1881

What is the study about?

This is a questionnaire study for gay men who are HIV negative. The study is looking to gather experiences and opinions from over 1000 gay men over a 3 year period.

The study will help us understand more about HIV transmission amongst gay men and how this changes over time. The results will also help us to develop specific strategies for gay men to remain healthy.

Who is taking part?

Gay men who are not diagnosed with HIV and who attended specific sexual health (GUM) clinics in London and Brighton are eligible to take part in AURAH2.

This includes those who took part in the original AURAH1 study and we would like as many of them as possible to participate. By taking part you would be making a valuable contribution to medical research.

What will I have to do?

The study will only entail answering brief online questions using a secure website approximately **every four months** (which will take 3-5 minutes to complete) with a slightly more detailed online questionnaire to complete **annually** (which will take around 20 minutes to complete).

You will not need to visit a clinic to answer questions for the AURAH2 study.

The study will continue for up to 3 years or as long as you are willing to participate in the study.

If you participate and were to receive a positive HIV test result at any point during the study, we would help to ensure that you get linked into an HIV clinic if you wanted this, but we would still like you to continue to participate in the study for its full 3 year term.

At the end of the study we also intend to see if the details of any of the participants in AURAH2 are also in the UK national HIV diagnosis database, or other UK national health databases, this will confirm their HIV status, or other health outcome. During the registration process we will ask for and securely store your name and date of birth to enable us to make this check.

When will I complete the online questionnaires?

The study coordinators will contact you by email to remind you and give you further information on when you should visit the secure website to answer the questions and this will happen approximately every four months. For each 4 month period you will receive a maximum of two reminders by email and, if necessary, one reminder by text. If you wish to withdraw from the study at any point or have any questions about the study you can contact the study researchers (see below).

Will my questionnaire responses be confidential?

Yes, completely. The online questionnaires will be made available on a secure website which can only be accessed using a link sent to your email address. After you have initially registered for the study, the website questionnaires will not ask you to enter any identifying personal details such as name, address or date of birth and will only be linked by a study number. Your answers to the online questionnaires will be stored in a confidential and secure manner.

What clinical information will be recorded?

If you agree to take part in the study, we will store the result of any HIV test that you did when you completed the original AURAH1 baseline questionnaire and during the time you are included in the study.

Will any other information about me be gathered?

The consent form asks you to provide contact information in the form of an email address and mobile phone number. This is to send you reminders and information about completing the online questionnaires. The contact details will also be used to notify you if you win an **annual £1000 prize** draw for people who participate in this study. You will also be asked to provide your name and date of birth to enable us to check the HIV status of all participants against the UK national HIV diagnosis database and other national health databases during and at the end of the study (as described above).

Any personally identifiable information that you provide will be securely stored, separately from the main study data, and used solely for the purposes described in this information sheet. After the study has finished and the data collected, all personal details (name, date of birth, email address and mobile number) will be deleted and the final study datasets will not include any of these details. If you decide to withdraw from the study we will, at your request, delete your details and will not contact you further.

What will happen to the information?

The information you give will be transferred to the Research Department of Infection & Population Health at UCL and analysed by computer. Your anonymised questionnaire responses will be added to everyone else's who has taken part in the study. The data will only be analysed for groups and not for individuals. The findings will be submitted to medical journals and national and international health conferences. Details of publications from this study will be made available on the study website (see below).

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 asked to sign the consent form at the bottom of this page.

If you agree to take part you can still change your mind later and decide not to complete the study or to leave the study at any point without explanation. If you choose not to take part in the study, this will not affect the standard of care you receive.

If you wish to withdraw from the study at any point or have any questions about the study you can email the research team at:

Contact person: Janey Sewell

Email: info@aurah2.org

Telephone: 020 7794 0500 extension 34673

Study website: www.aurah2.org

What if I want to withdraw from the study?

You can withdraw or stop participating in the study by emailing 'STOP' to info@aurah2.org

This will not affect the care that you receive at any sexual health centre.

You do not need to give us a reason for leaving the study. We will remove your email address from our email list and not contact you any further.

Are there any risks in taking part?

There is no risk to you in taking part in the study. If you find the questionnaire raises issues that concern you, or that you would like to discuss further, please contact your sexual health clinic.

What are the possible benefits of taking part in the study?

What we learn from this study will help us develop better interventions to protect people from getting HIV. You may benefit from this personally through the results of the study although this is not guaranteed. In addition all participants will be entered in an annual £1000 prize draw that will be established to encourage people to participate in this study.

What if there is a problem? (The following is standard advice that we give for all potential participants in research studies)

National Health Service or UCL complaints mechanisms are available to you. In the unlikely event that you are harmed by taking part in this study, and if you suspect that the harm is the result of the negligence of the Sponsor (University College London) or of the clinic where you originally completed the AURAH1 questionnaire, then you may be able to claim compensation. After discussing with the study researchers (see below for contact details, please make any claim in writing to Alison Rodger who is the Chief Investigator for the research and is based at UCL Research Department of Infection and Population Health, Royal Free Campus, Rowland Hill Street, London, NW3 2QG. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Who is leading this research?

A team of HIV specialists and researchers from around the UK is leading this study. The study is being coordinated by the UCL Research Department of Infection and Population Health, and is funded by the National Institute for Health Research. This study has been reviewed and approved by a research ethics committee.

Will I be paid expenses for taking part?

There will be no reimbursement of expenses for participants.

Who can I contact for any further information about the study?

You can get more information about the study using the following contact details:

Contact person:	Janey Sewell
Email:	info@aurah2.org
Telephone:	020 7794 0500 extension 34673
Study website:	www.aurah2.org

AURAH2 Participant Consent Form online - version 0.6

- I confirm that I have read and understand the information sheet (version 0.6) for this study
    - Yes
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
    - Yes
- I agree to take part in this study
    - Yes
- I understand that the information I give will be transferred to the research team at the UCL Research Department of Infection and Population Health
    - Yes
- I agree that the information from the AURAH study questionnaire that I previously completed can be used in this study
    - Yes
- I agree to enter my personal details below and understand that these will only be used for the purposes described in the information sheet
    - Yes

Name …… (Full name)

Date of birth …… (D-M-Y)

Email address …… (For reminders and information)

Mobile number …… (For reminder texts only)

(Your mobile number will *only* be used to send you one text to remind you to log-in to complete a questionnaire if you have not done so after being sent two email reminders.

If you would prefer not to be contacted by text please leave this blank.)

Appendix 5. AURAH2 in-clinic Patient Information Sheet and Consent form

Attitudes to and Understanding of Risk of Acquisition of HIV over Time:

The AURAH2 Study

Patient Information Sheet and Consent Form

V 0.5 18/11/2014

REC Ref: 14/LO/1881

We would like to invite you to take part in a research study. Please take some time to read this information about the study and decide whether or not to take part. Please ask the person who invited you to take part if anything is unclear or if you have any other questions.

What is the study about?

This is a questionnaire study for gay men who are HIV negative or unaware of their HIV status. The study is looking to gather experiences and opinions from over 1000 gay men for up to a 3 year period.

The study will help us understand more about HIV transmission amongst gay men attending sexual health clinics and how this changes over time. The results will also help us to develop specific HIV prevention strategies for gay men to remain healthy.

Who is taking part?

Gay men who are not diagnosed with HIV and who attend specific sexual health (GUM) clinics in London and Brighton are eligible to take part in AURAH2.

We would like as many men as possible to participate; by taking part you would be making a valuable contribution to medical research and provide gay men with more information on how to live healthily.

What will I have to do?

If you agree to take part you will be asked to complete a baseline questionnaire about your health and lifestyle at this visit. The questionnaire includes some personal questions about your sex life. You can complete the questionnaire on your own. It should take 15 to 20 minutes to complete.

The study will then entail answering brief online questions using a secure website approximately **every three to four months** (which will take less than 5 minutes to complete) with a slightly more detailed online questionnaire to complete **annually** (which will take less than 15 minutes to complete).

You will not need to visit a clinic to answer the online questions for the AURAH2 study.

The online questionnaires will **continue for up to 3 years** or as long as you are willing to participate in the study.

If you participate and were to receive a positive HIV test result at any point during the study from the GUM clinic that you attend, or through any other service, we would help to ensure that you get linked into an HIV clinic if you wanted this, but we would still like you to continue to participate in the study for its full 3 year term.

Both during and at the end of the study we also intend to check if the details of any of the participants in AURAH2 are in the UK national HIV diagnosis database to confirm their HIV status, or other UK national health databases, this will confirm their HIV status, or other health outcome. We will ask for and securely store your name and date of birth to enable us to make this check.

When will I complete the questionnaires?

We would like you to complete the first AURAH baseline questionnaire today, while you are here in the clinic, either before or after seeing the healthcare professional. There is a private space available for you to complete your questionnaire, if you would prefer this. The study nurse will make sure you don't miss your appointment in clinic.

The study coordinators will then contact you by email to remind you and give you further information on when you should visit the secure website to answer the questions and this will happen approximately every three months.

For each 3 -4 month period you will receive a maximum of two reminders by email and, if necessary, one reminder by text. If you wish to withdraw from the study at any point or have any questions about the study you can contact the study researchers (see below).

Will my questionnaire responses be confidential?

Yes, completely. Your name will NOT be written on the baseline questionnaire and your answers to it will NOT be seen by the doctors and nurses in the clinic. Your completed questionnaire can be placed in a sealed envelope which will not be opened by the clinic staff.

The online questionnaires will be made available on a secure website which can only be accessed using a link sent to your email address. The website questions will not ask you to enter any identifying personal details such as name, address or date of birth. Your answers to the online questionnaires will be stored in a confidential and secure manner.

What clinical information will be recorded?

If you agree to take part in the study, we will record the results of any HIV test that takes place today and during the time you are included in the study.

Will any other information about me be gathered?

The consent form asks you to provide contact information in the form of an email address and mobile phone number. This is to send you reminders and information about completing the online questionnaires. The contact details will also be used to notify you if you win an **annual**

£1000 prize draw for people who participate in this study. You will also be asked to provide your name and date of birth to enable us to check the HIV status of all participants against the UK national HIV diagnosis database and other national health databases during and at the end of the study (as described above).

Any personally identifiable information that you provide will be securely stored, separately from the main study data, and used solely for the purposes described in this information sheet. After the study has finished and the data collected, all personal details (name, date of birth, email address and mobile number) will be deleted and the final study datasets will not include any of these details. If you decide to withdraw from the study we will, at your request, delete your details and will not contact you further.

What will happen to the information?

Your anonymised responses will be added to everyone else's responses. The information you give will be transferred to the Research Department of Infection & Population Health at University College London (UCL) and analysed by computer. The data will only be analysed for groups and not for individuals. The findings will be submitted to medical journals and national and international health conferences. Details of publications from this study will be made available on the study website (see below).

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 given this information sheet to keep and be asked to sign the consent form.

If you agree to take part you can still change your mind later and decide not to complete the study or to leave the study at any point without explanation. If you choose not to take part in the study, this will not affect the standard of care you receive.

If you wish to withdraw from the study at any point or have any questions about the study you can email the research team at:

Contact person: Janey Sewell

Email: aurah2@ucl.ac.uk

Telephone: 020 7794 0500 extension 34673

Study website: http://www.aurah2.ucl.ac.uk/

Are there any risks in taking part?

There is no risk to you in taking part in the study. If you find the questionnaire raises issues that concern you, or that you would like to discuss further, please ask the person who invited you to take part to arrange for you to speak to the site lead researcher (see below) who will do their best to answer your questions.

What are the possible benefits of taking part in the study? What we learn from this study will help us develop better interventions to protect people from getting HIV. You may benefit

from this personally through the results of the study although this is not guaranteed. In addition all participants will be entered in an **annual £1000 prize draw** that will be established to encourage people to participate in this study.

What if there is a problem? (The following is standard advice that we give for all potential participants in research studies)

If you have a concern about any aspect of this study, you should ask to speak to the site lead researcher (see below) who will do their best to answer your questions. If you remain unhappy and wish to complain formally you can do this by contacting the Patient Advice and Liaison Service (see below).

National Health Service or UCL complaints mechanisms are available to you. In the unlikely event that you are harmed by taking part in this study, and if you suspect that the harm is the result of the negligence of the Sponsor (University College London) or of this clinic, then you may be able to claim compensation. After discussing with the site lead researcher, please make any claim in writing to Alison Rodger who is the Chief Investigator for the research and is based at UCL Research Department of Infection and Population Health, Royal Free Campus, Rowland Hill Street, London, NW3 2QG. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Who is leading this research?

A team of HIV specialists and researchers from around the UK is leading this study and the data from the study will make up part of a PhD at UCL for student Janey Sewell. The study is being coordinated by the UCL Research Department of Infection and Population Health, and is funded by the National Institute for Health Research. This study has been reviewed and approved by a research ethics committee.

Research Ethics Committee: Hampstead, London.

Will I be paid expenses for taking part?

There will be no reimbursement of expenses for participants.

Who can I contact for any further information about the study?

You can get more information about the study from your doctor or nurses at the clinic or contact the site lead researcher (see below).

Site lead researcher and contact details ……

Site Patient Advice and Liaison Service contact details……

Research Department of Infection and Population Health, University College London.

CONSENT FORM for AURAH2 Questionnaire Study.

Clinic ID: _____

AURAH2 Study ID: _____

1. I confirm that I have read and understand the information sheet (version 0.5 dated 18/11/2014) for this study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily.	☐ **Please initial**
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐ **Please initial**
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from UCL, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐ **Please initial**
4. I understand that the information I give will be transferred to the research team at the UCL Research Department of Infection and Population Health	☐ **Please initial**
5. I agree to take part in the study and by consenting to take part I agree to enter my personal details below and understand that these will only be used for the purposes described in the information sheet. **Full name:** **Date of birth:** **……** **(Email address)** **……** **(Mobile phone number for text messages)**	☐ **Please initial**

Please turn over the page to complete the consent process.

_____ __ __ /__ __ / __ __ __ __ _____

Name of patient Date Signature

_____ __ __ /__ __ / __ __ __ __ _____

Name of person taking consent Date Signature

When completed: 1 copy for participant if requested; 1 for researcher site file.

Appendix 6. AURAH2 study baseline questionnaire

(AURAH study questionnaire)

AURAH

MEN'S QUESTIONNAIRE

Version 4i 14/06/2013 REC Ref: 13/LO/0246

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those that apply to you.

Please do NOT write your name on this questionnaire. Your answers will NOT be seen by the doctors and nurses in the clinic

If you have any questions or need any help, please ask the person who gave you this questionnaire.

Please place your completed questionnaire in the envelope, seal the envelope and put in the box at reception, or give it back to the staff member who gave it to you.

If you have already completed this questionnaire recently, thank you. There is no need for you to complete it again.

Thank you for your help!

Study No. ☐☐☐☐☐ **Date:** ___ / ___ / ___

0

SECTION A: GENERAL INFORMATION

A1. Are you:

☐ Male ☐ Transgender (Female → Male)

A2. How old are you?

Please write in either the year of your birth: 1 9 __ __

Or your age in years: __ __

A3. Which ethnic group best describes you? (Please tick ONE ONLY)

A. White
☐ White British
☐ White Irish
☐ White other

B. Black or Black British
☐ Black African
☐ Black Caribbean
☐ Black other

C. Asian or Asian British
☐ Indian
☐ Pakistani
☐ Bangladeshi
☐ Asian other

D. Mixed
☐ White and Black African
☐ White and Black Caribbean
☐ White and Asian
☐ Mixed other

E. Chinese or other ethnic group
☐ Chinese
☐ Any other ethnic group

A4. Were you born in the UK?

☐ Yes → **IF YES, PLEASE GO TO QUESTION A5**
☐ No

If NO, which country were you born in? _____

1

When did you first move to the UK?

☐ Less than 1 year ago ☐ 1 to 5 years ago ☐ More than 5 years ago

How well do you speak English?

☐ Very well / fluent ☐ Quite well ☐ Not at all well

How well can you read English?

☐ Very well / fluent ☐ Quite well ☐ Not at all well

A5. What is your current work situation? (Please tick ONE ONLY)

☐ Employed or self-employed FULL-TIME (at least 30 hours per week)
☐ Employed or self-employed PART-TIME (less than 30 hours per week)
☐ Full time student / education / training
☐ Unemployed and registered for benefits
☐ Unemployed, NOT registered for benefits
☐ Permanently sick / disabled (for 3 months or more)
☐ Temporarily sick / disabled (for less than 3 months)
☐ Looking after home / family / dependants full-time
☐ Retired
☐ Other (please specify) .....

A6. What is your current housing situation?

☐ Own my own home (including with mortgage / loan / shared ownership)
☐ Renting from the council or housing association
☐ Renting from private landlord
☐ Temporary accommodation (hostel, shelter, bed & breakfast, squat)
☐ Staying with partner / friend(s) / family
☐ Homeless
☐ Other (please specify) .....

A7. Do you have enough money to cover your basic needs? (e.g. food, heating)

☐ Yes, all of the time
☐ Yes, most of the time
☐ Yes, some of the time
☐ No

A8. What is your current level of education? (Please tick ONE ONLY)

☐ Finished education with no qualifications
☐ O levels / GCSEs (or equivalent qualifications at age 16)
☐ A levels (or equivalent qualifications at age 18)
☐ University degree or above
☐ Other qualifications (please specify) .....

A9. Are you currently in an ongoing relationship with a partner (wife or civil partner or girlfriend / boyfriend)?

☐ Yes, I am in a relationship and living with my partner
☐ Yes, I am in a relationship but not living with my partner
☐ No, I am not currently in an ongoing relationship with a partner

If YES, overall, how long have you been in this relationship?
☐ Less than 1 year
☐ Between 1 and 3 years
☐ More than 3 years

If YES, is your partner HIV positive*?
**this means he/she has had an HIV test and been diagnosed with HIV*
☐ Yes ☐ No ☐ Don't know

A10. Do you have any children?

☐ Yes ☐ No

SECTION B: YOUR WELLBEING

In this part of the questionnaire, we are using some standard sets of questions to ask you about your wellbeing. We apologise if some of the questions seem repetitive, but please take the time to answer each section, as each one is important. If you are worried about any symptoms, please talk to your doctor. The answers from this survey will not be seen by anyone involved in your care. Thank you for your help!

B1. Below is a list of symptoms. Did you have any of these symptoms during the PAST 2 WEEKS? Please tick one box in each row to tell us whether you have had the symptom and, if so, how much it DISTRESSED or BOTHERED you.

Did you have any of these symptoms during the PAST 2 WEEKS?	No did not have the symptom	Yes, had symptom but it DID NOT BOTHER ME	Yes, had symptom and was bothered / distressed A LITTLE BIT	Yes, had symptom and was bothered / distressed QUITE A BIT	Yes, had symptom and was bothered / distressed VERY MUCH
1. Trouble remembering things	☐	☐	☐	☐	☐
2. Pain	☐	☐	☐	☐	☐
3. Headache	☐	☐	☐	☐	☐
4. Numbness, tingling or pain in hands/feet	☐	☐	☐	☐	☐
5. Muscle aches or joint pains	☐	☐	☐	☐	☐
6. Nausea	☐	☐	☐	☐	☐
7. Vomiting	☐	☐	☐	☐	☐
8. Diarrhoea	☐	☐	☐	☐	☐
9. Constipation	☐	☐	☐	☐	☐
10. Feeling bloated	☐	☐	☐	☐	☐
11. Dizziness	☐	☐	☐	☐	☐
12. Sweats/fever	☐	☐	☐	☐	☐
13. Cough	☐	☐	☐	☐	☐
14. Shortness of breath	☐	☐	☐	☐	☐
15. Problems with sexual interest/activity	☐	☐	☐	☐	☐
16. Skin problems (rash, itching, dryness)	☐	☐	☐	☐	☐
17. Lack of appetite	☐	☐	☐	☐	☐
18. Weight loss	☐	☐	☐	☐	☐

B2. Over the PAST 2 WEEKS, how often have you been bothered by any of the following problems? Please tick one box in each row.				
	Not at all	Several days	More than half the days	Nearly every day
1) Little interest or pleasure in doing things	☐	☐	☐	☐
2) Feeling down, depressed, or hopeless	☐	☐	☐	☐
3) Feeling sad	☐	☐	☐	☐
4) Feeling nervous, anxious or on edge	☐	☐	☐	☐
5) Not being able to stop or control worrying	☐	☐	☐	☐
6) Worrying too much about different things	☐	☐	☐	☐
7) Becoming easily annoyed or irritable	☐	☐	☐	☐
8) Trouble relaxing	☐	☐	☐	☐
9) Being so restless that it is hard to sit still	☐	☐	☐	☐
10) Feeling afraid as if something awful might happen	☐	☐	☐	☐
11) Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
12) Feeling tired or having little energy	☐	☐	☐	☐
13) Poor appetite or overeating	☐	☐	☐	☐
14) Feeling bad about yourself—or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
15) Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
16) Moving or speaking so slowly that other people could have noticed.	☐	☐	☐	☐
17) Thoughts that you would be better off dead, or of hurting yourself in some way	☐	☐	☐	☐
If you were bothered by any of these problems, how *difficult* have they made it for you to do your work, take care of things at home, or get along with other people?	☐ Not at all difficult ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult			

B3. Please indicate which statements best describe your own state of health TODAY. (Please tick one box in each section)

Mobility

☐ I have no problems in walking about
☐ I have some problems in walking about
☐ I am confined to bed

Self-care

☐ I have no problems with self-care
☐ I have some problems washing or dressing myself
☐ I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or leisure activities)

☐ I have no problems with performing my usual activities
☐ I have some problems with performing my usual activities
☐ I am unable to perform my usual activities

Pain / discomfort

☐ I have no pain or discomfort
☐ I have moderate pain or discomfort
☐ I have extreme pain and discomfort

Anxiety / depression

☐ I am not anxious or depressed
☐ I am moderately anxious or depressed
☐ I am extremely anxious or depressed

B4. Here is a list of some things that other people do for us that may be helpful or supportive. Please read each statement carefully and place a tick in the column that is closest to your situation. (Give only one answer for each row)

	As much as I would like	Almost as much as I would like	Some, but would like more	Less than I would like	Much less than I would like
a) I have people who care what happens to me	☐	☐	☐	☐	☐
b) I get love and affection	☐	☐	☐	☐	☐
c) I get chances to talk to someone I trust about my personal problems	☐	☐	☐	☐	☐
d) I get invitations to go out and do things with other people	☐	☐	☐	☐	☐
e) I get help when I am sick in bed	☐	☐	☐	☐	☐

SECTION C: YOUR GENERAL HEALTH

C1. Have you EVER been told by a doctor that you have any of the following conditions? (Please tick all those that apply)

☐ Cancer (not including non-melanoma skin cancer)
☐ Diabetes
☐ Stroke
☐ Heart disease / Coronary artery disease (e.g. heart attack, angina)
☐ High cholesterol requiring drug treatment
☐ Epilepsy
☐ High blood pressure requiring drug treatment
☐ Mental health condition (please specify)
.....
☐ Any other major condition (please specify)
.....

C2. Are you receiving medical treatment or therapy for DEPRESSION?

☐ Yes ☐ No

C3. Are you receiving medical treatment or therapy for any other MENTAL HEALTH condition?

☐ Yes → **If YES, please specify mental health condition**.....
☐ No

C4. Do you have either of the following conditions?

Chronic (long-term) Hepatitis B	☐ Yes	☐ No
Chronic (long-term) Hepatitis C	☐ Yes	☐ No

SECTION D: YOUR LIFESTYLE

D1. Do you smoke cigarettes regularly (at least 1 per day)?

☐ Yes → **If YES, please give approximate number smoked per day** .....
☐ No – I am an ex-smoker (given up smoking)
☐ No – I have never smoked

D2. How often do you have a drink that contains alcohol?

☐ Never → **IF NEVER, PLEASE GO TO QUESTION D8**
☐ Monthly or less
☐ 2 to 4 times a month
☐ 2 to 3 times a week
☐ 4 or more times a week

D3. How many units of alcohol* do you drink on a typical day when you are drinking?

**One unit=HALF a pint of beer / cider or a SMALL glass of wine or a SINGLE measure of spirits*

☐ 1 or 2
☐ 3 or 4
☐ 5 or 6
☐ 7 to 9
☐ 10 or more

D4 Have you ever felt you should cut down on your drinking?

☐ Yes ☐ No

D5. Have people annoyed you by criticising your drinking?

☐ Yes ☐ No

D6. Have you ever felt bad or guilty about your drinking?

☐ Yes ☐ No

D7. Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?

☐ Yes ☐ No

D8. In the PAST 3 MONTHS, have you used recreational drugs (e.g. poppers, cannabis, cocaine)?

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION D9**

If YES, which drugs have you used? (Please tick MORE THAN ONE box, if applicable)

☐ Acid / LSD / magic mushrooms
☐ Anabolic steroids
☐ Cannabis (marijuana, grass)
☐ Cocaine (coke)
☐ Crack
☐ Codeine
☐ Crystal meth (methamphetamine)
☐ Ecstasy (E)
☐ GHB (liquid ecstasy)
☐ Heroin
☐ Ketamine (K)
☐ Khat (chat)
☐ Mephedrone
☐ Morphine
☐ Opium
☐ Poppers (amyl nitrate)
☐ Speed (amphetamine)
☐ Viagra
☐ Other (please specify)
.....

D9. In the past 3 months, have you injected recreational drugs (e.g. heroin, crystal meth)?

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION E1**

If YES, did you use needles, syringes or 'works' previously used by another person?

☐ Yes ☐ No

SECTION E: YOUR SEXUAL HEALTH

E1. Why are you attending the clinic today? (Please tick all that apply)

☐ To get symptoms of infection checked or treated
☐ For a routine screening test
☐ To get contraception or contraceptive advice
☐ Other reasons (please specify)
……

E2. In the past year (BEFORE TODAY), have you been diagnosed with a sexually transmitted infection ?

☐ Yes
☐ No → **IF NO, PLEASE GO TO QUESTION E3**

If YES, have you had any of the following in the PAST YEAR? (Please tick MORE THAN ONE box, if applicable)

☐ Syphilis
☐ Gonorrhoea
☐ Chlamydia
☐ LGV
☐ New (acute) Hepatitis B
☐ New (acute) Hepatitis C
☐ Genital herpes (new or recurrent)
☐ Genital warts (new or recurrent)
☐ Trichomonas
☐ NSU (Non Specific Urethritis), NGU (Non Gonococcal Urethritis)
☐ Other (please specify) ……

E3. Do you currently have any of the following symptoms? (Please tick all that apply)

☐ Abnormal discharge from penis
☐ Anal discharge
☐ Pain on passing urine
☐ Pain in the genital area or anus
☐ Sores or rash on the genital area or anus

E4. Are you circumcised?

☐ Yes ☐ No

SECTION F: HIV

This section asks about Human Immunodeficiency Virus (HIV). A person known to be **HIV positive** has had an HIV test and been diagnosed with HIV. For HIV positive people, the **viral load** is a measure of HIV levels in the body.

F1. Are you HIV positive?

☐ No
☐ Don't know
☐ Yes → **If YES, this survey is only for people who have never been diagnosed with HIV. Please do not complete the rest of the questionnaire.**

F2. Are you having an HIV test today?

☐ Yes ☐ No ☐ Don't know / not sure

F3. Have you ever had an HIV test before?

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION F4**

If YES, approximately when was your last HIV test?
☐ Within the last 6 months
☐ More than 6 months ago and up to 2 years ago
☐ More than 2 years ago and up to 5 years ago
☐ More than 5 years ago

If YES, how many times have you had an HIV test in the past two years?
☐ Once
☐ Twice
☐ 3 or 4 times
☐ More than 4 times

F4. Here are some statements about HIV. Please read each statement carefully and place a tick in the box that is closest to your viewpoint. (Give only one answer for each row)					
	Strongly agree	**Tend to agree**	**Undecided / no opinion / not relevant to me**	**Tend to disagree**	**Strongly disagree**
a) I worry about getting HIV	☐	☐	☐	☐	☐
b) If I had HIV, I would feel comfortable telling others	☐	☐	☐	☐	☐
c) Modern HIV medications are easy to take and have few side effects	☐	☐	☐	☐	☐
d) If I had HIV and was being treated with modern HIV drugs, I would expect to have a normal lifespan	☐	☐	☐	☐	☐
e) If a person with HIV has an 'undetectable HIV viral load' this makes them less infectious to a sexual partner than if they had a high viral load.	☐	☐	☐	☐	☐
f) When HIV viral load is undetectable, a condom is not needed to prevent HIV transmission	☐	☐	☐	☐	☐

Post Exposure Prophylaxis (PEP)
This means taking antiretroviral (anti-HIV) drugs soon AFTER unprotected sex for 4 weeks to reduce the risk of becoming infected with HIV.

F5. Were you aware that you can take PEP to try to prevent HIV infection after sex without a condom?

☐ Yes ☐ No

Have you ever taken post exposure prophylaxis PEP?
☐ Yes ☐ No→ **IF NO, PLEASE GO TO QUESTION F6**

If YES, approximately how often did you take PEP in the last year?
☐ Never
☐ Once
☐ 2 to 3 times
☐ More than 3 times

PRe Exposure Prophylaxis (PREP)
This means taking antiretroviral (anti-HIV) drugs (usually a daily pill) to reduce the risk of becoming infected with HIV.

F6. Were you aware that you can take PREP to try to prevent HIV infection?

☐ Yes ☐ No

Have you ever taken PREP?
☐ Yes ☐ No

If YES, approximately for how many days did you take PREP in the last year?
☐ Between 1 and 4 days
☐ Between 5 and 19 days
☐ 20 to 50 days
☐ More than 50 days

If it were more widely available, would you be interested in taking PREP (or more PREP if you have taken it before) to try to prevent HIV infection?
☐ Yes ☐ No ☐ Don't know / need more information

SECTION G: YOUR SEXUAL IDENTITY

G1. How would you describe your sexuality?

☐ Straight / heterosexual → **IF YOU SELECT THIS OPTION, PLEASE GO TO QUESTION H1**
☐ Gay / homosexual
☐ Bisexual
☐ Other (please specify) .....

QUESTIONS G2 to G3 are for Gay or Bisexual Men

G2. What proportion of the following groups know that you are gay, bisexual and/or attracted to men?

	All or almost all	More than half	About half	Less than half	Few or none
Close family	☐	☐	☐	☐	☐
Friends	☐	☐	☐	☐	☐
Workmates	☐	☐	☐	☐	☐

G3. How often do you:

	Often (4+ times a month)	Sometimes (2-3 times a month)	Occasionally (Once a month)	Rarely (Less than once a month)	Never
Go to gay cafes, pubs, bars, nightclubs/discos	☐	☐	☐	☐	☐
Go to gay saunas	☐	☐	☐	☐	☐
Go to cruising areas where men meet for sex with men	☐	☐	☐	☐	☐
Use gay social networking websites or apps (e.g. Grindr, gay.com, gaydar.com)	☐	☐	☐	☐	☐

SECTION H: SEXUAL LIFESTYLE

This section asks about your recent sexual encounters. Remember this information is completely confidential. Your name or clinic number is NOT written on this questionnaire and your answers will NEVER be seen by the clinic staff.

H1. In the past 3 months, have you had sex* with a woman?

sex means **either vaginal sex (your penis in a woman's vagina) **or** anal sex (your penis in a woman's anus)*

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION H2**

If YES, did any of the sex within the last 3 months take place without a condom?

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION H2**

If YES:

(i) In the past 3 months, how many women did you have sex with, without a condom?

☐ One ☐ 2 to 4 ☐ 5 to 10 ☐ More than 10

Was this woman or one of these women your long-term partner?

☐ Yes ☐ No ☐ I don't have a long-term partner

(ii) In the past 3 months, did you have ANAL sex with a woman without a condom?

☐ Yes, at least once
☐ No, never

(iii) In the last 3 months, when you had sex without a condom, were the reasons for not using a condom in the following list? (Please tick all that apply)

☐ Trying for pregnancy
☐ Didn't think about using a condom or did not have a condom
☐ Don't like using condoms or it's more enjoyable / close without a condom
☐ My partner didn't want to use a condom
☐ Felt unable to discuss condom use
☐ Got carried away or was under the influence of alcohol or drugs
☐ Difficult to keep erection or ejaculate when using a condom

(iv) In the last 3 months, when you had sex without a condom, did you consider the risks of HIV infection?

☐ Yes ☐ No, I did not think about the risks at all

If YES, do any of these statements apply to you? (Please tick all that apply)
☐ I thought there was a very low risk of being infected with HIV
☐ I knew there was a risk of getting HIV but I am not so concerned about HIV that it made me want to have sex using a condom

(v) In the past 3 months, when you had sex without a condom, did you know the HIV status of your partner(s)?
☐ No, I did not know the HIV status of any of my partner(s) → **IF NO, GO TO QUESTION H2**
☐ Yes, I knew the HIV status of all my partner(s)
☐ Yes, I knew the HIV status of some of my partner(s)

(vi) In the past 3 months, did you have sex without a condom with a woman you knew was HIV positive?
☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION H2**

If YES, how many HIV positive women did you have sex with, without a condom, in the past 3 months?
☐ One ☐ Two ☐ 3 or more

If YES, was this woman or one of these women your long-term partner?
☐ Yes ☐ No ☐ I don't have a long-term partner

If YES, does the following statement apply to any of your HIV positive partners?
I thought the risks of catching HIV were low because my partner was taking anti-retroviral therapy
☐ Yes ☐ No

H2. In the past 3 months, have you had anal sex* with a man?

anal sex means your penis in a partner's anus (rectum or back passage), **OR a partner's penis in your anus (rectum or back passage),*

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION H3**

If YES, did any of the anal sex within the last 3 months take place without a condom?

☐ Yes ☐ No → **IF NO, PLEASE GO TO QUESTION H3**

If YES:

(i) In the past 3 months, how many men did you have anal sex with, without a condom?
☐ One ☐ 2 to 4 ☐ 5 to 10 ☐ More than 10

Was this man or one of these men your long-term partner?
☐ Yes ☐ No ☐ I don't have a long-term partner

(ii) In the past 3 months, when you had anal sex without a condom, which partner were you?

□ Always the insertive / top partner (your penis was inside your partner)
□ Always the receptive / bottom partner (your partner's penis was inside you)
□ Sometimes the insertive / top partner and sometimes the receptive / bottom partner

(iii) In the last 3 months, when you had anal sex without a condom, were the reasons for not using a condom in the following list? (Please tick all that apply)

□ Didn't think about using a condom or did not have a condom
□ Don't like using condoms or it's more enjoyable / close without a condom
□ My partner didn't want to use a condom
□ Felt unable to discuss condom use
□ Got carried away or was under the influence of alcohol or drugs
□ Difficult for me / partner to keep erection or ejaculate when using a condom

(iv) In the last 3 months, when you had anal sex without a condom, did you consider the risks of HIV infection?

□ Yes □ No, I did not think about the risks at all

If YES, do any of these statements apply to you? (Please tick all that apply)

□ I thought there was a very low risk of being infected with HIV
□ I knew there was a risk of getting HIV but I am not so concerned about HIV that it made me want to have sex using a condom

(v) In the past 3 months, when you had anal sex without a condom, did you know the HIV status of your partner(s)?

□ No, I did not know the HIV status of any of my partner(s) → **IF NO, GO TO QUESTION H3**
□ Yes, I knew the HIV status of all my partner(s)
□ Yes, I knew the HIV status of some of my partner(s)

(vi) In the past 3 months, did you have anal sex without a condom with a man you knew was HIV positive?

□ Yes □ No → **IF NO, PLEASE GO TO QUESTION H3**

If YES, how many HIV positive men did you have anal sex with, without a condom, in the past 3 months?

□ One □ 2 to 4 □ 5 to 10 □ More than 10

If YES, was this man or one of these men your long-term partner?

□ Yes □ No □ I don't have a long-term partner

If YES, does the following statement apply to any of your HIV positive partners?
I thought the risks of catching HIV were low because my partner was taking anti-retroviral therapy

☐ Yes ☐ No

H3. In the past 12 months, have you had any NEW* sexual partners?

**this means people you have not had sex with before*

☐ Yes ☐ No

If YES, how many NEW sexual partners have you had in the past 12 months?

☐ One ☐ 2 to 4 ☐ 5 to 10 ☐ 11 to 49 ☐ 50 to 99 ☐ 100 or more

H4. How much do you agree / disagree with the following statements? (Please give only one answer per row)

	Strongly agree	Tend to agree	Undecided / no opinion / not relevant to me	Tend to dis-agree	Strongly disagree
a) I feel confident that, if I want to, I can make sure a condom is used during sex with any partner, in any situation	☐	☐	☐	☐	☐
b) I'd expect to ask any new partner their HIV status before we have sex	☐	☐	☐	☐	☐
c) I would expect a new partner to tell me if they're HIV positive before we have sex	☐	☐	☐	☐	☐
d) I find it difficult to discuss condom use with any new sexual partner	☐	☐	☐	☐	☐
e) I am less likely to use a condom with a casual partner	☐	☐	☐	☐	☐

H5. In the past 3 months, have you used the internet to find a sexual partner?

☐ Yes ☐ No

H6. In the past 3 months, have you undertaken any of the following sexual practices?

Fisting	☐ Yes	☐ No
Use of sex toys	☐ Yes	☐ No

If YES to either of the above, did bleeding occur during sex as a result?

☐ Yes ☐ No

H7. In the past 3 months, have you participated in group sex*?

**this means sex with more than one other person on the same occasion*

☐ Yes ☐ No

H8. In the past 3 months, have you received money or drugs for having sex?

☐ Yes ☐ No

H9. Would you be interested in receiving further information about safer sex and protecting yourself from HIV infection?
(Please note you will NOT be contacted if you answer any of these questions)

☐ Yes ☐ No

If YES, please tell us your preferred information sources by selecting from the possibilities below. (Please tick all that apply)

Reading general information ...

☐ on websites
☐ in leaflets
☐ other (please specify) .....

Being on a distribution list to receive information ...

☐ by email
☐ by text message
☐ by post
☐ by phone call
☐ other (please specify) .....

Arranging to talk to a professional such as a ...

☐ doctor
☐ nurse
☐ community worker
☐ other (please specify) .....

Talking to others in the community such as …

☐ a group of people like me

☐ a person like me with training

☐ other (please specify) ……

Please use the space below if you want to comment on question H9 or you want to raise any other issues

AURAH

MEN'S QUESTIONNAIRE

Thank you very much for completing this questionnaire. Please either seal the questionnaire in the envelope provided and put it in the box at reception or, if you took the questionnaire away to complete it, please post it back using the pre-paid envelope.

Further information, advice and support services about HIV and AIDS are available from the Terence Higgins Trust:

THT DIRECT HELPLINE: 0808 802 1221

From 10am to 8pm Mon to Fri

Website: http://www.tht.org.uk

This project is coordinated by the Research Department of Infection and Population Health, University College London, in collaboration with our clinical partners. For further details see the AURAH website at:

http://www.astra-study.org/aurah

This project is funded by the National Institute for Health Research.

Appendix 7. AURAH2 study four-monthly questionnaire for HIV-negative

AURAH2 online: 4 monthly HIV Negative V1.0 (recall period 3 months)

1A) Approximately when was your last HIV test?

- …… (enter optional month and year) → 1Ai) What prompted you to test? (please select all that apply)
    - I test on a regular basis
    - I had condomless sex and was concerned
    - I went to a clinic to get PEP and was offered a test
    - A partner told me I should get tested
    - I was offered one in a clinic or hospital
    - 1Ai_other) Other ……

- I have never had an HIV test → 1Aii) Is there a reason you have not tested before? (please select all that apply)
    - Not enough time
    - Don't feel I need to
    - Worried about testing
    - Sexual health centre is too far or inconvenient
    - 1Aii_other) Other……

→Only show question 1B if there has been a previous HIV test

1B) What was the result?

- Negative
- Positive → Skip to first positive questionnaire
- Don't know

3A) Have you had anal sex with a man in the past 3 months?

- Yes
- No →Skip to next section

3B) In the past 3 months how many men did you have anal sex with*, without* a condom?

- None →Skip to next section
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3D) In the past 3 months when you had condomless anal sex, were you?

- Only insertive (top)
- Only receptive (bottom)
- Sometimes insertive / sometimes receptive

3E) In the past 3 months when you had anal sex without a condom, did you know the HIV status of your partner(s)?

- No, I did not know the status of any of my partners → Skip to question 3j
- Yes, I knew the status of **some** of my partners
- Yes, I knew the status of **all** of my partners

3F) In the past 3 months did you have anal sex without a condom with any men you knew were HIV positive?

- Yes → 3Fi) Were they on antiretroviral treatment?
    - Yes, all of them
    - Yes, some of them
    - No, none of them
- No
- Don't know

3J) In the past 3 months have you had group sex (i.e. sex involving more than two people)?

- Yes → 3Ji) Last time you had group sex how many men were in the group?
    - 3
    - 4 to 5
    - 6 to 10
    - More than 10
- No

4A) In the past 3 months have you been diagnosed with a sexually transmitted infection (STI)?

- Yes
- No →Skip to next section

4B) Do you know what STI it was? (please select all that are applicable)

- Syphilis
- Gonorrhoea→ 4Bi) where was the infection? (select all that are applicable) Throat/rectum/penis
- Chlamydia → 4Bii) where was the infection? (select all that are applicable) Throat/rectum/penis
- LGV
- New Hepatitis B
- New Hepatitis C
- Genital herpes (new or recurrent)
- Genital warts /HPV (new or recurrent)
- Trichomonas
- NSU (Non Specific Urethritis)
- NGU (Non Gonococcal Urethritis)
- Shigella
- Don't know
- 4B_other) Other (please specify) …….

7B) Have you used drugs before or during sex (chemsex) in the last 3 months?

- Yes → 7Bi) Which chemsex drugs have you used? (select as many as applicable)
    - Crystal meth/Tina

        - Mephedrone
        - GHB/GBL
        - 7Bi_other) Other (please specify)……
- No →Finish

7Bii) Approximately how often did you have chemsex in the last 3 months?

- Once
- Monthly
- Weekly

Finish - Thank you for completing your questionnaire – your answers are really valuable. We'll email you again in 4 months to remind you to log-in for your next questionnaire – Thanks for your time!

Appendix 8. AURAH2 study annual online HIV negative questionnaire

AURAH2 online: Annual HIV negative V1.0 (recall period 12 months unless otherwise stated)

Section 1 HIV tests

1a) Approximately when was your last HIV test?

- …… (month/year) → 1ai) What prompted you to test?
    - I test on a regular basis
    - I had unprotected sex and was concerned
    - I accessed PEP
    - A partner told me I should get tested
    - Other ……

- I have never had an HIV test → 1aii) Is there a reason for not testing?(please select)
    - not enough time
    - don't feel I needed to
    - worried about testing
    - too far to sexual health centre
    - Other……

1b) What was the result?

- Negative
- Positive → go to first positive
- Don't know

1c) In the last year when you last tested for HIV, did you test at home?

- Yes→ 1ci) Was that
    - self-testing (i.e. doing the test and getting the result yourself)
    - self-sampling (i.e. taking a sample and receiving the result at a later date)
- No

1d) Are you currently in an ongoing relationship with a partner (husband/civil partner/boyfriend)?

- Yes
- No

Section 3: Sex life

3a) Have you had anal sex with a man in the past 3 months?

- Yes
- No→3j

3b) In the past 3 months how many men did you have anal sex with*, without* a condom?

- None →Skip to next section

- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3bii) Was this man, or one of these men, your long-term (ongoing relationship) partner?

- Yes
- No

3c) How many of these men were new partners (i.e. ones that you had not had condom-less anal sex with before)?

- None
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3d) In the past 3 months when you had anal sex without a condom, were you?

- Only insertive (top)
- Only receptive (bottom)
- Sometimes insertive /sometimes receptive

3e) In the past 3 months when you had anal sex without a condom, did you know the status of your partner(s)?

- No, I did not know the status of any of my partners
- Yes, I knew the status of **some** of my partners
- Yes, I knew the status of **all** of my partners

3f) In the past 3 months did you have anal sex without a condom with any men you knew were HIV positive?

- Yes
- No
- Don't know

3j) In the past 3 months have you had group sex (i.e. with more than 2 people)?

- Yes→ Last time you had group sex how many men were in the group?
    - 3
    - 4 to 5
    - 6 to 10
    - More than 10
- No

3m) Where are you most likely to meet new partners? (Please select as many as appropriate)

- Cafes/pubs/bars/nightclubs
- Saunas
- Cruising areas
- Internet (e.g. Grindr/Manhunt/Gaydar/Scruff)

- Other – please specify ……..

Section 4 STI's

4a) In the past 3 months have you been diagnosed with an sexually transmitted infection (STI)?

- Yes
- No

4b) If Yes, do you know what it was? (please select more than one box if applicable)

- Syphilis
- Gonorrhoea→ where was the infection? (select all that are applicable) Throat/rectum/penis
- Chlamydia → where was the infection? (select all that are applicable) Throat/rectum/penis
- LGV
- New Hepatitis B
- New Hepatitis C
- Genital herpes (new or recurrent)
- Genital warts /HPV (new or recurrent)
- Trichomonas
- NSU (Non Specific Urethritis)
- NGU (Non Gonococcal Urethritis)
- Shigella
- Don't know
- Other (please specify) …….

Section 5 PEP

Post Exposure Prophylaxis (PEP)
This means taking antiretroviral (anti-HIV) drugs soon AFTER unprotected sex for 4 weeks to reduce the risk of becoming infected with HIV.

5a) Have you taken post exposure prophylaxis PEP in the past 12 months?

- Yes
- No

5b) Approximately how often did you take PEP in the last year?

- Once
- 2 to 3 times
- More than 3 times

5c) In the past year did you take PEP following chemsex (sex whilst taking drugs?)

- No, never
- Yes, once
- Yes, 2 to 3 times
- Yes, more than 3 times

Section 6 PrEP

Pre Exposure Prophylaxis (*PrEP)*
This means taking antiretroviral (anti-HIV) drugs (usually a daily pill) to reduce the risk of becoming infected with HIV.

6a) Have you taken PrEP in the past 12 months?

- Yes → 6a(i) Where did you access PrEP from? (please select any that are applicable)
    - From a clinic
    - From the internet
    - From a research study
    - From a friend
    - Other ……..
- No →Skip to next section

6b) Approximately how much of the time were you on PrEP in the last 12 months?

- Less than 3 months
- 3 to 6 months
- 6 to 9 months
- More than 9 months

6c) In the last 12 months, how many men did you have anal sex with, without a condom and without being on PrEP?

- None
- One
- 2 to 4
- 5 to 10
- More than 10

Section 7 Drugs

7a) In the past 3 months have you used recreational drugs?

- Yes
- No→8a

7b) Which drugs have you used? (please select as many as appropriate)?

- Acid/LSD/ magic mushrooms
- Anabolic steroids
- Cannabis (marijuana, grass)
- Cocaine (coke)
- Crack
- Codeine
- Crystal meth (methamphetamine)/ Tina
- Ecstasy (E)
- GHB/GBL (liquid ecstasy)
- Heroin
- Ketamine (K)
- Khat (chat)
- Mephedrone
- Morphine

- Opium
- Poppers (amyl nitrate)
- Speed (amphetamine)
- Viagra (Cialis)
- Other (please specify) …….

7bshort) Have you used drugs before or during sex (chemsex) in the last 3 months?

- Yes → 7b(i) Which chemsex drugs have you used? (select as many as applicable)
    - Crystal meth/Tina
    - Mephedrone
    - GHB/GBL
    - Cocaine
    - Poppers (amyl nitrate)
    - Ketamine (K)
    - Ecstasy (E)
    - Viagra/Cialis
    - Other ……
- No →7d

7b(ii) Approximately how often did you have chemsex in the last 3 months?

- Once
- Monthly
- Weekly

7d) In the past 3 months have you slammed/injected recreational drugs?

- Yes
- No →Go to question 7f

7e) Do you slam (inject) yourself or is it done by others?

- Self
- Others
- Both

7f) Over the last 3 months approximately how much of your sex life was chemsex?

- None
- Some of it
- Most of it
- All of it

Section 8 Alcohol

8a) In the last 12 months,

Did you have a drink that contained alcohol?

- Never →9a
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week

8b) How many units of alcohol did you drink on a typical day last year when you were drinking? (One unit = HALF a pint of beer/ cider or a SMALL glass of wine or a SINGLE measure of spirits)

- 1 or 2
- 3 or 4
- 5 or 6
- 7 to 9
- 10 or more

8c)

	Scoring system					Your score
	0	**1**	**2**	**3**	**4**	
How often have you had 8 or more units of alcohol on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Only show the following 3 questions if the answer above is Never (0), Less than monthly (1) or Monthly (2).						
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Section 9 Health and Well-being

9a) How much do you agree / disagree with the following statements?

	Strongly agree	**Tend to agree**	**Undecided / no opinion / not relevant to me**	**Tend to disagree**	**Strongly disagree**
a) I feel confident that, if I want to, I can make sure a condom is used during sex with any partner, in any situation	□	□	□	□	□
b) I'd expect to ask any new partner their HIV status before we have sex	□	□	□	□	□
c) I would expect a new partner to tell me if they're HIV positive before we have sex	□	□	□	□	□
d) I find it difficult to discuss condom use with any new sexual partner	□	□	□	□	□
e) I am less likely to use a condom with a casual partner	□	□	□	□	□

9b) Please indicate which statements best describe your own state of health TODAY? (Please select one box in each section)

Mobility

- I have no problems in walking about
- I have some problems walking about
- I am confined to bed

Self-care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

9c) Over the past 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1) Little interest or pleasure in doing things	□	□	□	□
2) Feeling down, depressed, or hopeless	□	□	□	□
3) Feeling sad	□	□	□	□
4) Feeling nervous, anxious or on edge	□	□	□	□
5) Not being able to stop or control worrying	□	□	□	□
6) Worrying too much about different things	□	□	□	□
7) Becoming easily annoyed or irritable	□	□	□	□
8) Trouble relaxing	□	□	□	□
9) Being so restless that it is hard to sit still	□	□	□	□
10) Feeling afraid as if something awful might happen	□	□	□	□
11) Trouble falling or staying asleep, or sleeping too much	□	□	□	□
12) Feeling tired or having little energy	□	□	□	□
13) Poor appetite or overeating	□	□	□	□

14) Feeling bad about yourself—or that you are a failure or have let yourself or your family down	□	□	□	□
15) Trouble concentrating on things, such as reading the newspaper or watching television	□	□	□	□
16) Moving or speaking so slowly that other people could have noticed.	□	□	□	□
17) Thoughts that you would be better off dead, or of hurting yourself in some way	□	□	□	□
If you were bothered by any of these problems, how *difficult* have they made it for you to do your work, take care of things at home, or get along with other people?	□ Not at all difficult □ Somewhat difficult □ Very difficult □ Extremely difficult			

9cii) Are you receiving medical treatment or therapy for depression?

- Yes
- No

9ciii) Are you receiving medical treatment or therapy for any other mental health conditions?

- Yes
- No

3h) Finally, Please think back over the last year, how many men have you had anal intercourse with without using a condom?

…… (Range: 0-997)

Appendix 9. AURAH2 study 1st HIV positive questionnaire for participants who reported an HIV diagnosis

AURAH2 online: 1st HIV positive questionnaire 4.0

Section 2 Engagement in care

2a) Have you been seen by a doctor or specialist healthcare professional since your diagnosis?

- Yes
- No

2b) Are you now taking antiretroviral treatment for HIV?

- Yes → When did you start? Month/year
- No

Section 3: Sex life:

3g) In the 3 months *before* your HIV diagnosis did you have anal sex with a man?

- Yes
- No→Skip to next section

3h) In the 3 months *before* your HIV diagnosis, how many men did you have anal sex with, *without* a condom?

- None → Skip to next section
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3i) In the 3 months *before* your HIV diagnosis, how many of these were men new partners (i.e. partners that you had not had condom-less anal sex with before)?

- None
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

Section 4 STI's

4ai) In the past 3 months *before* your HIV diagnosis had you been diagnosed with a sexually transmitted infection (STI)?

- Yes
- No

4b) Do you know what STI it was? (please select all that are applicable)

- Syphilis

- Gonorrhoea→ where was the infection? (select all that are applicable) Throat/rectum/penis
- Chlamydia → where was the infection? (select all that are applicable) Throat/rectum/penis
- LGV
- New Hepatitis B
- New Hepatitis C
- Genital herpes (new or recurrent)
- Genital warts /HPV (new or recurrent)
- Trichomonas
- NSU (Non Specific Urethritis)
- NGU (Non Gonococcal Urethritis)
- Shigella
- Don't know
- Other (please specify) …….

Section 7 Drugs/chemsex (shorter version)

7c(ii) In the 3 months before your HIV diagnosis did you use drugs before or during sex (chemsex)?

- Yes→7c(iii) If yes, which chemsex drugs did you use *before* your diagnosis (please select any that you have used)?
    - Crystal meth/Tina
    - Mephedrone
    - GHB/GBL
    - Cocaine
    - Poppers (amyl nitrate)
    - Ketamine (K)
    - Ecstasy (E)
    - Viagra/Cialis
    - Other……
- No

7c(iv) Approximately how often did you have chemsex in the 3 months before your HIV diagnosis?

- Once
- Monthly
- Weekly

7(ii) Do you believe you became HIV positive whilst you were using drugs during chemsex?

- Yes
- No

7iii) Has your drug use changed since your HIV diagnosis?

- Yes→ increased
    - decreased
- No

Appendix 10. AURAH2 study four-monthly questionnaire for HIV-diagnosed participants

AURAH2 online: 4 monthly HIV Positive V3 (recall period 3 months)

Section 2 Engagement in care

2c) Have you been seen by an HIV doctor or specialist healthcare professional since you were diagnosed HIV positive?

- Yes
- No

2b) Are you now taking antiretroviral treatment for HIV?

- Yes → Approximately when did you start? Month/year
- No→Skip to next section

2e) Do you know your viral load?

- Yes→ Is it?:
  - Undetectable (<40 copies/ml)
  - Detectable (>40 copies/ml)
- No

Section 3: Sex life:

3a) Have you had anal sex with a man in the past 3 months?

- Yes
- No→4a

3b) In the past 3 months how many men did you have anal sex with*, without* a condom?

- None →Skip to next section
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e) In the past 3 months when you had anal sex without a condom, did you know the HIV status of your partner(s)?

- No, I did not know the status of any of my partners → Skip to question 3j
- Yes, I knew the status of **some** of my partners
- Yes, I knew the status of **all** of my partners

3e(i) In the past 3 months, have you had anal sex without a condom, with a man you knew also had HIV?

- Yes
- No

3e(ii) If Yes, how many HIV positive men have you had sex with, without a condom in the past 3 months?

- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e(iii) In the past 3 months, have you had anal sex, without a condom, with a man who did not have HIV or whose HIV status you didn't know?

- Yes
- No

3e(iv) If Yes, in the past 3 months, how many men who did you have anal sex with, without a condom, who did not have HIV or whose HIV status you didn't know?

- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e(v) In the past 3 months when you had anal sex without a condom with men who are HIV negative or whose HIV status you did not know, were you?

- Only insertive (top)
- Only receptive (bottom)
- Sometimes insertive / sometimes receptive

3j) In the past 3 months have you had group sex (i.e. sex involving more than two people)?

- Yes→ Last time you had group sex how many men were in the group?
    - 3
    - 4 to 5
    - 6 to 10
    - More than 10
- No

Section 4 STI's

4a) In the past 3 months have you been diagnosed with a sexually transmitted infection (STI)?

- Yes
- No

4b) Do you know what STI it was? (please select all that are applicable)

- Syphilis
- Gonorrhoea→ where was the infection? (select all that are applicable) Throat/rectum/penis
- Chlamydia → where was the infection? (select all that are applicable) Throat/rectum/penis
- LGV
- New Hepatitis B
- New Hepatitis C

- Genital herpes (new or recurrent)
- Genital warts /HPV (new or recurrent)
- Trichomonas
- NSU (Non Specific Urethritis)
- NGU (Non Gonococcal Urethritis)
- Shigella
- Don't know
- Other (please specify) …….

Section 7 Drugs/chemsex (shorter version)

7bshort) Have you used drugs before or during sex (chemsex) in the last 3 months?

- Yes → 7b(i) Which chemsex drugs have you used? (select as many as applicable)
    - Crystal meth/Tina
    - Mephedrone
    - GHB/GBL
    - Cocaine
    - Poppers (amyl nitrate)
    - Ketamine (K)
    - Ecstasy (E)
    - Viagra/Cialis
    - Other ……
- No

7b(ii) Approximately how often did you have chemsex in the last 3 months?

- Once
- Weekly
- Monthly

Appendix 11. AURAH2 study annual questionnaire for HIV-diagnosed participants

Annual HIV positive V3 (recall period up to 12 months unless otherwise stated)

Section 2 Engagement in care

2d) Do you regularly attend an HIV unit for care (i.e. at least every 6 months or annually?)

- Yes
- No

2b) Are you now taking antiretroviral treatment for HIV?

- Yes → Approximately when did you start? Month/year
- No

2e) Do you know your viral load?

- Yes→ Is it?:
  - Undetectable (<40 copies/ml)
  - Detectable (>40 copies/ml)
- No

1d) Are you currently in an ongoing relationship with a partner (husband/civil partner/boyfriend)?

- Yes
- No

Section 3: Sex life:

3a) Have you had anal sex with a man in the past 3 months?

- Yes
- No→3a

3b) In the past 3 months how many men did you have anal sex with*, without* a condom?

- None →Skip to next section
- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3bii) Was this man, or one of these men, your long-term (ongoing relationship) partner?

- Yes
- No

3c) How many of these men were new partners (i.e. ones that you had not had condom-less anal sex with before)?

- None
- One

- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e) In the past 3 months when you had anal sex without a condom, did you know the HIV status of your partner(s)?

- No, I did not know the status of any of my partners → Skip to question 3j
- Yes, I knew the status of **some** of my partners
- Yes, I knew the status of **all** of my partners

3e(i) In the past 3 months, have you had anal sex without a condom, with a man you knew also had HIV?

- Yes
- No

3e(ii) If Yes, how many HIV positive men have you had sex with, without a condom in the past 3 months?

- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e(iii) In the past 3 months, have you had anal sex, without a condom, with a man who did not have HIV or whose HIV status you didn't know?

- Yes
- No

3e(iv) If Yes, in the past 3 months, how many men who did you have anal sex with, without a condom, who did not have HIV or whose HIV status you didn't know?

- One
- 2 to 4
- 5 to 10
- 11 to 49
- More than 50

3e(v) In the past 3 months when you had anal sex without a condom with men who are HIV negative or whose HIV status you did not know, were you?

- Only insertive (top)
- Only receptive (bottom)
- Sometimes insertive / sometimes receptive

3j) In the past 3 months have you had group sex (i.e. sex involving more than two people)?

- Yes→ Last time you had group sex how many men were in the group?
    - 3
    - 4 to 5
    - 6 to 10
    - More than 10

- No

3m) Where are you most likely to meet new partners? (Please select as many as appropriate)

- Cafes/pubs/bars/nightclubs
- Saunas
- Cruising areas
- Internet (e.g. Grindr/Manhunt/Gaydar)
- Other – please specify ……..

Section 4 STI's

4a) In the past 3 months have you been diagnosed with a sexually transmitted infection (STI)?

- Yes
- No

4b) Do you know what STI it was? (please select all that are applicable)

- Syphilis
- Gonorrhoea→ where was the infection? (select all that are applicable) Throat/rectum/penis
- Chlamydia → where was the infection? (select all that are applicable) Throat/rectum/penis
- LGV
- New Hepatitis B
- New Hepatitis C
- Genital herpes (new or recurrent)
- Genital warts /HPV (new or recurrent)
- Trichomonas
- NSU (Non Specific Urethritis)
- NGU (Non Gonococcal Urethritis)
- Shigella
- Don't know
- Other (please specify) ……..

7a) In the past 3 months have you used recreational drugs?

- Yes
- No →Skip to next section

7b) Which drugs have you used? (Please select as many as appropriate)?

- Acid/LSD/ magic mushrooms
- Anabolic steroids
- Cannabis (marijuana, grass)
- Cocaine (coke)
- Crack
- Codeine

- Crystal meth (methamphetamine)/ Tina
- Ecstasy (E)
- GHB/GBL (liquid ecstasy)
- Heroin
- Ketamine (K)
- Khat (chat)
- Mephedrone
- Morphine
- Opium
- Poppers (amyl nitrate)
- Speed (amphetamine)
- Viagra / Cialis
- Other (please specify) …….

7bshort) Have you used drugs before or during sex (chemsex) in the last 3 months?

- Yes → which drugs have you used before or during sex (chemsex)?
    - Crystal meth/Tina
    - Mephedrone
    - GHB/GBL
    - Cocaine
    - Poppers (amyl nitrate)
    - Ketamine (K)
    - Ecstasy (E)
    - Viagra/Cialis
    - Other ……
- No → go to 7d)

7b(ii) Approximately how often did you have chemsex in the last 3 months?

- Once
- Monthly
- Weekly

7d) In the past 3 months have you slammed/injected recreational drugs?

- Yes
- No →Go to question 7g

7e) Do you slam (inject) yourself or is it done by others?

- Self
- Others
- Both

7f) Over the last 3 months approximately how much of your sex life was chemsex?

- None
- Some of it
- Most of it
- All of it

Section 8 Alcohol

8a) In the last 12 months, how often did you have a drink that contained alcohol?

- Never →Go to next section
- Monthly or less
- 2 to 4 times a month
- 2 to 3 times a week
- 4 or more times a week

8b) How many units of alcohol did you drink on a typical day last year when you were drinking? (One unit = HALF a pint of beer/ cider or a SMALL glass of wine or a SINGLE measure of spirits)

- 1 or 2
- 3 or 4
- 5 or 6
- 7 to 9
- 10 or more

8c)

	Scoring system					**Your score**
	0	**1**	**2**	**3**	**4**	
How often have you had 8 or more units of alcohol on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Only show the following 3 questions if the answer above is Never (0), Less than monthly (1) or Monthly (2).						
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Section 9 Health and Well-being

9a) How much do you agree / disagree with the following statements?

	Strongly agree	**Tend to agree**	**Undecided / no opinion / not relevant to me**	**Tend to disagree**	**Strongly disagree**
a) I feel confident that, if I want to, I can make sure a condom is used during sex with any partner, in any situation	□	□	□	□	□

b) I'd expect to ask any new partner their HIV status before we have sex	□	□	□	□	□
c) I would expect a new partner to tell me if they're HIV positive before we have sex	□	□	□	□	□
d) I find it difficult to discuss condom use with any new sexual partner	□	□	□	□	□
e) I am less likely to use a condom with a casual partner	□	□	□	□	□

9b) Please indicate which statements best describe your own state of health TODAY? (Please select one box in each section)

Mobility

- I have no problems in walking about
- I have some problems walking about
- I am confined to bed

Self-care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

9c) Over the past 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1) Little interest or pleasure in doing things	□	□	□	□
2) Feeling down, depressed, or hopeless	□	□	□	□
3) Feeling sad	□	□	□	□
4) Feeling nervous, anxious or on edge	□	□	□	□
5) Not being able to stop or control worrying	□	□	□	□
6) Worrying too much about different things	□	□	□	□
7) Becoming easily annoyed or irritable	□	□	□	□

8) Trouble relaxing	□	□	□	□
9) Being so restless that it is hard to sit still	□	□	□	□
10) Feeling afraid as if something awful might happen	□	□	□	□
11) Trouble falling or staying asleep, or sleeping too much	□	□	□	□
12) Feeling tired or having little energy	□	□	□	□
13) Poor appetite or overeating	□	□	□	□
14) Feeling bad about yourself—or that you are a failure or have let yourself or your family down	□	□	□	□
15) Trouble concentrating on things, such as reading the newspaper or watching television	□	□	□	□
16) Moving or speaking so slowly that other people could have noticed.	□	□	□	□
17) Thoughts that you would be better off dead, or of hurting yourself in some way	□	□	□	□
If you were bothered by any of these problems, how *difficult* have they made it for you to do your work, take care of things at home, or get along with other people?	□ Not at all difficult □ Somewhat difficult □ Very difficult □ Extremely difficult			

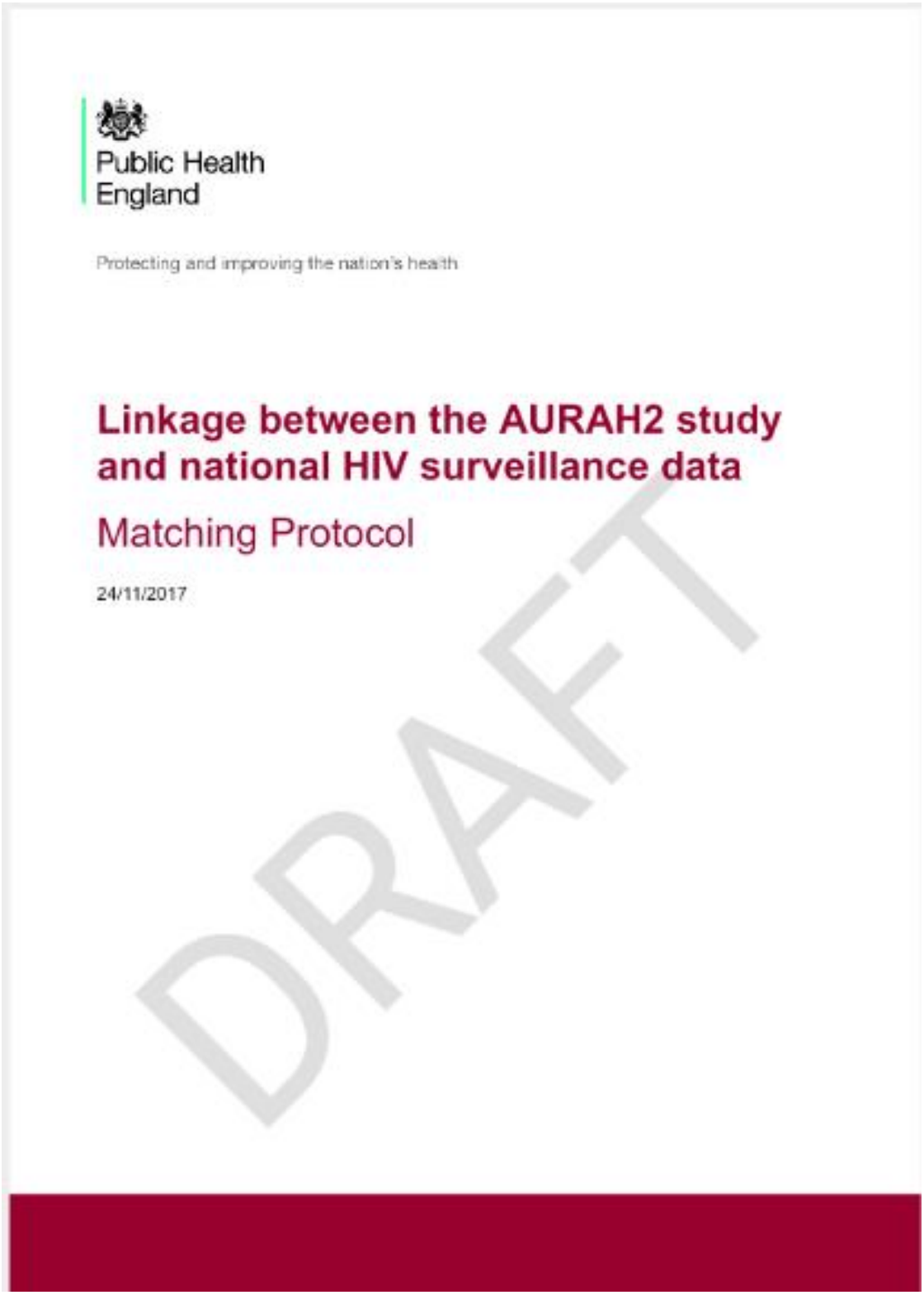
9cii) Are you receiving medical treatment or therapy for depression?

- Yes
- No

9ciii) Are you receiving medical treatment or therapy for any other mental health conditions?

- Yes
- No

Appendix 12. AURAH2 study and National HIV Surveillance data matching protocol



Public Health England

Protecting and improving the nation's health

Linkage between the AURAH2 study and national HIV surveillance data

Matching Protocol

24/11/2017

DRAFT

Document purpose

This document summarises the matching protocol, including data items and timescales, for linking data collected in the AURAH2 study (Attitudes to and Understanding of Risk of Acquisition of HIV over Time) to national HIV surveillance data managed by Public Health England (PHE).

Background of the AURAH2 study

The AURAH2 study aims to study the incidence and predictors of new infections among HIV negative MSM at risk of acquiring HIV, and to assess changes over time in risk behaviour and testing practices within individuals.

Male participants who had not at that stage been diagnosed HIV positive were recruited to this longitudinal observational study in one of three GUM clinics. Participants completed a baseline paper questionnaire at that time covering demographic, social, lifestyle, physical and psychological symptoms, attitudes to HIV transmission, disclosure, treatment, use of PEP and PreP, attitudes to PreP, HIV-testing preferences and recent sexual behaviour. They were then invited to register on a website to continue to complete similar online surveys approximately 3-4 monthly for a period of up to three years.

The study is looking to match participants to their PHE HIV surveillance data to verify the numbers of HIV diagnoses reported by the participants and to discover any diagnoses within the cohort that have not been reported.

Data items collected

The following data items are collected at various timepoints in the AURAH2 study and required in order to match to national HIV surveillance data:

- Gender identity (Male or Transgender (Female to Male))
- Date of birth (where available)
- Year of birth
- Surname (soundex*)

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- First name (initial)
- Alternative surname (if any) (soundex)
- Alternative first name (if any) (initial)
- Ethnicity
- Country of birth (if born outside UK)
- Years in UK (if born outside UK) (<1 year, 1 to 5 years, >5 years)
- Originating clinic (Dean Street, Mortimer Market, Brighton)

Soundex

Soundex is an indexing system for encoding surnames:

- It provides an anonymised representation of a surname.
- It consists of the initial letter of the surname and three digits.
- No soundex is unique to a single name, and a name cannot be recreated from a soundex code.

The Soundex algorithm used by PHE is the original variant (in contrast to the American Soundex). Soundex codes may be generated with the use of the accompanying Excel sheet.

National HIV surveillance data

The HIV and AIDS Reporting Section at PHE undertake timely and comprehensive data from a range of UK settings on:

- People receiving HIV care (collected quarterly)
- First HIV and AIDS diagnoses (collected annually)
- Deaths among HIV positive individuals (collected annually)
- Late HIV diagnoses (collected annually)

Data items collected include geography of residence, a pseudonymised name (soundex code), date of birth, gender, probable route of exposure and other demographic factors.

Matching Process

The matching between the AURAH2 data and national HIV surveillance data will be carried out using the Stata software. Matching will take the form of a deterministic, hierachical algorithm. Deterministic matching algorithms have been shown to be effective for record linkage using indirect identiers and are routinely used by Public Health England for deduplication and cross-system linkages.

The following matching criteria will be used:

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1. Soundex (or alternate soundex), Initial (or alternate initial), Gender, DOB (or YOB), Clinic, Ethnicity, COB
2. Soundex (or alternate soundex), Initial (or alternate initial), Gender, DOB (or YOB), Ethnicity, COB
3. Soundex (or alternate soundex), Initial (or alternate initial), Gender, DOB (or YOB), Ethnicity
4. Soundex (or alternate soundex), Gender, DOB (or YOB), Ethnicity
5. Soundex (or alternate soundex), Initial (or alternate initial), Gender, DOB (or YOB), Clinic
6. Soundex (or alternate soundex), Initial (or alternate initial), Gender, DOB (or YOB)
7. Initial (or alternate initial), Gender, DOB (or YOB), Clinic, additional manual review
8. Soundex (or alternate soundex), DOB (or YOB), Clinic, additional manual review

Additional criteria will be added dependent upon data completeness.

For each of the matching criteria, a Stata algorithm will compare records in the AURAH2 dataset to the national HIV databases. The following example code demonstrates the process of cleaning a dataset, linking records and assigning a 'matchtype' variable to indicate the matching criteria .

```
use "data/tmp_aurah2.dta", clear
keep apid soundex initial gender dob postcode ethnicity cob
drop if soundex==""
drop if initial==""
drop if gender=="" | gender==9
drop if dob==.
drop if postcode==""
drop if ethnicity=="" | ethnicity=="Z"
drop if cob=="" | cob=="ZZZ"
duplicates drop
save "data/tmp_aurah2_primed.dta", replace

use "data/drv_hivs.dta", clear
keep hpid soundex initial gender dob postcode ethnicity cob
drop if soundex==""
drop if initial==""
drop if gender=="" | gender==9
drop if dob==.
drop if postcode==""
drop if ethnicity=="" | ethnicity=="Z"
drop if cob=="" | cob=="ZZZ"
duplicates drop
bysort soundex initial gender dob postcode ethnicity cob: gen many=_n
save "data/tmp_aurah2_primed.dta", replace

summarize many
```


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```
forval i = 1(1)`r(max)' {
use "data\tmp_aurah2_primed.dta", clear
drop if many!= `i'
drop many
merge 1:m soundex initial gender dob postcode ethnicity cob using "data\tmp_hars_primed.dta", keep(match) nogen
if `i'!=1 append using "data/dhv_matched.dta"
save "data/dhv_matched.dta", replace
}
gen matchtype=1
save "data/dhv_matched.dta", replace
```

For each record matched, a two-stage eyeballing process will be used to verify that the linkage is correct, with data being reviewed by a data analyst and scientist at PHE.

Outputs from matching process

For each individual who is verified to have been matched, PHE will provide the following data items to the AURAH2 research team for analyses:

- Date of diagnosis
- Region of diagnosis
- CD4 at HIV diagnosis
- Viral load at HIV diagnosis
- GUM clinic attendance history (ongoing)
- Clinical outcome information (link to care, treatment)

HARS Submission Deadlines for 2016/17 data

The following chart indicates the deadline for submission of quarterly HIV attendance data to PHE by HIV clinics. Follow-up and cleaning processes may require up to 1 month before data is ready for matching to AURAH2 records.

Q4 2017	- Friday 20th January 2018
Q1 2018	- Friday 14th April 2018
Q2 2018	- Friday 14th July 2018
Q3 2018	- Friday 20th October 2018
Q4 2018	- Friday 19th January 2019

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Annual HIV diagnosis and death data is collected on an annual basis and will be ready for matching in summer of the following year e.g. 2016 diagnosis data will be ready in summer of 2017.

Data Security and Confidentiality

To ensure the highest level of data security and confidentiality, data forwarded to PHE should not contain patient names. All surnames are replaced with a soundex code at the reporting clinic or laboratory. The soundex code is a simple coding of names to their initial letter and three digits - no code is unique to a single surname, but their use allows the recognition of records relating to the same individual.

Data is submitted to PHE via the secure HIV & STI Web Portal and is then password protected and stored on a secure network drive and handled according to Caldicott guidance.
https://hivstiwebportal.phe.org.uk/

A generic webpage explaining PHE's Personal Information Charter and how we handle personal information can be found at the following web address:
https://www.gov.uk/government/organisations/public-health-england/about/personal-information-charter

To eliminate the risk of deductive disclosure, any data provided will be masked in line with the PHE HIV & STI data sharing policy, more information explaining how data is masked can be found at the following web address:
https://www.gov.uk/government/publications/hiv-and-sti-data-sharing-policy

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Matching Timeline

	Jan 2018	Feb 2018	Mar 2018	Aug 2018	Sep 2018	Feb 2019	Mar 2019	Aug 2019	Sep 2019
Clean Match data will be extracted, formatted and prepared (there are 763 consented AURIN2 participants & these data will not change)	X								
Transfer Data Match data transferred to PHE	X								
Matching Matching the available data to the HARS system		X		X		X		X	
Eyeball Matching Matches are reviewed manually to ensure accuracy		X		X		X		X	
Transfer Data PHE will send back the output from the matching process			X		X		X		X

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Appendix 13. Associations between ethnicity, education, and employment characteristics with sexual behavior measures at baseline among 1162 GBMSM in AURAH2 study*

		CLS	CLS ≥2 partners	Group sex	Non-injection chemsex	Injection drug use	Bacterial STI	PEP use	PrEP use
	N (%)	%	%	%	%	%	%	%	%
Born in the UK and ethnicity									
Yes, white	568 (49.4%)	62.2%	32.6%	42.9%	26.8%	3.2%	32.4%	17.6%	4.9%
Yes, other ethnicity	60 (5.2%)	65.0%	38.3%	40.%	20.%	5.0%	42.3%	25.0%	6.7%
No, white	374 (32.5%)	64.7%	35.3%	44.1%	30.2%	3.2%	**44.9%**	23.3%	5.1%
No, other ethnicity	148 (12.9%)	67.6%	44.6%	45.3%	29.1%	3.4%	39.9%	25.7%	4.7%
		p=0.626	*p=0.053*	*p=0.893*	*p=0.683*	*p=0.683*	***p=0.001***	*0.054*	*0.945*
University Education									
Yes	853 (73.4%)	62.4%	34.2%	43.4%	26.1%	3.2%	36.2%	20.2%	4.7%
Other qualification	272 (23.4%)	67.3%	38.6%	43.8%	33.1%	3.7%	43.0%	22.4%	5.9%
No qualification	21 (1.8%)	85.7%	38.6%	33.3%	28.6%	0%	38.1%	33.3%	9.5%
		p=0.038	*p=0.327*	*p=0.646*	*p=0.308*	*p=0.308*	*p=0.133*	*p=0.270*	*p=0.473*
Employed									
Yes	952 (82.9%)	64.1%	36.5%	43.9%	29.4%	3.0%	38.1%	21.1%	5.5%
No	197 (17.1%)	62.9%	30.5%	41.6%	20.3%	4.6%	38.1%	19.3%	3.1%
		p=0.763	*p=0.109*	*p=0.556*	***p=0.009***	*p=0.009*	*p=0.988*	*p=0.566*	*p=0.158*

***Pearson χ^2 test

GBMSM gay, bisexual, and other men who have sex with men; CL condomless anal sex; STI sexually transmitted infections; PEP post-exposure prophylaxis; PrEP pre-exposure prophylaxis.

Appendix 14. The Guy's and St. Thomas' study protocol

PROTOCOL TITLE:

Total Cost of Treatment and Care for Newly Diagnosed People Living with HIV in London

Sponsor

Name: Guy's & St. Thomas' NHS Foundation Trust

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CONTENTS

Study Synopsis

Title of observational study		**Total(Direct and Indirect) Cost of Treatment and Care for Newly Diagnosed People Living with HIV (PLHIV) in London 2013-2014**
Protocol Short Title/Acronym		Total Cost of HIV Treatment and Care
Study Phase if not mentioned in title		
Sponsor name		Guys and St Thomas' NHS Trust
Chief Investigator		Dr Julie Fox
REC number		
Medical condition or disease under investigation		HIV infection
Purpose of observational study		To calculate the direct and indirect cost of people with newly diagnosed HIV infection.
Primary objective		To calculate the direct and indirect cost of PLHIV in the first 12 months following diagnosis of HIV infection and entering treatment and care
Secondary objective (s)		1. To calculate the direct and indirect cost of people newly diagnosed with HIV infection stratified by CD4 cell count. 2. To calculate the cost-effectiveness of people newly diagnosed with HIV infection comparing those diagnosed with a CD4<350 cells/ml) with those diagnosed with a CD4 >350 cells/ml. 3. To evaluate the change in sexual behaviour, and therefore HIV transmission risk, following HIV diagnosis.

Tertiary objectives	1. To investigate the direct and indirect cost of newly diagnosed people living with HIV (PLHIV) in the 6 months prior to their diagnosis of HIV infection and entering treatment and care. 2. To investigate missed opportunities for testing for HIV both in community and hospital settings and calculate the potential cost savings at each opportunity for HIV diagnosis. 3. To evaluate the impact of notifications of missed HIV diagnoses to health care professionals 4. To develop recommendations on how healthcare professionals, community members and other relevant stakeholders can improve earlier diagnosis and access to treatment for PLHIV. 5. To compare the direct and indirect cost of HIV treatment and care in those people newly diagnosed with HIV (ND-HIV) compared with those known to have been living with HIV for more than two years (not newly diagnosed with HIV – NND-HIV)and stable on antiretroviral therapy for at least one year, stratified by age and CD4 count. 6. To evaluate the effect of age on the total cost of HIV stratified by CD4 count
Study design	Observational study of people newly diagnosed with HIV at Guys and St Thomas' NHS Trust and prospectively followed up for 12 months
Primary Endpoint	The direct and indirect cost of newly diagnosed PLHIV in the first 12 months following diagnosis of HIV infection
Secondary Endpoints:	1. The direct and indirect cost of people diagnosed with HIV infection stratified by CD4 count. 2. The cost effectiveness of treatment and care since diagnosis of HIV infection CD4<350 compared to CD4≥350 3. The change in HIV transmission risk behaviour following HIV diagnosis
Sample Size	125 ND-HIV (assuming 10% loss to follow up, total N remains above 100).
Summary of eligibility criteria	Inclusion criteria: - Male or female over 18 years old - Newly diagnosed with HIV-1 diagnosis within the previous 4 months and attending St Thomas' Hospital - **Or for sub study:** living with HIV for more than two years (not newly diagnosed with HIV – NND-HIV)and stable on antiretroviral therapy for at least one year - Able to understand and consent to study Exclusion criteria: - Documented HIV-2 Ab detected

1. Background & Rationale

Due to increased life expectancy of PLHIV on anti-retroviral therapy (ART) and to a continuous high HIV incidence , the global number of PLHIV continues to increase including in the UK. The increasing need for medical and social services is already placing economic pressures on the NHS (Mandalia et al., 2010). Of the estimated 96,000 PLHIV in the UK, an estimated 24% are unaware that they are living with HIV. (HPA, 2012). When they are eventually diagnosed and access services, they have a low CD4 which is associated with worse outcomes and increased cost for treatment and care (Krenz et al., 2004; Lucas et al., 2008; Beck et al., 2011a). A recent analysis demonstrated that around 25% of UK PLHIV diagnosed between 1996 and 2008 accessed services with a CD4 less than 200 cells/mm^3 (Beck et al., 2011b). This study also demonstrated the cost-effectiveness of diagnosing PLHIV and accessing services early so they can be monitored and start anti-retroviral therapy at an optimum CD4 count (Beck et al., 2011b).

Reducing late stage diagnosis of HIV is a key priority for BHIVA and the Department of Health (DOH 2010) as this group may also act as a reservoir for continuing transmissions of HIV; reduced transmission of HIV is pivotal to the success of the UK's response to its HIV epidemic and broader sexual health strategy. A number of studies have modelled the effectiveness or cost-effectiveness of expanded testing and treatment programmes, but many of these studies did not have information on the sexual behaviour of PLHIV once they know their sero-status or have started antiretroviral therapy (ART) (Long et al 2010).

Knowing direct and indirect costs of medical and social services used by PLHIV will provide UK policy-makers and other stakeholders with more robust and updated information of the cost and cost-effectiveness of the various programmatic responses in the UK. These pieces of information are crucial to assess for example the cost-effectiveness of expanded testing and treatment programmes and the provision of medical and social services for PLHIV.

The lifetime cost of treatment of a person living with HIV was estimated to range from £135,000-£180,000 in 2001 (DOH 2001) and to be £347,500 in 2009 (Phillips personal communication). The major cost driver has shifted over time from inpatient to outpatient services including ART (Mocroft et al., 2003). Various studies estimated ART costs to comprise 56%-73% of the total costs (Ewings et al., 2008; Krentz et al., 2003; Shackman et al., 06). In a recent UK analysis ART cost for first-line therapy varied from 46 to 59% (Beck et al., 2011a). Starting ART with CD4 counts > 200cells/mm^3 generated lower annual cost, due to less inpatient care. non-nucleoside reverse transcriptase inhibitors (NNRTI) containing regimes were also associated with lower hospital costs compared to boosted PI regimens (Beck et al., 2011a).

Many of these studies focused on the use and cost of hospital services and did not usually take into account indirect costs to the individual or cost of using medical or social HIV services outside of the hospital (Mullens et al., 2000). Use of health and social services and indirect health costs were investigated in the early 1990's (Renton et al., 1996; Petrou et al., 1996; Mullens et al., 2000) but have not been quantified or costed since then. They studied how individuals and households were affected by living with a PLHIV as well as the societal impact, including the employment history and personal expenditures when using community and social services. Given changing treatment regimens and associated costs, increased life-expectancy and related increased need for additional services, especially for older PLHIV, an urgent need exists to estimate the current use and cost of hospital, community and social services for PLHIV.

A recent audit performed at Guys and St Thomas' NHS Trust identified missed opportunities for early diagnosis in non-GUM settings, in both hospital outpatient and community setting. This has both important medical and cost implications in terms of hospital and intensive care unit (ITU) admissions (Read et al., 2010). An understanding of the reasons for late presentation is required to more effectively reduce the number of PLHIV presenting with low CD4 counts as to date little progress has been made despite high profile campaigns to increase HIV testing. Evaluating approaches to feedback of missed HIV diagnoses to healthcare professionals is one aspect of this study.

More robust and updated estimates of the total cost of treating PLHIV are necessary to evaluate the cost-effectiveness of various prevention and therapeutic programmes in the UK, including the option of expanding HIV testing and treatment in the UK.

Given the high costs of treating HIV-related diseases and the fact that people who are diagnosed are probably less likely to transmit HIV, due to reduced viral load associated with ART and possibly reduced risk behaviour,, interventions which increase HIV testing could be highly cost-effective. To evaluate this hypothesis, in addition to cost data, data are needed regarding changes in sexual behaviour following an HIV diagnosis. Once a person has been diagnosed with HIV better data on costs of care for people diagnosed at different levels of CD4 count are required to cost specific programmes and enhance relevant cost-effectiveness models (Public Health Interventions Advisory Committee, 2010). Lambeth is the London Borough with the highest HIV prevalence in the UK and accounts for 28% of HIV infections in London (HPA 2011; Brixton HNA 2010). Guys and St Thomas' NHS Trust has - on average 25 new HIV diagnoses per month and approximately 35% are diagnosed with a CD4<350 cells/ml.

Novelty of the study:

1. Capturing the total direct and indirect cost of providing services for people newly diagnosed with HIV based on their use of hospital, community and social services.

2. Provide important information on changes in sexual behaviour of newly diagnosed people who live with HIV

3. Investigating feedback of missed HIV testing to Health care professionals

Clinical relevance of study:

Evaluation of the use and cost incurred by PLHIV in the first twelve months following HIV diagnosis will provide policy makers and other stakeholders with more robust and up to date information on the total cost of services contributed by this group of patients. This will enable policymakers, health professionals and civil society members, including PLHIV, to improve the effectiveness and efficiency of the response to the HIV epidemic in London and the UK.

This will facilitate resource planning for both HIV prevention and the management of HIV infection.

Hypotheses:

1.0 Diagnosis of HIV in people with lower CD4 counts is associated with higher direct and indirect costs, both before and after diagnosis.

2.0 There is no difference in sexual risk behaviour in the three months before HIV diagnosis compared with 12 months after HIV diagnosis

The observational study - will be conducted in compliance with the principles of the Declaration of Helsinki (specifying which amendment), the principles of GCP and all (if any) applicable regulatory requirements. The protocol will be submitted for approval by an NHS Research Ethics Committee (REC). The name of the Ethics Committee will be stated in the protocol.

2. Study Objectives, Design and Statistics

2.1. Study Objectives

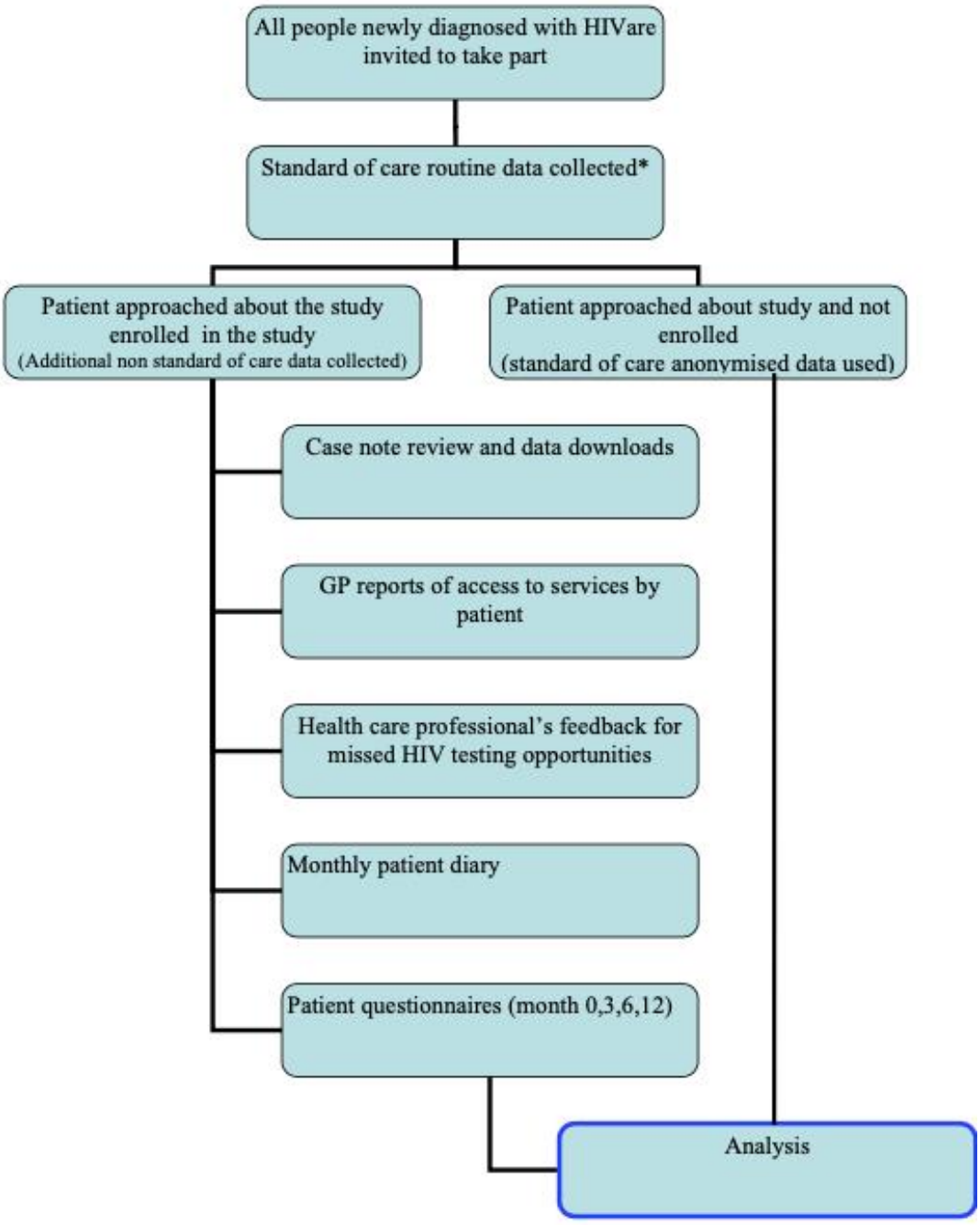
Overall Aim: To estimate the direct and indirect cost of people diagnosed with HIV infection at different CD4 cell counts in the first 12 months following diagnosis of HIV infection and to investigate the cost-effectiveness of early versus late diagnosis.

Primary objective	To calculate the direct and indirect cost of PLHIV in the first 12 months following diagnosis of HIV infection and entering treatment and care
Secondary objective (s)	1. To calculate the direct and indirect cost of people newly diagnosed with HIV infection stratified by CD4 cell count. 2. To calculate the cost-effectiveness of people newly diagnosed with HIV infection comparing those diagnosed with a CD4<350 cells/ml with those diagnosed with CD4 >350 cells/ml. 3. To evaluate the change in sexual behaviour, and therefore HIV transmission risk , following HIV diagnosis.

Tertiary objectives	1. To investigate the direct and indirect cost of newly diagnosed PLHIV in the 6 months prior to diagnosis of HIV infection and entering treatment and care. 2. To investigate missed opportunities for testing for HIV both in community and hospital settings and calculate the potential cost savings at each opportunity for HIV diagnosis. 3. To evaluate the impact of notifications of missed HIV diagnoses to health care professionals 4. To develop recommendations on how healthcare professionals, community members and other relevant stakeholders can improve earlier diagnosis and treatment for PLHIV. 5. To compare the direct and indirect cost of HIV treatment and care in those people newly diagnosed with HIV compared with those known to have been living with HIV for more than two years and stable on antiretroviral therapy for at least one year, stratified by age and CD4 count. 6. To evaluate the effect of age on the total cost of HIV stratified by CD4 count

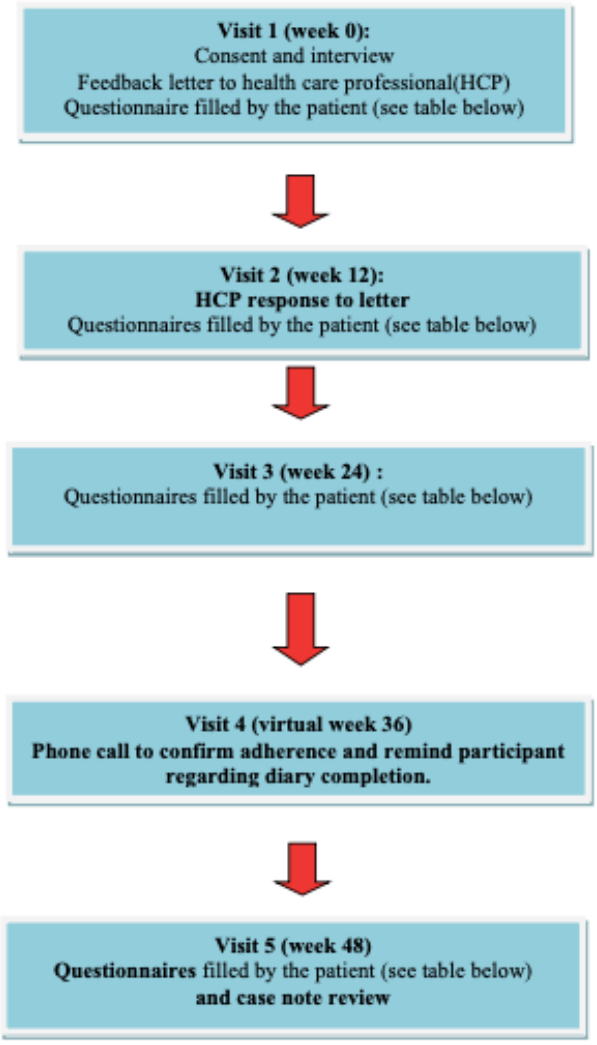
2.2 Study Design & Flowchart

Study design: Prospective observational study of people newly diagnosed with HIV and attending Guys and St Thomas' NHS Trust



*currently new patient database used, to replaced by enoting new patient proforma.

Flow chart of visit schedule for participants



1.3

Timing of questionnaires and activities

	Week number				
	Baseline	12 (+/- 4 weeks)	24 (+/- 4 weeks)	36 (+/- 4 weeks)	48 (+/-4 weeks)
Informed Consent					
Questionnnaire					
Section A: GENERAL INFORMATION 1-6	X				
: GENERAL INFORMATION 7-13	X		X		X
SECTION B:YOU & HIV	X	X	X		X
SECTION C: YOUR VIEWS ON HIV TRANSMISSION RISK	X	X	X		X
SECTION D_1: YOUR HEALTH & WELLBEING	X	X	X		X
D_2: SYMPTOMS (MSAS)	X	X	X		X
D_3: PATIENT HEALTH (PHQ-9)	X	X	X		X
D_4: HEALTH OUTCOME (EQ-5D)	X	X	X		X
D_5: SOCIAL SUPPORT (DUKE UNC FUNCTIONAL SOCIAL)					
SECTION E: LIFESTYLE	X	X	X		X
SECTION F_1: HIV TREATMENT	X	X	X		X
F_2: ADHERENCE (*FOR THOSE ON ART*)		X	X	X**	X
SECTION G_1: SEXUAL BEHAVIOUR/HISTORY	X	X			X
SECTION G_2:SEXUAL LIFESTYLE BEFORE HIV DIAGNOSIS	X				
G_3: SEXUAL LIFESTYLE SINCE HIV DIAGNOSIS		X			X
Data download-Hospital Community (Rio)					X
GP feedback on patient attendance					X
Diary* (monthly)	X	X	X	X**	X
Patient feedback to encourage testing					X
HCP feedback regarding HIV testing		X	x		
Case note review	X				X

*stamped addressed envelopes
**Phone call and text/email reminders for diary completion

Data Collection

Patients will be recruited from the GUM/HIV department at Guys and St Thomas' NHS trust. Those wishing to take part in the study will sign a consent form. Recruitment will take place over a 14 month period with one year follow up. Depending on how well the individual is coping after having received their HIV diagnosis, individuals will be approached anytime between diagnosis and 4 months following this (as assessed by study team). During the first 4 months of any HIV diagnosis individuals attend the unit on approximately 3 occasions to see a health advisor, clinic nurse and clinic doctor during which routine data are collected. There will therefore be approximately 3 occasions to approach individuals about participation in the study. As this is a non-intervention study, individuals may consent immediately, others will be given the opportunity to contact the department after a longer period of consideration.

There are no potential risks to the participants. The routine HIV care of the individual will be carried out by the HIV clinician and study visits will be arranged around these. Individuals will be referred by NHS staff to the research unit and consented to the study by either the study nurse or doctor. Due to the time taken to complete the forms, patients will be reimbursed £10 per visit.

After signing the consent form individuals will complete structured questionnaires- this includes questions on demographics, service utilization in the preceding 6 months and HIV testing history. They will then be asked to complete a confidential questionnaire which includes questions on sexual behaviour, quality of life (EQ-5D and MSAS). These questionnaires can be completed on paper or electronically, depending on which the participant prefers. For those with poor literacy or English as a second language, they will be asked permission to complete this section with a health care assistant. The time taken to complete these questionnaires is approximately 25 minutes. A letter will be sent to all health care professionals who were reported to have seen the individual in the 6 months preceding HIV diagnosis and not offered a HIV test (Appendix 1). A follow up letter will be sent or phone call made 12 weeks after sending this letter to assess how useful the health care professional found the feedback and whether it had changed their testing practise (Appendix 2)

At entry to the study individuals will be asked about all health and social services that they used 6 months before their HIV diagnosis and the period of time since their HIV diagnosis and entry into the study. In addition they will be asked to collect information on use of all medical or social service, formal or informal used either in the community, hospital(s) or both on a daily basis on a diary. To give them an idea of what type of information should be collected a list of services (appendix 3) and staff types (appendix 4) will be provided. Individuals will be asked to complete the diary for the entire duration of the study (12 months) with support from a research nurse. Stamped addressed envelopes will be provided for individuals to send diaries in on a monthly basis. The information recorded will include facilities use by children of the patients enrolled in the study during the period of follow up, who they saw during the most recent health visit (any non-HIV clinic visit) or inpatient stay, the reason for using the services and the outcome of the episode. As a reminder to complete the diaries, monthly text messages, emails or phone calls will be used depending on the patients preference.
The services use to be recorded on the diary are indicated in Appendix 3. This list is not an exclusive list and some may be added at discretion of the patient. Individuals will be encouraged to record in the diary as much detail as possible of the visits. Alternatively

patients will be given the option of emailing the research team when they attend an appointment. Cost of service will be assigned in terms of the professional or volunteer they saw during that services as well as associated indirect cost or overheads if a facility. The professionals are indicated in Appendix 4, but this is not necessarily an exhaustive list.

If patient consent, individual GP practices will be contacted and they will be asked to provide information on the encounters with the patients for the six months before and the twelve months since the patient was diagnosed with HIV. Contact will be made through a letter of introduction (appendix 5). A self-reported questionnaire will be attached together with the copy of patient consent form.

Should recruitment be rapid and additional resources be obtained, we would like to recruit a further cohort of HIV infected individuals attending the clinic who have been living with HIV for more than two years and been stable on antiretroviral therapy for at least one year (NND-HIV). This cohort will be recruited at St Thomas Hospital and matched to the new HIV diagnosis cohort by age and CD4 count and the methods used to gain information from the NND-HIV cohort will be the same for the ND-HIV cohort. Having the additional information on indirect cost of non-newly diagnosed will strengthen the findings even further and will provide policy-makers with additional important cost information. .

Methods of data collection:

1. Patient questionnaires -Appendix 6:

- a. General socio demographic information
- b. You and HIV
- c. Your views on HIV transmission risk
- d_1 Your health & wellbeing
- d_2 Symptoms (MSAS)
- d_3 Patient Health (PHQ-9)
- d_4 Health Outcome (EQ-5D)
- d_5 Social Support (Duke UNC Functional Social)
- e. Lifestyle
- f_1 HIV treatment
- f_2 Adherence (*for those on ART*)
- g_1 Sexual behaviour/history
- g_2 Sexual lifestyle before HIV Diagnosis
- g_3 Sexual lifestyle since HIV diagnosis

2. Diaries with -monthly reminders

3.Case note review (Appendix 7)

4. Data download on whole cohort for all investigations carried out at Guys and St Thomas' NHS Trust

5. GP provided information on encounter data, referrals and hospital attendances (12 only) (appendix 5). Community services download (RIO): this captures community health service

encounters in Lambeth and Southwark and has nationally recognized attributable reference costs (Appendix 8).

The research team will supervise handing out of the paper questionnaires to individuals when they are attending for their routine HIV, or give them access to the electronic questionnaire.

Summary of content of data collection (appendices 7 and 8):

1. ***Baseline only***
    a. ***General information/socio demographic***

Education and employment status
Social and domestic relationships
Housing
Benefits received
Postcode

b. HIV testing history

Presumed mode of transmission
HIV testing history and date of first positive test
Missed opportunities for testing
Identify factors that would have led to earlier testing

c. Use of health services

Utilization of community services

2. ***Baseline and longitudinal questionnaires***

a. QOL/your health and well being

Health Related Quality of Life

b. Sexual behaviour

- Sexual behaviour and potential risk of HIV transmission: at baseline and one year (0, 3, and 12 months);

c. Loss to society

Personal cost- employment, days lost from work (i.e loss of income) in past 3 months, relationships (include a sub-study of qualitative interviews), health and HIV status of children and partner. Who is primary career of children, Quality of life

d. Indirect healthcare costs

- transport cost (to patient or paid for by NHS),
- benefits
- incident STI during the year,

e. Direct community costs

- Visits to other health services- specialty, treatment received.,
- use of social services/ CNS nurses/mental health services
- payment to complimentary therapies etc

3. ***Direct hospital healthcare costs (HIV related and Non HIV related):***

For hospital attendances; Trust HRCG code cost; Actual cost- Payment by results Department of Health (DOH) categories

a. HIV St Thomas' Hospital visits: inpatient, outpatient (routine and emergency clinic)
b. Non HIV St Thomas' visits (GUM/ inpatient, outpatient, ITU, high dependency unit)
c. Drug cost (HIV and non-HIV):

i. HIV related drug cost: ART regime initiated/ switches; Number of ART regimen;
ART toxicity events:
HIV drug resistance test: baseline and subsequent genotypes, OI prophylaxis (eg septrin, fluconazole)
ii. Non HIV drug costs: Drug start and stop date/on-going

d. clinical conditions – HIV-related (using BHIVA list of clinical indicators of HIV) and non-HIV related
e. laboratory tests costs
f. Hospital St Thomas' visits/ procedure/investigation costs
g. GP visits/ A&E attendance ,non-Guys and St Thomas' Hospital admissions and clinic visits

4. Impact of informing health care professional of a missed HIV diagnosis

- Letter to HCP at two time points

2.4 Statistics

Routine data collected on all new patients diagnosed with HIV will be downloaded from the clinic database with all patients identifiers removed. This data will form denominator data.

Intent-to-treat (ITT) **Population** will include all subjects who attended for baseline visit and recruited into the study, including those who do not complete the study.

A Statistical Analysis plan (SAP) describing in detail the analysis that will be conducted will be developed as a separate document.. All costing work will be performed using methods used in other cost studies published by Ms Mandalia and Dr Beck (Mandalia et al., 2010; Beck et al., 2011a; Beck et al., 2011b) one of whom was also involved with the UK community services and indirect costs studies of the 1990s (Petrou S et al 1995, 1996a, 1996b, 1996c; Mullins CD et al 2000).

All data analyses will be performed in SAS® V9.1 (or higher) and all p-values presented will be two tailed.

2.4.1 Sample Size

We aim to recruit a minimum of 125 individuals newly diagnosed with HIV during the study period. On average we expect to recruit 10 newly HIV diagnosed patients per month out of the 25 new diagnoses that on average occur at St Thomas Hospital. We therefore anticipate recruitment to take approximately 12 months. If possible we will recruit a further 125 PLHIV to comprise the NND-HIV cohort.

2.4.2 Randomisation

There is no randomisation

2.4.3 Analysis

Primary analysis

Estimate the direct and indirect cost of those PLHIV in the first 12 months following diagnosis of HIV infection

Secondary analyses

1. The direct and indirect cost of people diagnosed with HIV infection stratified by CD4 count at diagnosis.
2. The cost effectiveness of treatment and care since diagnosis of HIV infection in those diagnosed with CD4 count below 350 cells/mm^3 compared to those diagnosed with CD4 above 350 cells/mm^3.
3. The change in sexual behaviour following HIV diagnosis

In order to carry out the above objectives, the use of all health and social services and the sexual behaviour of PLHIV when first diagnosed at Guys and St Thomas' hospital for one year from time of diagnosis will be recorded prospectively and retrospectively. The cost of services provided at Guys and St Thomas' hospital and other health- and social care providers during the year of follow up will be estimated. The mean use of services will be multiplied by unit costs for health- and social-care services to arrive at cost for service provision. The employment status of the study participants before and after diagnosis of HIV infection will be reviewed.

Analysis of sexual behaviour data

The aim is to evaluate whether there are changes over time in reported sexual risk behaviour. Information on sexual risk behaviour will refer to the three months before HIV diagnosis (collected at baseline), the 3 months following diagnosis (collected at visit two) and the three months before one year since diagnosis (collected in visit 4).
These changes will be evaluated using a mixed effects longitudinal model.
The main outcome is the proportion who reported having at least one partner they have condomless sex with in the last 3 months.

3 Selection and Withdrawal of Subjects

3.1 Inclusion Criteria

Inclusion criteria:

- Male or female over 18 years old
- Newly diagnosed with HIV-1 diagnosis within the previous 4 months and attending St Thomas' Hospital
- **Or for sub study:**
  living with HIV for more than two years (not newly diagnosed with HIV – NND-HIV)and stable on antiretroviral therapy for at least one year
- Able to understand and consent to study

3.2 Exclusion Criteria

Exclusion criteria:

- Documented HIV-2 Ab detected
- Unwilling or unable to consent to the study
- Unwilling or unable to comply with protocol

3.3 Withdrawal of Subjects

People recruited in the study can withdraw from it at any point in time. They will be asked permission to continue collecting laboratory measurements and their data will be included in analysis unless they request otherwise. Subjects who withdrawal in the first 6 months of the study will be replaced.

4. Trial Steering Committee

N/A

5. Direct Access to Source Data and Documents

The Investigator(s) will permit trial-related monitoring, audits, REC review, and regulatory inspections (where appropriate) by providing direct access to source data and other documents (ie patients' case sheets, blood test reports, X-ray reports, histology reports etc).

6. Ethics & Regulatory Approvals

This protocol and related documents will be submitted for review to NRES Committee – London Westminster. Annual progress reports and a final report at conclusion of the trial will be submitted to REC in accordance with regulatory requirements.

7. Quality Assurance, Data Handling, Publication Policy and Finance

Monitoring of this study will be to ensure compliance with Good Clinical Practice and scientific integrity will be managed and oversight retained; by the CTU within Harrison Wing.

8. Signatures

To be signed by Chief Investigator minimum and statistician if applicable.

_____	_____
Chief Investigator	Date
Print name	
_____	_____
Statistician	Date
Print name	

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Appendix 15. The Guy's and St. Thomas' study GP information request form

Appendix 5: request of information from GP

St Thomas' Hospital
Westminster Bridge Road
London SE1 7EH

Reception: 020 7188 6666
Secretaries: 020 7188 2662 / 2663 / 7791
Fax: 020 7188 2646
Main Switchboard: 020 7188 7188

Clinic Name: **Harrison Wing - STH**
Consultant: Fox
Clinic Date:

Dear Dr xxxxxx (Via Email)

Re:
Hospital No:
Address:

Date of Birth:
NHS No:

Dear Doctor,

This man/woman was diagnosed HIV positive on xxxx and has kindly agreed to participate in a study investigating the total cost of HIV. The community and personal cost of HIV has not been investigated before. In order to capture all costs we would be grateful if you could provide us with the following information for the patient in the past 18 months from x to y (please see table 1). We would be grateful of any way that is convenient for you to provide this information e.g. by a print out of all contacts/referrals or by completing the table to the next page.

I enclose a copy of the patients consent.

If you would like to discuss the case further, please do not hesitate to contact me on 020 71882636.

Could you either post or email to our study administrator Alice Sharp (alice.sharp@kcl.ac.uk)
Harrison wing Research unit
St Thomas' Hospital

Yours sincerely,

Dr Julie Fox
Consultant HIV Physician
Guys and St Thomas' NHS Trust
London SE1 9RT

Julie.fox@gstt.nhs.uk

Table 1: list of encounters of interest for GP

	6 months prior to HIV diagnosis (The date of diagnosis is indicated above)	12 months following HIV diagnosis(The date of diagnosis is indicated above)
Number of doctor or nurse consultations		
Number of phone consultations		
No. of referrals		
No. of A&E attendances		
No. of attendances at all hospitals		
No. of attendances requiring a blood test		
No. of attendances resulting in a prescription		
No. of HIV tests carried out		
list of drugs prescribed		
No. of DVLA reports written		
Number of Medical reports, housing letters or other forms completed (please list type of report)		

Table 2: alternative format for Gps to provide information

Either a print out of all consultations of the following information for each consultation:

- Date of visit
- HIV test Y/N
- Blood test request Y/N
- Prescription given: if y what drugs
- Referral written: to what specialty

- A&E attendances: date
- Hospital attendances: date, hospital, inpatient number of days and specialty
- DVLA report: ever y/N. date of report(s)

Appendix 16. The Guy's and St. Thomas' study patients' questionnaires

Summary of questions for participants to complete online or on paper

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No.* __ __ __ *Date:* ____ / ____ / ____
- *Visit No.* __ __ *Wk no:* __ __

Is this questionnaire being completed by (please tick)

a. *Participant* ☐
b. *Health worker* ☐

SECTION A: GENERAL INFORMATION:

Questions 1 to 6 Baseline (week 0) only

1. Which ethnic group best describes you? (*Please tick ONE ONLY)*

- ***A. White***

White British ☐
White Irish ☐
White other ☐

D. Mixed

White and Black African ☐
White and Black Caribbean ☐
White and Asian ☐
Mixed other ☐

- ***B. Black or Black British***

Black African ☐
Black Caribbean ☐
Black other ☐

- ***C. Asian or Asian British***

Indian ☐
Pakistani ☐
Bangladeshi ☐

Asian other □
Chinese or other ethnic group □
Chinese □
Any other ethnic group □

2. ***Were you born in the UK?***
   1 Yes □**→ *PLEASE GO TO QUESTION 3***
   2 No □ *if no, which country were you born in? ……*

3. ***When did you first move to the UK?***
   Less than 1 year ago □
   1 to 5 years ago □
   More than 5 years ago □

4. ***What is your highest level of education?***
   University □
   In between secondary (high school) level and university (e.g further education) □
   Secondary or high school □
   Primary school or less □
   Other, please specify □

5 . What is the most likely way that you became infected with HIV? Choose the most likely way, even if you are uncertain:

Sex with a man who was HIV positive □
Sex with a woman who was HIV positive □
Shared needles or other injection equipment with a person who was HIV positive □
Blood transfusion, blood products or medical procedure □
Needle stick or other exposure while at work (occupational exposure) □
Born with HIV infection □
Other (please specify)□ ……
Unknown □

6 . Had you previously been tested for HIV?

Yes □
No □

If yes:
- *when was your last HIV test month/ year _ _/_ _ _ _*

If no:

- *what were the reasons that you had not previously tested for HIV tick all that apply*
    - *never thought I was at risk* ☐
    - *doctor didn't offer test* ☐
    - *didn't want to know* ☐
    - *other reasons (please specify) ……*

7. In the PAST 2 YEARS, have you had a sexual health screen (tests for sexually transmitted infections)?

a. *Yes* ☐
b. *No* ☐
c. *Don't know* ☐

SECTION A (cont'd): GENERAL INFORMATION:

General Questions for Baseline (w0), W12,w24, w48

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __/__/__ Date: ____ /____ /____*
  Is this questionnaire being completed by (please tick)
  a. *Participant* ☐
  b. *Health worker* ☐

---

8. What is your current work situation?

Please tick ONE ONLY

Employed or self-employed full-time (at least 30 hours per week) ☐
Employed or self-employed part-time (less than 30 hours per week) ☐
Full time student / education / training ☐
Unemployed and registered for benefits ☐
Unemployed, NOT registered for benefits ☐
Permanently sick / disabled (for 3 months or more) ☐
Temporarily sick / disabled (for less than 3 months) ☐
Looking after home / family / dependants full-time ☐
Retired ☐
Other (please specify) ☐ .....

9. If you are working, how many days of sick leave have you had in the past 3 months
.....

10. What is your current housing situation?

Own my own home (including with mortgage / loan / shared ownership) ☐

Renting from the council or housing association	☐
Renting from private landlord	☐
Temporary accommodation (hostel, shelter, bed & breakfast, squat)	☐
Staying with partner / friend(s) / family	☐
Homeless	☐
Other (please specify) ……	☐

13. Do you find it difficult to pay for the cost of heating your home in the winter?

Yes ☐
No ☐

14. Do you receive any benefits? (*This information is completely confidential and WILL NOT be released to any other organisation.)*

Yes ☐
No ☐

If yes, do you receive any of the following?

Income Support	☐
Pension Credit	☐
Housing Benefit	☐
Working Tax Credit	☐

15. How much did it cost you to come to hospital today (return journey)
£

16. Did you arrive by hospital transport today?

Yes ☐
No ☐

SECTION B: YOU AND HIV. Completed at Baseline (w0), W12,w24, w48

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

a. *Participant* ☐
b. *Health worker* ☐

---

17. Apart from health care staff, have you told anyone that you have HIV?

Yes ☐

No ☐→ *PLEASE GO TO QUESTION 18*

If YES:

I have told my partner / wife / husband Yes ☐ No ☐ Not applicable ☐

I have told other family members:	None ☐	some ☐	most or all ☐
I have told my friends	None ☐	some ☐	most or all ☐
I have told my work colleagues	None ☐	some ☐	most or all ☐

18. how do you feel about testing now that you know that the test was positive:

glad that I tested ☐
wish that I hadn't tested ☐
not sure ☐

19. Are you currently in a relationship with a partner (wife / husband/ civil partner or girlfriend / boyfriend)?

Yes, I am in a relationship and living with my partner ☐
Yes, I am in a relationship but not living with my partner ☐
No, I am not currently in a relationship with a partner ☐

- *If YES:*
  Overall, how long have you been in this relationship? __ __ months __ __ years

20. Does your partner have HIV?

Yes ☐
No ☐
Don't know ☐
I do not have a partner ☐

21. Do you have any children?

Yes ☐
No ☐

If YES, please complete the following for each child:

	Age of child	*do they have HIV*		
1	.....	*Yes* ☐	*No* ☐	*not tested* ☐
2	.....	*Yes* ☐	*No* ☐	*not tested* ☐
3	.....	*Yes* ☐	*No* ☐	*not tested* ☐
4	.....	*Yes* ☐	*No* ☐	*not tested* ☐
5	.....	*Yes* ☐	*No* ☐	*not tested* ☐

SECTION C: YOUR VIEWS ON HIV TRANSMISSION RISK .
Completed at <u>Baseline (w0), W12,w24, w48</u>

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

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- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

c. *Participant* ☐

d. *Health worker* ☐

---

22. Here are some statements about HIV. Please read each statement carefully and place a tick in the box that is closest to your viewpoint. Give only one answer for each row.

Strongly agree=5 Tend to Agree =4 Undecided or no opinion=3 Tend to disagree=2 Strongly disagree=1

a) In my opinion, because of improvements in HIV treatments, people are more willing to take a chance of getting infected or infecting someone else with HIV.

5☐ 4☐ 3☐ 2☐ 1☐

b) In my opinion, a person on HIV treatment who has an undetectable viral load is less likely to transmit HIV to a sexual partner than someone with a high viral load.

5☐ 4☐ 3☐ 2☐ 1☐

c) In my opinion, if an HIV-positive person's viral load is undetectable, it is not necessary to use a condom to prevent transmission of HIV.

5☐ 4☐ 3☐ 2☐ 1☐

SECTION D: YOUR HEALTH AND WELLBEING:
Completed at <u>Baseline (w0), W12,w24, w48</u>

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

e. Participant ☐

f. Health worker ☐

In this part of the questionnaire, we are using some standard sets of questions to ask you about your health. We apologize if some of the questions seem repetitive, but please take the time to answer each section, as each one is important. Thanks for your help!

23. Are you currently receiving treatment (medicine or other therapy) for depression?

Yes ☐

No ☐

24. Are you currently receiving treatment (medicine or other therapy) for any other mental health condition ?

Yes ☐ *(please specify condition)……*

No ☐

Symptoms (Memorial Symptom Assessment Scale MSAS
completed at Baseline (w0), W12,w24, w48

25. Below is a list of symptoms. If you have had the symptom DURING THE PAST 2 WEEK please tick YES, and please tick the box that tells us how much the symptom DISTRESSED or BOTHERED you.					
Tick all the symptoms you have had during the PAST 2 WEEKS.	*Yes*	*IF YES: How much did it DISTRESS or BOTHER you?*			
		it DID NOT BOTHER ME	*A LITTLE BIT*	*QUITE A BIT*	*VERY MUCH*
Difficulty concentrating		*0*	*1*	*2*	*3*
Difficulty sleeping		*0*	*1*	*2*	*3*
Lack of energy		*0*	*1*	*2*	*3*
Feeling drowsy / tired		*0*	*1*	*2*	*3*
Pain		*0*	*1*	*2*	*3*
Headache		*0*	*1*	*2*	*3*
Numbness or tingling in hands or feet		*0*	*1*	*2*	*3*
Nausea		*0*	*1*	*2*	*3*
Vomiting		*0*	*1*	*2*	*3*
Diarrhoea		*0*	*1*	*2*	*3*
Constipation		*0*	*1*	*2*	*3*
Feeling bloated		*0*	*1*	*2*	*3*
Dizziness		*0*	*1*	*2*	*3*
Sweats / fever		*0*	*1*	*2*	*3*
Cough		*0*	*1*	*2*	*3*
Shortness of breath		*0*	*1*	*2*	*3*
Problems urinating		*0*	*1*	*2*	*3*
Problems with sexual		*0*	*1*	*2*	*3*

interest / activity					
Skin problems (e.g. rash, itching, dryness)		*0*	*1*	*2*	*3*
Mouth sores		*0*	*1*	*2*	*3*
Dry mouth		*0*	*1*	*2*	*3*
Lack of appetite		*0*	*1*	*2*	*3*
Changes in way food tastes		*0*	*1*	*2*	*3*
Weight loss		*0*	*1*	*2*	*3*
Changes in fat in face or body		*0*	*1*	*2*	*3*

26. We would like to know how you have been feeling recently. Please indicate, by ticking the box, whether you have experienced the following feelings DURING THE PAST 1 WEEK and, if so, HOW OFTEN they occurred.				
Tick the feelings that you have experienced during the PAST 1 WEEK. *Yes* *IF YES: How OFTEN did it occur?*	*Yes √*	*OCCASIONALLY*	*FREQUENTLY*	*ALMOST CONSTANTLY*
Feeling sad		*1*	*2*	*3*
Worrying		*1*	*2*	*3*
Feeling nervous		*1*	*2*	*3*
Feeling irritable		*1*	*2*	*3*
Suicidal thoughts		*1*	*2*	*3*

Patient Health questionnaire (PHQ-9)

completed at Baseline (w0), W12,w24, w48

27. Over the PAST 1 WEEK, how often have you been bothered by any of the following problems? (use a circle to indicate your answer)				
	Not at all	*Several days*	*More than half the days*	*Nearly every day*
Little interest or pleasure in doing things	0	*1*	*2*	*3*
Feeling down, depressed, or hopeless	0	*1*	*2*	*3*
Trouble falling or staying asleep, or sleeping too much	0	*1*	*2*	*3*
Feeling tired or having little energy	0	*1*	*2*	*3*
Poor appetite or overeacting?	0	*1*	*2*	*3*
Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	*1*	*2*	*3*
Trouble concentrating on things, such as reading the newspaper or watching television	0	*1*	*2*	*3*
Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	*1*	*2*	*3*
Thoughts that you would be better off dead, or of hurting yourself in some way	0	*1*	*2*	*3*
If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	*1 Not at all difficult* *2 Somewhat difficult* *3 Very difficult* *4 Extremely difficult*			

Health outcome (EQ-5D)

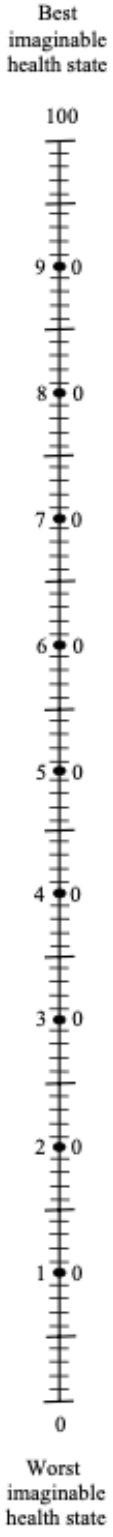
completed at w0,w12, w24, w48

28. Please indicate which statement best describes your own state of health TODAY.	
Mobility	*I have no problems walking about* ☐ *I have some problems walking about* ☐ *I am confined to bed* ☐
Self-care	*I have no problems with self-care* ☐ *I have some problems with performing my usual activities* ☐ *I am unable to wash or dress myself* ☐
Usual activities (e.g. work, study, housework, leisure activities)	*I have no problems with performing my usual activities* ☐ *I have some problems with performing my usual activities* ☐ *I am unable to perform my usual activities* ☐
Pain/discomfort	*I have no pain or discomfort* ☐ *I have moderate pain or discomfort* ☐ *I have extreme pain and discomfort* ☐
Anxiety/depression	*I am not anxious or depressed* ☐ *I am moderately anxious or depressed* ☐ *I am extremely anxious or depressed* ☐

29. To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 (on top) and the worst state you can imagine is marked 0 (at the bottom).

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



46

Social support (Duke UNC functional social)
completed at Baseline (w0), W12,w24, w48

30. Here is a list of some things that other people do for us that may be helpful or supportive. Please read each statement carefully and place a tick in the column that is closest to your situation. Give only one answer for each row.					
	As much as I would like	*Almost as much as I would like*	*Some, but would like more*	*Less than I would like*	*Much less than I would like*
I have people who care what happens to me					
I get love and affection					
I get chances to talk to someone I trust about my personal problems					
I get invitations to go out and do things with other people					
I get help when I am sick in bed					

SECTION E LIFESTYLE:

Completed at Baseline (w0), W12,w24, w48

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- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

g. Participant ☐

h. Health worker ☐

---

31. Have you ever felt you should Cut down on your drinking?

Yes ☐

No ☐

32. Have people Annoyed you by criticizing your drinking?

Yes ☐

No ☐

33. Have you ever felt bad or Guilty about your drinking?

Yes ☐

No ☐

34. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)?

35. In the PAST 3 MONTHS, have you used recreational drugs?

Yes ☐

No ☐

SECTION F: HIV TREATMENT:
Completed at Baseline (w0), W12,w24, w48

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

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- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

i. Participant ☐

j. Health worker ☐

---

36. Have you ever taken HIV treatment (antiretroviral treatment / HAART)?

a. Yes

b. No → PLEASE GO TO QUESTION 45

FOR ALL PATIENTS WHO ARE TAKING OR HAVE EVER TAKEN HIV TREATMENT

37. When did you start taking HIV treatment?

Month: __ __ __ Year: __ __ __ __

38. Why did you start antiretroviral treatment (*Please tick all that apply)*

was HIV making you ill?	☐
was your CD4 count low but you had no symptoms	☐
to prevent transmitting HIV to your partner	☐
because you had hepatitis B or hepatitis C	☐
because you wanted to start even though your results were good	☐

39. Please tick which response is closest to your own view: "Compared to what I expected before starting HIV treatment, taking treatment was..."

Much worse than I expected	☐
A bit worse than I expected	☐
About the same as I expected	☐
A bit better than I expected	☐
Much better than I expected	☐
Don't know / can't remember	☐

40. Have you ever changed your HIV treatment because it was not keeping your viral load down?

Yes	☐
No	☐
Don't know	☐

41. Are you currently taking HIV treatment?

Yes → PLEASE GO TO QUESTION 42

No

If NO:

When did you stop taking treatment?

Less than 1 month ago	☐
1 to 6 months ago	☐
More than 6 months ago	☐

Why did you stop taking treatment?

Please tick all that apply

I took HIV treatment only because I was pregnant	☐
I took HIV treatment only as part of a clinical trial	☐
My HIV doctor advised me to stop taking treatment	☐
I stopped because of treatment side effects	☐
I wanted a break from treatment	☐
I stopped because treatment was not working	☐
I found it difficult to take regular treatment	☐
Other (please specify)	☐

.....

If you are no longer taking HIV treatment please go to question 44

For individuals on HIV antiretroviral therapy:

Adherence (for those on ART completed at w12, w24, w48)

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- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

k. Participant ☐

l. Health worker ☐

42. How often do you need to take your HIV treatment?

Once a day ☐

Twice a day ☐

Other (please specify) ☐……

43. In the LAST 2 WEEKS, how many doses of HIV treatment have you missed? (In the last 2 weeks, if you took all your once a day treatment, that would be 14 doses. In the last 2 weeks, if you took all your twice a day treatment, that would be 28 doses.)

Missed no doses in last 2 weeks (took all my treatment) ☐

Missed 1 dose ☐

Missed 2 doses ☐

Missed 3 doses ☐

Missed 4 to 6 doses ☐

Missed 7 to 9 doses ☐

Missed 10 or more doses (please give approximate number missed……) ☐

If you missed at least one dose in the LAST 2 WEEKS: what were the reasons for this? Please tick all that apply

Treatment was making me feel ill	*Yes*	☐	*No* ☐
I forgot to take pills	*Yes*	☐	*No* ☐
I was away from home and forgot to bring my pills	*Yes*	☐	*No* ☐
I ran out of pills	*Yes*	☐	*No* ☐
I was in a public place	*Yes*	☐	*No* ☐
I was with people who did not know I had HIV	*Yes*	☐	*No* ☐
I was fed up with taking pills	*Yes*	☐	*No* ☐
I was feeling depressed / low	*Yes*	☐	*No* ☐

Other (please specify)……. ☐

44. In the PAST 3 MONTHS, have you ever missed your HIV treatment for two or more days at a time?

a. *Yes* ☐
b. *No* ☐
c. *Don't know / Can't remember* ☐

If YES, on how many occasions in the past 3 months has this happened?

a. *Once* ☐
b. *2 or 3 times* ☐
c. *More than 3 times* ☐

PLEASE GO TO QUESTION 47

FOR individuals WHO HAVE NEVER TAKEN HIV TREATMENT

45. Here are some statements about starting HIV treatment. Please read each statement carefully and place a tick in the box that is closest to your viewpoint. Give only one answer for each row.

5 =Strongly agree 4= Tend to Agree 3= Undecided or no opinion 2=Tend to disagree 1= Strongly disagree

a) I would prefer to delay starting HIV treatment for as long as possible, even if this meant a small increased risk of getting a serious illness.

5 4 3 2 1

b) I would want to start HIV treatment now, if I knew that being on treatment would slightly reduce my risk of getting a serious illness.

5 4 3 2 1

c) I would want to start HIV treatment now, if I knew that being on treatment would reduce the risk of transmitting HIV to a sexual partner (even if there was no benefit to my own health).

5 4 3 2 1

46. Has your HIV doctor ever advised you to start HIV treatment?

Yes ☐

No ☐

If YES, please tick the main reasons for not starting treatment:
Please tick all that apply

a) I was worried about the side effects of treatment *Yes* ☐ *No* ☐

b) I was worried about others knowing I had HIV *Yes* ☐ *No* ☐

c) I was worried about developing resistance to treatment *Yes* ☐ *No* ☐

d) I didn't want to take regular medication *Yes* ☐ *No* ☐

e) I wanted to delay starting treatment that I would have to take for the rest of my life *Yes* ☐ *No* ☐

f) I felt well and didn't see the need for treatment *Yes* ☐ *No* ☐

g) I didn't think treatment would help me *Yes* ☐ *No* ☐

h) I would rather let HIV take its natural course *Yes* ☐ *No* ☐

i) Other (please specify)..... ☐

Section G: Sexual behaviour/history questionnaire – completed at w0, w12, w48

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

m. Participant ☐

n. Health worker ☐

Section G_1 (week 0, 12, 48)

47. In the PAST 3 MONTHS, have you been diagnosed with a sexually transmitted infection?

Yes ☐

No ☐

If YES, have you had any of the following in the PAST 3 MONTHS?
Please tick MORE THAN ONE box, if applicable

1 Syphilis ☐
2 Gonorrhoea ☐
3Chlamydia ☐
4 LGV ☐
5 New Hepatitis C ☐
6 Genital herpes (new or recurrent) ☐
7 Genital warts (new or recurrent) ☐
8 Trichomonas ☐
9.NSU (Non Specific Urethritis), ☐
10.NGU (Non Gonococcal Urethritis) ☐
11 Other (please specify) ……

48. Have you ever been told by a doctor that you have Hepatitis C?

a. Yes ☐

b. No ☐

Section G_2 (week 0 only) SEXUAL LIFESTYLE BEFORE HIV DIAGNOSIS

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

o. *Participant* ☐

p. *Health worker* ☐

TO BE INCLUDED IN MEN'S QUESTIONNAIRE

This section asks about your recent sex life. Remember this information is completely confidential. Your name or clinic number is NOT written on this questionnaire and your answers WILL NOT be seen by the routine clinic staff.

The questions ask about vaginal sex and anal sex, IN THE PAST 3 MONTHS. 'Vaginal sex' means a man's penis is in a woman's vagina. 'Anal sex' means a man's penis in a partner's anus (rectum or back passage). Sex means vaginal or anal sex.

SEX WITH WOMEN

49. In the past 3 months, have you had sex (vaginal or anal sex) with a woman?

Yes ☐

No ☐ *→ PLEASE GO TO QUESTION 58*

If YES, how many women have you had sex (vaginal or anal sex) with in the past 3 months?

1 woman - regular / long-term partner ☐

1 woman - casual / short-term partner ☐

2 to 5 women ☐

More than 5 women (please give approximate number _____) ☐

50. In the past 3 months, have you ever used a condom when you had sex (vaginal or anal sex) with a woman?

Yes ☐

No ☐

51. In the past 3 months, have you had sex (vaginal or anal sex) with a woman WITHOUT using condom?

Yes ☐

No ☐ → *PLEASE GO TO QUESTION 58*

IF YES, IN THE PAST 3 MONTHS:

(i) How many women did you have sex (vaginal or anal sex) with, WITHOUT USING a condom?

1 woman - regular / long-term partner ☐

1 woman - casual / short-term partner ☐

2 to 5 women ☐

More than 5 women (please give approximate number _____) ☐

(ii) Overall, how many times did you have sex (vaginal or anal sex) WITHOUT a condom?

1. Once ☐

2. 2 to 10 times ☐

3. 11 to 30 times ☐

4. More than 30 times (please give approximate number _____) ☐

(iii) When you had sex with women WITHOUT a condom, did you have anal sex?

1 Yes, at least once ☐

2 No, never ☐

(iv) When you had sex (vaginal or anal sex) WITHOUT a condom, did you ejaculate (come) inside your partner?

1. *Yes – some or all of the times* ☐
2. *No – none of the times* ☐

(v) The last time you had sex (vaginal or anal sex) with a woman without a condom, what were the reasons for not using a condom

Please tick all that apply

a) Trying for pregnancy	*Yes* ☐	*No* ☐
c) I didn't think about using a condom	*Yes* ☐	*No* ☐
d) My partner didn't want to use a condom	*Yes* ☐	*No* ☐
e) I felt unable to discuss condom use	*Yes* ☐	*No* ☐
f) We did not have a condom	*Yes* ☐	*No* ☐
g) It's more enjoyable / close without a condom	*Yes* ☐	*No* ☐
h) I got carried away	*Yes* ☐	*No* ☐
i) I was under the influence of alcohol or drugs	*Yes* ☐	*No* ☐

j) Difficult to keep erection or ejaculate using a condom *Yes* ☐ *No* ☐
k) I am relaxed about having unprotected sex *Yes* ☐ *No* ☐
l) Other, please specify .....

SEX WITH MEN

These questions ask about anal sex with another man – this means your penis in a partner's anus (rectum or back passage), OR a partner's penis in your anus.

52. In the past 3 months, have you had anal sex with a man?

Yes ☐
No ☐ → *PLEASE GO TO QUESTION 58*

If YES, how many men have you had anal sex with in the past 3 months?

1. *1 man - regular/long-term partner*
2. *1 man - casual/short-term partner*
3. *2 to 5 men*
4. *More than 5 men (please give approximate number _____)*

53. In the past 3 months, have you had anal sex with a man, WITHOUT using condom?

Yes ☐
No ☐ → *PLEASE GO TO QUESTION 58*

IF YES, IN THE PAST 3 MONTHS:

(i) How many men did you have anal sex with, WITHOUT using condom? 1 man - regular/long-term partner ☐
1 man - casual/short-term partner ☐
2 to 5 men ☐
More than 5 men (please give approximate number _____) ☐

(ii) Overall, how many times did you have anal sex WITHOUT using condom?

Once ☐
2 to 10 times ☐
11 to 30 times ☐
More than 30 times (please give approximate number _____) ☐

(iii) When you had anal sex WITHOUT a condom, which partner were you?

Always the insertive partner (your penis was inside your partner) ☐
Always the receptive partner (your partner's penis was inside you) ☐
Sometimes the insertive partner and sometimes the receptive partner ☐

(iv) When you had insertive anal sex WITHOUT a condom, did you ejaculate (come) inside your partner?

Yes, always ☐
Yes, sometimes ☐
No, never ☐

(v) The last time you had anal sex with a man without a condom, what were the reasons for not using a condom?

Please tick all that apply

b) I didn't think about using a condom	*Yes* ☐	*No* ☐
c) My partner didn't want to use a condom	*Yes* ☐	*No* ☐
d) I felt unable to discuss condom use	*Yes* ☐	*No* ☐
e) We did not have a condom	*Yes* ☐	*No* ☐
f) It's more enjoyable / close without a condom	*Yes* ☐	*No* ☐
g) I got carried away	*Yes* ☐	*No* ☐
h) I was under the influence of alcohol or drugs	*Yes* ☐	*No* ☐
i) Difficult for me / partner to keep erection or ejaculate when using a condom	*Yes* ☐	*No* ☐
j) I am relaxed about having unprotected sex	*Yes* ☐	*No* ☐

k) Other, please specify .....

TO BE INCLUDED IN WOMEN'S QUESTIONNAIRE

54. Are you pregnant?

Yes ☐
No ☐
Not sure ☐

This section asks about your recent sex life. Remember this information is completely confidential. Your name or clinic number is NOT written on this questionnaire and your answers WILL NOT be seen by the clinic staff.

The questions ask about vaginal sex and anal sex, in the past 3 months. With 'Vaginal sex' we mean a man's penis is in a woman's vagina. With 'Anal sex' we mean a man's penis in a woman's anus (rectum or back passage). With "Sex" we mean either "vaginal" or "anal sex".

55. In the past 3 months, have you had sex (vaginal or anal sex) with a man?

1 Yes ☐
2 No ☐ → *PLEASE GO TO QUESTION 58*

If YES, how many men have you had sex with in the past 3 months?

1 man - regular/long-term partner ☐

1 man - casual/short-term partner ☐

2 to 5 men ☐

More than 5 men (please give approximate number _____) ☐

56. In the past 3 months, have you EVER used a condom when you had sex (vaginal or anal sex) with a man?

Yes, always ☐

Yes, sometimes ☐

No, never ☐

57. In the past 3 months, have you had sex (vaginal or anal sex) with a man WITHOUT using condom?

Yes ☐

No ☐ *→ PLEASE GO TO QUESTION 58*

IF YES, IN THE PAST 3 MONTHS:

(i) How many men did you have sex (vaginal or anal sex) with, WITHOUT using condom?

1 man - regular/long-term partner ☐

1 man - casual/short-term partner ☐

2 to 5 men ☐

More than 5 men (please give approximate number _____) ☐

(ii) Overall, how many times did you have sex (vaginal or anal sex) WITHOUT using a condom?

Once ☐

2 to 10 times ☐

11 to 30 times ☐

More than 30 times (please give approximate number _____) ☐

(iii) When you had sex with men without a condom, did you have anal sex?

Yes, at least once ☐

No, never ☐

(iv) The last time you had sex (vaginal or anal sex) with a man WITHOUT using condom, what were the reasons for not using a condom?

Please tick all that apply

a) Trying for pregnancy	*Yes* ☐	*No* ☐
b) I believe the risk of HIV transmission is very low	*Yes* ☐	*No* ☐

c) I didn't think about using a condom	*Yes* ☐	*No* ☐
d) My partner didn't want to use a condom	*Yes* ☐	*No* ☐
e) I felt unable to discuss condom use	*Yes* ☐	*No* ☐
f) We did not have a condom	*Yes* ☐	*No* ☐
g) It's more enjoyable / close without a condom	*Yes* ☐	*No* ☐
h) I got carried away	*Yes* ☐	*No* ☐
i) I was under the influence of alcohol or drugs	*Yes* ☐	*No* ☐
j) Difficult for partner to keep erection or ejaculate when using a condom	*Yes* ☐	*No* ☐
k) I am relaxed about having unprotected sex	*Yes* ☐	*No* ☐
l) Other, please specify ……	*Yes* ☐	*No* ☐

58 . How much do you agree / disagree with the following statements? Please give only one answer per row.

5= Strongly agree 4= Tend to Agree 3=Undecided or no opinion 2=Tend to disagree 1=Strongly disagree

a) I feel confident that, if I want to, I can make sure a condom is used when I have sex with any partner, in any situation

5 4 3 2 1

b) I'd expect to ask a new partner their HIV status before we have sex

5 4 3 2 1

c) I'd expect to tell a new partner that I'm HIV-positive before we have sex

5 4 3 2 1

d) I find it difficult to discuss condom use with a new sexual partner

5 4 3 2 1

59. In the past 3 months, have you used the internet to find a sexual partner?

Yes ☐

No ☐

60. In the past 3 months, have you participated in group sex?

Yes ☐

No ☐

61. In the past 3 months, have you received money for having sex?

Yes ☐

No ☐

Thank you very much for completing this questionnaire. Please place in the envelope provided in put in the box at reception.

If you took the questionnaire away to complete it, please post it back using the pre-paid envelope. Thank you.

Section G_3 (week 12, week 48): SEXUAL LIFESTYLE SINCE HIV DIAGNOSIS

This questionnaire is self-completed and will be handed to clinic staff in a sealed envelope.

Thank you for agreeing to complete this confidential questionnaire. Please answer all the questions as fully as you can. You are free to leave any question you do not want to answer – although we hope that you will answer all those thatapply to you.

- *Your answers WILL only be seen by the research team and NOT by the doctors and nurses in the clinic, and your answers WILL NOT be recorded in your clinic notes.*

- *If you have any questions or need any help, please ask the nurse who gave you this questionnaire.*

- *Study No. __ __ __* *Date: ____ / ____ / ____*
- *Visit No. __ __* *Wk no: __ __*

Is this questionnaire being completed by (please tick)

q. Participant ☐

r. Health worker ☐

TO BE INCLUDED IN MEN'S QUESTIONNAIRE

This section asks about your recent sex life. Remember this information is completely confidential. Your name or clinic number is NOT written on this questionnaire and your answers WILL NOT be seen by the clinic staff.

The questions ask about vaginal sex and anal sex, IN THE PAST 3 MONTHS. With 'Vaginal sex' we mean/refer to a man's penis is in a woman's vagina. With 'Anal sex' we mean a man's penis in a partner's anus (rectum or back passage). With "Sex" we mean either "vaginal" or "anal" sex.

SEX WITH WOMEN

62. In the past 3 months, have you had sex (vaginal or anal sex) with a woman?

Yes ☐

No ☐

→ PLEASE GO TO QUESTION 73

If YES, how many women have you had sex (vaginal or anal sex) with in the past 3 months?

1 woman - regular / long-term partner

1 woman - casual / short-term partner

2 to 5 women

More than 5 women (please give approximate number _____)

63. In the past 3 months, have you ever used a condom when you had sex (vaginal or anal sex) with a woman?

Yes ☐

No ☐

64. In the past 3 months, have you had sex (vaginal or anal sex) with a woman WITHOUT using condom?

Yes ☐

No ☐

→ PLEASE GO TO QUESTION 73

65. In the past 3 months, have you had sex (vaginal or anal sex) WITHOUT using condom, with a woman who you knew also had HIV?

Yes ☐

No ☐

IF YES:

How many HIV-positive women have you had sex with, without a condom, in the past 3 months?

1 woman - regular / long-term partner ☐

1 woman - casual / short-term partner ☐

2 to 5 women ☐

More than 5 women (please give approximate number _____) ☐

66. In the past 3 months, have you had sex (vaginal or anal sex) WITHOUT using condom, with a woman who did not have HIV or whose HIV-status you didn't know?

Yes ☐

No ☐*→ PLEASE GO TO QUESTION 73*

IF YES, IN THE PAST 3 MONTHS:

(i) How many women did you have sex (vaginal or anal sex) with, WITHOUT usingcondom, who did not have HIV or whose HIV-status you didn't know? Count only women who did not have HIV, or whose HIV-status you didn't know.

1 woman - regular / long-term partner ☐

1 woman - casual / short-term partner ☐

2 to 5 women ☐

More than 5 women (please give approximate number _____) ☐

(ii) Overall, how many times did you have sex (vaginal or anal sex) WITHOUT using condom? Count only times you had sex with women who did not have HIV, or whose HIV-status you didn't know.

Once ☐
2 to 10 times ☐
11 to 30 times ☐
More than 30 times (please give approximate number _____) ☐

(iii) When you had sex with women WITHOUT using condom, did you have anal sex? Count only sex with women who did not have HIV, or whose HIV-status you didn't know.

Yes, at least once ☐
No, never ☐

(iv) When you had sex (vaginal or anal sex) WITHOUT using , did you ejaculate (come) inside your partner? Count only sex with women who did not have HIV, or whose HIV-status you didn't know.

Yes – some or all of the times ☐
No – none of the times ☐

(v) The last time you had sex (vaginal or anal sex) with a woman WITHOUT using condom, what were the reasons for not using a condom? This is for sex with a woman who did not have HIV or whose HIV-status you didn't know.

Please tick all that apply

a) Trying for pregnancy	*Yes* ☐	*No* ☐
b) I believe the risk of HIV transmission is very low	*Yes* ☐	*No* ☐
c) I didn't think about using a condom	*Yes* ☐	*No* ☐
d) My partner didn't want to use a condom	*Yes* ☐	*No* ☐
e) I felt unable to discuss condom use	*Yes* ☐	*No* ☐
f) We did not have a condom	*Yes* ☐	*No* ☐
g) It's more enjoyable / close without a condom	*Yes* ☐	*No* ☐
h) I got carried away	*Yes* ☐	*No* ☐
i) I was under the influence of alcohol or drugs	*Yes* ☐	*No* ☐
j) Difficult to keep erection or ejaculate using a condom	*Yes* ☐	*No* ☐
k) I am relaxed about having unprotected sex	*Yes* ☐	*No* ☐
l) Other, please specify		

SEX WITH MEN

These questions ask about anal sex – this means your penis in a partner's anus (rectum or back passage), OR a partner's penis in your anus.

67. In the past 3 months, have you had anal sex with a man?

Yes ☐
No ☐ → *PLEASE GO TO QUESTION 71*

If YES, how many men have you had anal sex with in the past 3 months?
1. 1 man - regular/long-term partner ☐
2. 1 man - casual/short-term partner ☐
3. 2 to 5 men ☐
4. More than 5 men (please give approximate number _____) ☐

68. In the past 3 months, have you ever used a condom when you had anal sex with a man?

Yes, always ☐
Yes, sometimes ☐
No,never ☐

69. In the past 3 months, have you had anal sex with a man, WITHOUT using condom?

Yes ☐
No ☐ → *PLEASE GO TO QUESTION 72*

70. In the past 3 months, have you had anal sex WITHOUT using condom, with a man you knew also had HIV?

Yes ☐
No ☐

IF YES:
How many HIV-positive men have you had sex with, ***WITHOUT using*** *condom, in the past 3 months?*
1 man - regular/long-term partner ☐
1 man - casual/short-term partner ☐
2 to 5 men ☐
More than 5 men (please give approximate number _____) ☐

71. In the past 3 months, have you had anal sex WITHOUT using condom with a man who did not have HIV or whose HIV-status you didn't know?

Yes ☐
No ☐ → *PLEASE GO TO QUESTION 72*

IF YES, IN THE PAST 3 MONTHS:

*(i) How many MEN did you have anal sex with, **WITHOUT using** condom? Count only men who did not have HIV, or whose HIV-status you didn't know.*

1 man - regular/long-term partner ☐

1 man - casual/short-term partner ☐

2 to 5 men ☐

More than 5 men (please give approximate number _____) ☐

*(ii) Overall, how many TIMES did you have anal sex **WITHOUT using** condom? Count only times you had sex with men who did not have HIV, or whose HIV-status you didn't know.*

Once ☐

2 to 10 times ☐

11 to 30 times ☐

More than 30 times (please give approximate number _____) ☐

*(iii) When you had anal sex **WITHOUT using** condom, which partner were you? Count only sex with men who did not have HIV, or whose HIV-status you didn't know.*

Always the insertive partner (your penis was inside your partner) ☐

Always the receptive partner (your partner's penis was inside you) ☐

Sometimes the insertive partner and sometimes the receptive partner ☐

*(iv) When you had INSERTIVE anal sex **WITHOUT using** condom, did you ejaculate (come) inside your partner? Count only sex with men who did not have HIV, or whose HIV-status you didn't know.*

1 Yes – some or all of the times ☐

2 No – none of the times ☐

*(v) The last time you had anal sex with a man **WITHOUT using** condom, what were the reasons for not using a condom? This is for sex with a man who did not have HIV or whose HIV-status you didn't know.*

72. Please tick all that apply

a) I believe the risk of HIV transmission is very low	*Yes* ☐	*No* ☐
b) I didn't think about using a condom	*Yes* ☐	*No* ☐
c) My partner didn't want to use a condom	*Yes* ☐	*No* ☐
d) I felt unable to discuss condom use	*Yes* ☐	*No* ☐
e) We did not have a condom	*Yes* ☐	*No* ☐
f) It's more enjoyable / close without a condom	*Yes* ☐	*No* ☐
g) I got carried away	*Yes* ☐	*No* ☐
h) I was under the influence of alcohol or drugs	*Yes* ☐	*No* ☐
i) Difficult for me / partner to keep erection or ejaculate when using a condom	*Yes* ☐	*No* ☐
j) I am relaxed about having unprotected sex	*Yes* ☐	*No* ☐

k) Other, please specify .....

TO BE INCLUDED IN WOMEN'S QUESTIONNAIRE

73. Are you pregnant?

Yes ☐

No ☐

Not sure ☐

This section asks about your recent sex life. Remember this information is completely confidential. Your name or clinic number is NOT written on this questionnaire and your answers WILL NOT be seen by the clinic staff.

The questions ask about vaginal sex and anal sex, in the past 3 months. 'Vaginal sex' means a man's penis is in a woman's vagina. 'Anal sex' means a man's penis in a woman's anus (rectum or back passage). Sex means vaginal or anal sex.

74. In the past 3 months, have you had sex (vaginal or anal sex) with a man?

Yes ☐

No ☐→ *PLEASE GO TO QUESTION 79*

If YES, how many men have you had sex with in the past 3 months?
1 1 man - regular/long-term partner
2 1 man - casual/short-term partner
3 2 to 5 men
4 More than 5 men (please give approximate number _____)

75. In the past 3 months, have you ever used a condom when you had sex (vaginal or anal sex) with a man?

Yes ☐

No ☐

76. In the past 3 months, have you had sex (vaginal or anal sex) with a man without a condom?

Yes ☐

No ☐ → *PLEASE GO TO QUESTION 79*

77. In the past 3 months, have you had sex (vaginal or anal sex) without a condom, with a man you knew also had HIV?

Yes ☐

No ☐

IF YES:
How many HIV-positive men have you had sex with, without a condom, in the past 3 months?

1. *1 man - regular/long-term partner* ☐

2. *1 man - casual/short-term partner* ☐
3. *2 to 5 men* ☐
4. *More than 5 men (please give approximate number _____)* ☐

78. In the past 3 months, have you had sex (vaginal or anal sex) without a condom with a man who did not have HIV or whose HIV-status you didn't know?

Yes ☐
No ☐
→ PLEASE GO TO QUESTION 79

IF YES, IN THE PAST 3 MONTHS:
(i) How many men did you have sex (vaginal or anal sex) with, without a condom? Count only men who did not have HIV, or whose HIV-status you didn't know.

1. 1 man - regular/long-term partner ☐

3. *1 man - casual/short-term partner* ☐
4. *2 to 5 men* ☐
5. *More than 5 men (please give approximate number _____)* ☐

(ii) Overall, how many times did you have sex (vaginal or anal sex) without a condom? Count only times you had sex with men who did not have HIV, or whose HIV-status you didn't know.

1. *Once* ☐
2. *2 to 10 times* ☐
3. *11 to 30 times* ☐
4. *More than 30 times (please give approximate number _____)* ☐

(iii) When you had sex with men without a condom, did you have anal sex? Count only sex with men who did not have HIV, or whose HIV-status you didn't know.

Yes, at least once ☐
No, never ☐

(iv) The last time you had sex (vaginal or anal sex) with a man without a condom, what were the reasons for not using a condom? This is for sex with a man who did not have HIV or whose HIV-status you didn't know.

Please tick all that apply

a) Trying for pregnancy *Yes* ☐ *No*
b) I believe the risk of HIV transmission is very low *Yes* ☐ *No*
c) I didn't think about using a condom *Yes* ☐ *No*
d) My partner didn't want to use a condom *Yes* ☐ *No*
e) I felt unable to discuss condom use *Yes* ☐ *No*
f) We did not have a condom *Yes* ☐ *No*
g) It's more enjoyable / close without a condom *Yes* ☐ *No*
h) I got carried away *Yes* ☐ *No*

i) I was under the influence of alcohol or drugs *Yes* ☐ *No*
j) Difficult for partner to keep erection or ejaculate
when using a condom *Yes* ☐ *No*
k) I am relaxed about having unprotected sex *Yes* ☐ *No*
l) Other, please specify .....

79 . How much do you agree / disagree with the following statements? Please give only one answer per row.

5= Strongly agree 4= Tend to Agree 3=Undecided or no opinion 2=Tend to disagree 1=Strongly disagree
a) I feel confident that, if I want to, I can make sure a condom is used when I have sex with any partner, in any situation
5 4 3 2 1
b) I'd expect to ask a new partner their HIV status before we have sex
5 4 3 2 1
c) I'd expect to tell a new partner that I'm HIV-positive before we have sex
5 4 3 2 1
d) I find it difficult to discuss condom use with a new sexual partner
5 4 3 2 1

80. In the past 3 months, have you used the internet to find a sexual partner?
Yes ☐
No ☐

81 . In the past 3 months, have you participated in group sex?
Yes ☐
No ☐

82 .
In the past 3 months, have you received money for having sex?
Yes ☐
No ☐

Thank you very much for completing this questionnaire. Please place in the envelope provided in put in the box at reception.

If you took the questionnaire away to complete it, please post it back using the pre-paid envelope. Thank you.

Appendix 17. The Guy's and St. Thomas' study case note review

Appendix 7: Information obtained from case note review, booking system and /or clinic database (week 0 and week 48)

1. Routine data from clinic database (including Date of birth)
2. Postcode,
3. Ethnicity
4. Gender
5. GP name
6. Diagnosis date
7. Date of ART initiation
8. Start and stop dates of all current drugs and for w48 , all drugs in past 48 weeks.
9. Number of previous HIV negative test
3. *Date of last HIV negative test*
4. *HIV STARHS incident test result*
5. *Date of attendance and type of healthcare professional seen (Appendix 5) in Guys and St Thomas' NHS trust in past 12 months*
    a. *non HIV outpatients*
    b. *HIV outpatients*
    c. *Accident and emergency*

1. *referrals carried out*
    a. *other hospital specialties (list)*
    b. *mental health and/or counselling services*

For each emergency clinic visit need reason for attendance:

a. *antiretroviral related reasons (needs to start, suspected drug reaction)*
b. *severe illness requiring admission*
c. *mild illness not requiring admission*

Appendix 18. The Guy's and St. Thomas' study – the use and cost of community and hospital services data

Appendix 8: Capturing the Use and Cost of Community and Hospital Services

Heath/social costs service utilization

1. Information to be collected in a monthly Diary

Diaries will be completed at baseline and then at monthly intervals thereafter. At baseline , diaries will be completed referring to the previous 6 months. Thereafter the diaries will be completed in real time.

Information to be collected for non-hospital health services

a. Date of visit
b. Service used
c. Reason for using service
d. Type of staff member seen
e. Cost of travel to the service
f. Cost of service (e.g. complimentary therapies)
g. outcome (including any treatment) of visit:

Information to be collected for hospital services

a. Date of visit
b. Hospital In or outpatient
c. What speciality
d. Type of staff member seen
e. Cost of travel to the service
f. No. of days an inpatient

2. Information to be collected from Rio Lambeth Health services system

a. Date of visit
b. Service used
c. Type of staff member seen
d. Cost of service

Appendix 19. The AURAH2 study results paper "Use of HIV pre-exposure among men who have sex with men in England: data from the AURAH2 prsopective study

Use of HIV pre-exposure prophylaxis among men who have sex with men in England: data from the AURAH2 prospective study

*Nadia Hanum, Valentina Cambiano, Janey Sewell, Andrew N Phillips, Alison J Rodger, Andrew Speakman, Nneka Nwokolo, David Asboe, Richard Gilson, Amanda Clarke, Ada R Miltz, Simon Collins, Fiona C Lampe, for the AURAH2 Study Group**

Summary

Background Since October, 2017 (and until October, 2020), pre-exposure prophylaxis (PrEP) has only been available in England, UK, through the PrEP Impact Trial, by purchasing it from some genitourinary medicine clinics, or via online sources. Here we report changes from 2013 to 2018 in PrEP and postexposure prophylaxis (PEP) awareness and use among HIV-negative gay, bisexual, and other men who have sex with men (MSM) and assess predictors of PrEP initiation.

Methods In the prospective cohort study Attitudes to, and Understanding of Risk of Acquisition of HIV 2 (AURAH2), MSM were recruited from three sexual health clinics in England: two in London and one in Brighton, UK. Men were eligible if they were aged 18 years or older and HIV-negative or of unknown HIV status. Participants self-completed a baseline paper questionnaire at one of the three clinics between July 30, 2013, and April 30, 2016, and were subsequently able to complete 4-monthly and annual online questionnaires, which were available between March 1, 2015, and March 31, 2018, and collected information on sociodemographics, health and wellbeing, HIV status, and sexual behaviours. PrEP and PEP use in the previous 12 months was obtained at baseline and in annual questionnaires. We assessed trends over calendar time in 3-month periods from first enrolment to the end of the study period (July–December, 2013, was counted as one period) in use of PrEP and PEP using generalised estimating equation logistic models. We used age-adjusted Poisson models to assess factors associated with PrEP initiation among participants who reported never having used PrEP at baseline.

Findings 1162 men completed a baseline questionnaire, among whom the mean age was 34 years (SD 10·4), and of those with available data, 942 (82%) of 1150 were white, 1076 (94%) of 1150 were gay, and 857 (74%) of 1159 were university educated. 622 (54%) of 1162 men completed at least one follow-up online questionnaire, of whom 483 (78%) completed at least one annual questionnaire. Overall, PrEP use in the past year increased from 0% (none of 28 respondents) in July to December, 2013, to 43% (23 of 53) in January to March, 2018. The corresponding increase in PrEP use among men who reported condomless sex with two or more partners was from 0% (none of 13 respondents) to 78% (21 of 27). PEP use peaked in April to June, 2016, at 28% (41 of 147 respondents), but decreased thereafter to 8% (four of 53) in January to March, 2018. Among 460 men who had never used PrEP at baseline, predictors of initiating PrEP included age 40–44 years (incidence rate ratio [IRR] 4·25, 95% CI 1·14–15·79) and 45 years and older (3·59, 1·08–11·97) versus younger than 25 years; and after adjustment for age, recent HIV test (5·17, 1·89–14·08), condomless sex (5·01, 2·16–11·63), condomless sex with two or more partners (5·43, 2·99–9·86), group sex (1·69, 1·01–2·84), and non-injection chemsex-related drugs use (2·86, 1·67–4·91) in the past 3 months, PEP use (4·69, 2·83–7·79) in the past 12 months, and calendar year (Jan 1, 2017, to March 31, 2018 *vs* July 30, 2013, to Dec 31, 2015: 21·19, 9·48–47·35). Non-employment (0·35, 0·14–0·91) and unstable or no housing (*vs* homeowner 0·13, 0·02–0·95) were associated with reduced rates of PrEP initiation after adjustment for age. About half of PrEP was obtained via the internet, even after the PrEP Impact trial had started (11 [48%] of 23 respondents in January to March, 2018).

Interpretation PrEP awareness and use increased substantially from 2013 to 2018 among a cohort of MSM in England. Improving access to PrEP by routine commissioning by National Health Service England could increase PrEP use among all eligible MSM, but should include public health strategies to target socioeconomic and demographic disparities in knowledge and use of PrEP.

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Introduction

The PROUD study, an open-label randomised controlled trial carried out at 13 sites in England, UK, in 2015, reported that daily oral pre-exposure prophylaxis (PrEP) with tenofovir–emtricitabine resulted in an 86% reduction in HIV infection in gay, bisexual, and other

Research in context

Evidence before this study

Pre-exposure prophylaxis (PrEP) taken daily or on-demand has been shown to be highly effective for prevention of HIV infection among men who have sex with men (MSM) in clinical trials and open-label studies. PrEP is recommended by WHO for HIV-negative individuals at substantial risk of sexually acquired HIV, including MSM. We searched PubMed for longitudinal cohort studies in English that included MSM in England, UK, published from database inception up to Jan 31, 2020, using key search terms including "pre-exposure prophylaxis", "PrEP", "HIV", "MSM", "homosexual", "men who have sex with men", "gay", "bisexual men", "longitudinal", "cohort", and "prospective". We identified 83 articles, which included articles of clinical trials, demonstration projects, and cohort studies mostly done in high-income countries. Apart from reports on PrEP uptake and associated factors, among these articles were studies about sexual behaviours, sexually transmitted infections, and HIV incidence among PrEP users; PrEP awareness, acceptability, and willingness to use; PrEP retention, engagement, adherence, and discontinuation; and characteristics of PrEP users. We identified two studies run in England, two articles from the PROUD trial, and one article from our research group (the Attitudes to, and Understanding of Risk of Acquisition of HIV [AURAH] and AURAH2 study) that measured changes in the prevalence of sexual behaviours and PrEP use, by comparing data from the AURAH cross-sectional study with baseline data from the AURAH2 prospective cohort. To our knowledge, no data have been published from longitudinal cohort studies in England, excluding those from clinical trials or PrEP demonstration projects.

Added value of this study

This study provides the first estimates of trends in PrEP use and predictors of PrEP initiation among HIV-negative MSM in England, using data from a prospective cohort, at a critical time in planning the roll-out of PrEP in England. We found that, despite free PrEP availability in England being only through the PrEP Impact trial, both awareness and use of PrEP increased substantially from 2013 to 2018 among MSM attending three sexual health clinics in south-east England. In 2018, PrEP use was almost 80% among men with multiple condomless sex partners. A substantial proportion of men accessing PrEP obtained it via the internet. PrEP use was lower among those with lower socioeconomic status than among those of higher socioeconomic status.

Implications of all the available evidence

The available evidence highly supports the addition of PrEP to the standard of care for MSM who would benefit from the preventive prophylaxis. Sociodemographic and economic barriers associated with PrEP use should be promptly addressed via routine commissioning of PrEP.

men who have sex with men (hereafter referred to as men who have sex with men [MSM]).[1] A subsequent modelling study has shown that the introduction of a PrEP programme for MSM in the UK would be cost-effective and possibly cost-saving in the long term.[2] In England, PrEP is freely available to people at risk of HIV only in the context of the PrEP Impact trial by Public Health England that launched across England in October, 2017. All trial participants will get National Health Service (NHS) England funded PrEP until at least October, 2020 (the end of the trial). Otherwise, people can legally purchase PrEP for their own use via the internet or from some genitourinary medicine clinics. A nationally commissioned PrEP programme for England has been agreed and should be operational by the end of the PrEP Impact trial.

For more on the **PrEP Impact trial** see https://www.prepimpacttrial.org.uk/

For more on **purchasing PrEP online** see https://www.iwantprepnow.co.uk/buy-prep-now/

Among gay and bisexual men in the UK, modelling of available data suggests that the estimated annual number of new HIV infections has decreased by 71%, from 2800 in 2012, to 800 in 2018.[3] The annual number of HIV diagnoses recorded among gay and bisexual men in the UK has also decreased by 35%, from 3480 in 2014, to 2250 in 2018.[3] Based on a CD4 cell count back-calculation model, the modelled number of incident infections among gay and bisexual in England has decreased by 65% since 2014, with the most rapid decrease occurring after 2016.[3] A combination of PrEP scale-up, a large increase in ever and repeat HIV testing, and rapid antiretroviral therapy initiation at diagnosis are most likely responsible for these steep decreases in new infections, largely among MSM.[4] Similar decreases in HIV diagnoses among MSM have also been reported in San Francisco, CA, and New York City, NY, in the USA,[5,6] and New South Wales, Australia.[7]

To date, little information exists on trends in PrEP awareness and uptake and predictors of PrEP initiation in England. Such data would be helpful to further inform the unrestricted PrEP implementation programme in England in 2020, in which PrEP will be made routinely available after completion of the PrEP Impact trial.[8]

The Attitudes to, and Understanding of Risk of Acquisition of HIV 2 (AURAH2) study is among the first prospective cohort studies of MSM in England. We assessed changes in awareness of, and use of, PrEP and postexposure prophylaxis (PEP), predictors of PrEP initiation, and factors associated with reporting the recent use of PrEP among initially HIV-negative MSM between 2013 and 2018.

Methods

Study design and participants

The AURAH2 study was a prospective cohort study that recruited MSM who were HIV negative or of unknown HIV status from two large sexual health clinics in London (56 Dean Street and Mortimer Market Centre) and one in Brighton (Claude Nicol clinic), between July 30, 2013, and April 30, 2016.[9] Additionally, participants were

eligible if they were aged 18 years or older and attending or had attended the study clinics for routine sexually transmitted infection (STI) or HIV testing. Individuals who consented to participation in the study completed a confidential baseline paper questionnaire in the clinic. During the follow-up period, participants self-completed subsequent 4-monthly and annual questionnaires that were available online from March, 2015, until March, 2018; hence, maximum follow-up was 3 years. The baseline and follow-up questionnaires gathered information on demographic and socioeconomic factors, health and wellbeing, knowledge and understanding of HIV, lifestyle, sexual health, recent sexual behaviour, and PrEP and PEP use. The study protocol has been described previously.[9]

All participants provided written informed consent before taking part. The AURAH2 study was approved by the designated research ethics committee, The National Research Ethics Service committee London-Hampstead (14/LO/1881), in November, 2014. Based on the research protocol and all versions of study documents, the AURAH2 study subsequently received permission for clinical research at three participating NHS sites: Chelsea and Westminster NHS Foundation Trust, Central and North West London NHS Foundation Trust, and the Brighton and Sussex University Hospitals NHS Trust.

	Baseline questionnaire	Annual questionnaire
PrEP awareness	Were you aware that you can take PrEP to try to prevent HIV infection? • Yes or no	NA
PEP awareness	Were you aware that you can take PEP to try to prevent HIV infection after sex without a condom? • Yes or no	NA
PrEP use in the past 12 months	Have you ever taken PrEP? • Yes or no	Have you taken PrEP in the past 12 months? • Yes or no
	If yes, approximately for how many days did you take PrEP in the last year? • 1–4 days • 5–19 days • 20–50 days • >50 days	Approximately how much of the time were you on PrEP in the last 12 months? • <3 months • 3–6 months • 6–9 months • >9 months
PEP use in the past 12 months	Have you ever taken PEP? • Yes or no	Have you taken PEP in the past 12 months? • Yes or no
	If yes, approximately how often did you take PEP in the last year? • Never • Once • 2 to 3 times • >3 times	Approximately how often did you take PEP in the last year? • Once • 2 to 3 times • >3 times
Source of PrEP	NA	Where did you access PrEP from? • Clinic, the internet, research study, a friend, or other source

Figure 1: **PrEP and PEP measures in the AURAH2 study***
AURAH2=Attitudes to and Understanding of Risk of Acquisition of HIV 2. NA=not applicable. PrEP=pre-exposure prophylaxis. PEP=postexposure prophylaxis. *PrEP data were not collected in the 4-monthly online questionnaire.

Measures

All measures were self-reported from participant questionnaires. Information on PrEP and PEP use was collected in the baseline and annual questionnaires, with information on PrEP and PEP awareness collected at baseline only. The main outcomes of interest were PrEP and PEP awareness and reported PrEP and PEP use in the previous 12 months. Study definitions and questions are shown in figure 1. To be classified as positive for having taken PrEP or PEP in the past 12 months, at baseline or at the annual questionnaire, participants were required to have answered "yes" to the question on having ever taken PrEP or PEP, and subsequently indicated use in the past year on the question on frequency of use. Missing answers to PrEP and PEP use questions were classified as no use.

Sociodemographic variables of interest included age group (<25, 25–29, 30–34, 35–39, 40–44, ≥45 years), country of birth and ethnicity (white UK born, other ethnicity UK born, white non-UK born, other ethnicity non-UK born), sexual identity (gay, bisexual or other), university education (yes, no), ongoing relationship (yes, no), employment status (employed, not employed), sufficient money for basic needs (all of the time, most of the time, sometimes or no), and housing status (homeowner, renting, unstable or other). We considered the following seven measures of HIV risk and related behaviours and activities (in the past 3 months, unless otherwise stated): condomless anal sex (condomless sex), condomless sex with two or more partners, group sex (sex involving more than two participants on the same occasion), recreational drug use classified into four groups (none; drug use but not injection or chemsex-related; use of at least one chemsex-related drug [crystal methamphetamine, γ-hydroxybutyrate (GHB), γ-butyrolactone (GBL), or mephedrone] but no injection drug use; injection drug use), STI diagnosis (in the past 12 months at the baseline questionnaire, and in the past 3 months at the annual questionnaire), PrEP or PEP use in the past 12 months, and having had a recent HIV test (in the past 6 months at the baseline questionnaire, and in the past 3 months at the annual questionnaire). Mental health and lifestyle factors of interest included depressive symptoms (a score of ≥10 on the Patient Health Questionnaire-9),[10] anxiety symptoms (a score of ≥10 on the Generalised Anxiety Disorder-7 test),[11] and higher alcohol consumption (a score of ≥6 on the WHO alcohol screening tool audit, Alcohol Use Disorders Identification Test-consumption [AUDIT-C], questionnaire; first two questions only).[12] Ethnicity, sexual identity, education, employment, financial status, and housing status were fixed variables derived from the baseline questionnaire, whereas age, depressive symptoms, anxiety symptoms, alcohol consumption, and HIV risk and related behaviours were time-varying variables derived from baseline and annual questionnaires. We treated missing values as "no" answers (these accounted for <5% for each variable), except for the few individuals with

	Completed baseline questionnaire (n=1162)	Completed at least one follow-up questionnaire (n=622)	Completed at least one annual questionnaire (n=483)
Sociodemographics			
Age, years			
Mean	34 (10·4)	34 (11·3)	35 (11·2)
Median	31 (26–39)	33 (26–41)	33 (26–42)
<25	275/1153 (23·9%)	132/613 (21·5%)	103/479 (21·5%)
25–29	207/1153 (17·9%)	86/613 (14·0%)	69/479 (14·4%)
30–34	226/1153 (19·6%)	121/613 (19·8%)	87/479 (18·2%)
35–39	157/1153 (13·6%)	89/613 (14·5%)	68/479 (14·2%)
40–44	121/1153 (10·5%)	70/613 (11·4%)	55/479 (11·5%)
≥45	167/1153 (14·5%)	114/613 (18·6%)	97/479 (20·2%)
Country of birth and ethnicity			
Born in the UK, white	568/1150 (49·4%)	317/611 (51·9%)	262/479 (54·7%)
Born in the UK, other ethnicity*	60/1150 (5·2%)	29/611 (4·7%)	20/479 (4·2%)
Non-UK born, white	374/1150 (32·5%)	195/611 (31·9%)	149/479 (31·1%)
Non-UK born, other ethnicity*	148/1150 (12·9%)	70/611 (11·5%)	48/479 (10·0%)
Sexual identity			
Gay	1076/1150 (93·6%)	581/614 (94·6%)	455/480 (94·8%)
Bisexual or other	74/1150 (6·4%)	33/614 (5·4%)	25/480 (5·2%)
University education			
Yes	857/1159 (73·9%)	471/619 (76·1%)	365/483 (75·6%)
No	302/1159 (26·1%)	148/619 (23·9%)	118/483 (24·4%)
Employed			
Yes	1053/1159 (90·9%)	548/619 (88·5%)	431/483 (89·2%)
No	106/1159 (9·1%)	71/619 (11·5%)	52/483 (10·8%)
Money to cover basic needs			
All of the time	896/1158 (77·4%)	509/618 (82·4%)	404/481 (84·0%)
Most of the time	194/1158 (16·8%)	81/618 (13·1%)	58/481 (12·1%)
Sometimes or no	68/1158 (5·8%)	28/618 (4·5%)	19/481 (3·9%)
Housing status†			
Homeowner	314/1147 (27·4%)	200/607 (33·0%)	168/475 (35·4%)
Renting	680/1147 (59·3%)	328/607 (54·0%)	250/475 (52·6%)
Unstable or other	153/1147 (13·3%)	79/607 (13·0%)	57/475 (12·0%)
HIV risk and behaviours			
Ongoing relationship			
Yes	465/1159 (40·1%)	257/619 (41·5%)	202/481 (42·0%)
No	694/1159 (59·9%)	362/619 (58·5%)	279/481 (58·0%)
Recent HIV test			
No	322/1159 (27·8%)	155/619 (25·0%)	123/481 (25·6%)
Yes	837/1159 (72·2%)	464/619 (75·0%)	358/481 (74·4%)
Condomless sex in the past 3 months			
No	418/1159 (36·1%)	224/619 (36·2%)	172/480 (35·8%)
Yes	741/1159 (63·9%)	395/619 (63·8%)	308/480 (64·2%)
Condomless sex with ≥2 partners in past 3 months			
No	749/1159 (64·6%)	385/619 (62·2%)	299/480 (62·3%)
Yes	410/1159 (35·4%)	234/619 (37·8%)	181/480 (37·7%)
Group sex in the past 3 months			
No	659/1159 (56·9%)	327/619 (52·8%)	247/480 (51·5%)
Yes	500/1159 (43·1%)	292/619 (47·2%)	233/480 (48·5%)

(Table 1 continues on next page)

missing values for the variables of age, country of birth and ethnicity, sexual identity, financial status, and housing status, who were excluded from analyses for those variables.

Statistical analysis

In preparation for the analyses, we considered calendar year 3-month periods from the first enrolment (July, 2013) to the end of the study period (March, 2018). Information from each participant's questionnaires was ascribed to the 3-month period in which the questionnaire was completed. We combined data for the last two quarters of 2013 as one calendar period (July–December, 2013) because recruitment started on July 30, 2013, and so the third quarter of 2013 was less than 3 months; the number recruited by September, 2013, was too small to have a separate period. To describe the prevalence of PrEP and PEP awareness at baseline, we used data from all available baseline questionnaires. We assessed trends over calendar time in the proportion of participants who indicated PrEP and PEP awareness at baseline over the period from July, 2013, to April, 2016 (enrolment stage), and did a χ^2 test for linear trends in proportions.

To examine trends in past 12-month PrEP and PEP use over the entire study period, we used pooled data from all available baseline and annual questionnaires. We used univariate generalised estimation equation (GEE) models with a logit link and robust SEs to assess trends over calendar time during the period July, 2013, to March, 2018, in the proportion of questionnaires for which PrEP and PEP use were reported, accounting for multiple questionnaire responses from individual participants. Calendar year was fitted as a continuous variable to obtain a test for linear trend. Similarly, we investigated trends over calendar time in the proportion of men who reported condomless sex with two or more partners, and trends in PrEP use among these men specifically. We also assessed trends over time (in 6-month calendar periods) in source of PrEP, using questionnaires in which PrEP use was reported.

We assessed, in a longitudinal analysis, factors associated with PrEP initiation during follow-up among those who reported not using PrEP at baseline and who had completed at least one annual questionnaire. PrEP initiation was defined as the first report of PrEP use in the past 12 months from an annual questionnaire; time to initiation was the time from baseline to the date of completion of the questionnaire in which PrEP was first reported, or from baseline to the end of follow-up if PrEP was not initiated. We considered each factor separately in age-adjusted Poisson models (using age as a continuous variable) with robust SEs. The predictors considered included sociodemographic factors, mental health, lifestyle factors, and sexual health and behaviours reported in past questionnaires associated with subsequent PrEP initiation. We present these results as age-adjusted incidence rate ratios (IRRs) with their corresponding 95% CIs.

We did an additional cross-sectional analysis to examine factors associated with being on PrEP, using all available baseline and annual questionnaires. We used GEE models with a logit link function, adjusted for age (as a continuous variable). Also, separately among PrEP users, we analysed factors associated with reporting non-prescribed PrEP (ie, PrEP obtained via the internet, friends, or others sources) using all available annual questionnaires in which PrEP use was reported. We present these results as age-adjusted odds ratios (ORs) with their corresponding 95% CIs.

p values below 0·05 were considered to be significant. We did all analyses using STATA (version 15.1).

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

1162 men enrolled in the study between July 30, 2013, and April 30, 2016 (table 1). The mean age at baseline was 34 years (SD 10·4). Of those with available data, participants were predominantly of white ethnicity (942 [82%] of 1150), self-reported being gay (1076 [94%] of 1150), had a university degree (857 [74%] of 1159), reported being employed (1053 [91%] of 1159), and always had money to cover basic needs (896 [77%] of 1158). Regarding sexual behaviour in the past 3 months, 741 (64%) of 1159 men reported condomless sex, 410 (35%) of 1159 reported condomless sex with two or more partners, 500 (43%) of 1159 reported group sex, and 695 (60%) of 1159 reported the use of at least one recreational drug; including 38 (3%) who reported injection drug use. In the previous 12 months, 440 (38%) of 1159 men reported they had been diagnosed with an STI, 240 (21%) reported taking PEP, and 58 (5%) reported taking PrEP.

622 (54%) of 1162 men completed at least one online follow-up questionnaire, of whom 483 (78%) completed at least one annual questionnaire. A higher proportion of participants who were older, had greater financial security, and with more stable housing status continued on the study than did those who were younger, who only sometimes or did not have money to cover basic needs and who had unstable or no housing (table 1). The number of follow-up questionnaires (4-monthly and annual) completed by the end of the study period was 3277.

To describe PrEP and PEP awareness at enrolment by calendar period of baseline questionnaire, we used data from 1161 of 1162 participants who completed a baseline questionnaire (one questionnaire was excluded from the analysis due to missing data). Overall, at baseline, 838 (72%) of 1161 participants were aware of PrEP and 1074 (93%) were aware of PEP. The proportion of men who at baseline reported PrEP awareness increased significantly over calendar time of recruitment, from 12 (43%) of 28 men recruited in July to December, 2013, to 58 (92%) of 63 men recruited in April to June, 2016 (p_{trend}<0·0001; breakdown by quarters not shown). The awareness of PEP was already high in the first period of recruitment (26 [93%] of 28 men recruited in July to December, 2013) and remained so over the recruitment period (61 [97%] of 63 recruited in April to June, 2016; p_{trend}=0·69).

To describe changes in past 12 month PrEP and PEP use over calendar time, we used data from 2079 questionnaires

	Completed baseline questionnaire (n=1162)	Completed at least one follow-up questionnaire (n=622)	Completed at least one annual questionnaire (n=483)
(Continued from previous page)			
Recreational drug use			
None	464/1159 (40·0%)	229/619 (37·0%)	181/480 (37·7%)
Drug use, non-injection, non-chemsex-related	336/1159 (29·0%)	179/619 (28·9%)	145/480 (30·2%)
Use of ≥1 chemsex-related drug, non-injection	321/1159 (27·7%)	192/619 (31·0%)	139/480 (29·0%)
Injection drug use	38/1159 (3·3%)	19/619 (3·1%)	15/480 (3·1%)
STI diagnoses‡			
No	719/1159 (62·0%)	384/619 (62·0%)	297/480 (61·9%)
Yes	440/1159 (38·0%)	235/619 (38·0%)	183/480 (38·1%)
PEP use in the past 12 months			
No	919/1159 (79·3%)	496/619 (80·1%)	387/481 (80·5%)
Yes	240/1159 (20·7%)	123/619 (19·9%)	94/481 (19·5%)
PrEP use in the past 12 months			
No	1101/1159 (95·0%)	589/619 (95·2%)	460/481 (95·6%)
Yes	58/1159 (5·0%)	30/619 (4·8%)	21/481 (4·4%)
Mental health and lifestyle			
Higher risk alcohol consumption§			
No	1008/1159 (87·0%)	537/619 (86·8%)	418/483 (86·5%)
Yes	151/1159 (13·0%)	82/619 (13·2%)	65/483 (13·5%)
Depressive symptoms¶			
No	1018/1159 (87·8%)	544/619 (87·9%)	424/483 (87·8%)
Yes	141/1159 (12·2%)	75/619 (12·1%)	59/483 (12·2%)
Anxiety symptoms‖			
No	1033/1159 (89·1%)	562/619 (90·8%)	440/483 (91·1%)
Yes	126/1159 (10·9%)	57/619 (9·2%)	43/483 (8·9 %)

Data are n/N (%), mean (SD), or median (IQR). Data are from baseline paper questionnaire. Condomless sex refers to condomless anal sex. Data are missing from the baseline questionnaire as follows: age (n=9), money status (n=4), housing status (n=15); country of birth and ethnicity (n=12), sexual identity (n=12), university education (n=3), employment (n=3), relationship (n=3), HIV test (n=3), condomless sex in the past 3 months (n=3), condomless sex with ≥2 partners in the past 3 months (n=3), group sex in the past 3 months (n=3), PEP use (n=3), PrEP use (n=3), recreational drug use (n=3), STI diagnoses (n=3), alcohol consumption (n=3), depressive symptoms (n=3), and anxiety symptoms (n=3). AURAH2=Attitudes to and Understanding of Risk of Acquisition of HIV 2. PrEP=pre-exposure prophylaxis. PEP=postexposure prophylaxis. STI=sexually transmitted infection. *Other ethnicity includes Black, Asian, Mixed, and other ethnic groups. †Renting housing includes private renting and renting from council or housing association; unstable or other housing includes temporary accommodation, staying with friends or family, other accommodation, and homeless. ‡In the past 12 months at the baseline questionnaire and in the past 3 months at the annual questionnaire. §Higher risk defined as a score of ≥6 on the WHO modified alcohol screening tool audit, Alcohol Use Disorders Identification Test-consumption, questionnaire. ¶Defined as a score of ≥10 on the Patient Health Questionnaire-9. ‖Defined as a score of ≥10 on the Generalised Anxiety Disorder-7.

Table 1: Baseline sociodemographic, health and lifestyle characteristics, sexual behaviour, and PrEP and PEP use among participants who completed the baseline, follow-up, and annual questionnaires in the AURAH2 study, 2013–18

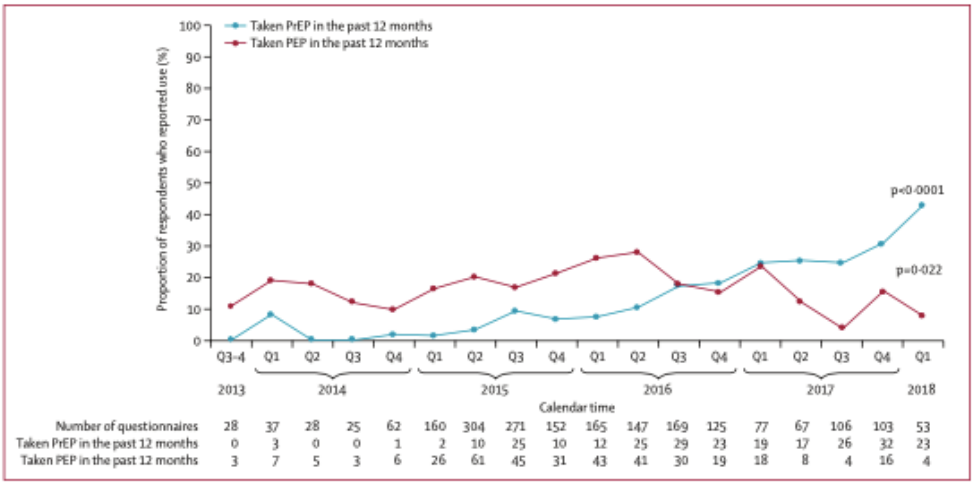

Figure 2: **Prevalence of PrEP and PEP use in the past 12 months over time among MSM, 2013–18**
Data are from baseline and annual questionnaires, missing values on use of PrEP and PEP questions were treated as "no" answers. 1161 participants provided 2079 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment. p values are for linear trends. MSM=men who have sex with men. PrEP=pre-exposure prophylaxis. PEP=postexposure prophylaxis. Q=quarter.

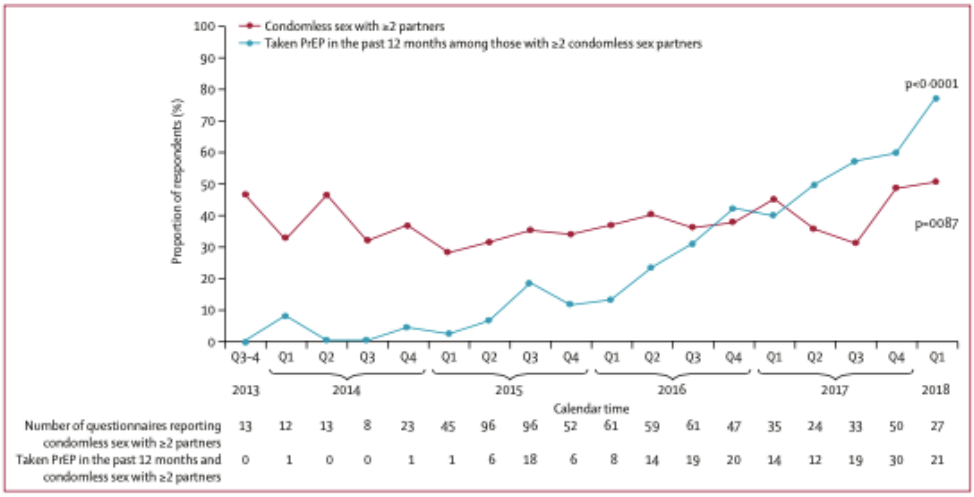

Figure 3: **Prevalence of condomless sex with two or more partners and prevalence of PrEP use among these men, 2013–18**
Data for condomless sex with ≥2 partners are from all baseline and annual questionnaires (ie, 1161 participants provided 2079 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment). Data on PrEP use in the past 12 months is from those with ≥2 condomless sex partners at baseline and in the annual questionnaires (n=755 questionnaires; one questionnaire was excluded from the analysis due to missing data on year of enrolment). Condomless sex is condomless anal sex. p values are for linear trends. PrEP=pre-exposure prophylaxis. Q=quarter.

(baseline and annual follow-up) from 1161 participants. Overall, PrEP use in the past 12 months was reported in 248 (12%) questionnaires. PrEP use increased significantly from 0% (none of 28 respondents) in the last two quarters of 2013 to 43% (23 of 53) by January to March, 2018 (p value for linear trend from GEE-logistic model <0·0001; figure 2). By contrast, some fluctuation was seen in the trend of past 12-month use of PEP. PEP use was reported in 371 (18%) questionnaires. PEP use was consistently higher than PrEP use until the period July to September, 2016, but after reaching a peak of 28% (41 of 147 respondents) in April to June, 2016, the

proportion of men who reported PEP use began to decrease significantly to a low of 8% (four of 53 respondents) by January to March, 2018 (p value for linear trend from GEE=0·022). From the 2079 questionnaires (of which one questionnaire was excluded from analysis due to missing data on year of enrolment), 755 (36%) reported condomless sex with two or more partners; we observed a slight increase in this prevalence from 46% (13 of 28 respondents) in the period July to December, 2013, to 51% (27 of 53) in January to March, 2018 (p value for linear trend from GEE=0·087). Of 755 questionnaires, 190 (25%) reported having taken PrEP in the past 12 months. PrEP use increased significantly among men who reported condomless sex with two or more partners, from 0% (none of 13 respondents) in July to December, 2013, to 78% (21 of 27) in January to March, 2018 (p value for linear trend from GEE <0·0001; figure 3).

Of all available annual questionnaires that reported PrEP sources (n=190), 112 (59%) indicated PrEP had been obtained from the internet, 65 (34%) from clinics, and 13 (7%) from friends or other sources. In October, 2017, to March, 2018, (after the PrEP Impact trial started), the proportion of respondents who reported sourcing PrEP from the internet was 65% (36 of 55), from a clinic was 25% (14 of 55), and from friends or other sources was 9% (five of 55). The proportion of respondents who reported PrEP use who also reported sourcing their PrEP from the internet increased over time. This proportion was 0% (none of 12) in the period of July to December, 2015, 67% (six of nine) in January to June, 2016, 58% (30 of 52) in July to December, 2016, 67% (24 of 36) in January to June, 2017, 71% (41 of 58) in July to December, 2017 (the period in which the Impact Trial started), and 48% (11 of 23) in January to March, 2018.

To examine factors associated with initiating PrEP, we restricted our analysis to the 460 participants who reported no previous PrEP use in the baseline questionnaire and who completed at least one annual follow-up questionnaire (data from 875 questionnaires). Age-adjusted IRRs for factors associated with initiating PrEP are shown in table 2. The PrEP initiation rate increased substantially from 2013 to 2018. When considering year as a continuous variable, the age-adjusted IRR per calendar year was 5·91 (3·68–9·49; p<0·0001). Compared with the category of younger than 25 years, rate of PrEP initiation was increased in the age categories of 40–44 years and age 45 years and older. In age-adjusted models, non-employment and unstable housing were significantly associated with a reduced rate of PrEP initiation compared with being a homeowner. Behavioural factors associated with higher rates of PrEP initiation within the past 12 months were having a recent HIV test; reporting condomless sex; condomless sex with two or more partners, group sex, use of non-injected chemsex-related drugs, and use of PEP in the past 12 months (table 2).

To assess factors associated with reporting PrEP use in the previous year, we used data from 2080 questionnaires representing 1162 respondents (baseline and follow-up; table 2). The predictors for PrEP use in the previous year were similar to those associated with initiating PrEP. In particular, older age and later calendar year were strongly associated with increased use of PrEP, while unstable or other housing was associated with less use of PrEP than

	Predictors of initiating PrEP (n=460)*		Factors associated with past 12-month use of PrEP (n=1162)†	
	Age-adjusted IRR (95% CI)	p value	Age-adjusted OR (95% CI)	p value
Age (time-updated) per year‡	1·02 (1·01–1·04)	0·0010	1·04 (1·03–1·05)	<0·0001
Age (time-updated) category, years‡				
<25	1 (ref)	0·0050	1 (ref)	<0·0001
25–29	1·76 (0·47–6·56)	..	1·13 (0·49–2·57)	..
30–34	2·42 (0·69–8·45)	..	2·86 (1·44–5·68)	..
35–39	1·93 (0·49–7·59)	..	3·04 (1·47–6·29)	..
40–44	4·25 (1·14–15·79)	..	3·89 (1·80–8·36)	..
≥45	3·59 (1·08–11·97)	..	3·54 (1·77–7·09)	..
Country of birth and ethnicity				
Born in the UK, white	1 (ref)	0·42	1 (ref)	0·52
Born in the UK, other ethnicity§	1·52 (0·46–5·03)	..	1·74 (0·84–3·59)	..
Non-UK born, white	1·19 (0·68–2·11)	..	1·17 (0·79–1·71)	..
Non-UK born, other ethnicity§	1·34 (0·56–3·24)	..	1·08 (0·63–1·87)	..
Sexual identity				
Bisexual or other	1 (ref)	0·79	1 (ref)	0·29
Gay	1·21 (0·29–4·95)	..	1·53 (0·69–3·38)	..
University education				
Yes	1 (ref)	0·24	1 (ref)	0·63
No	0·67 (0·34–1·31)	..	0·91 (0·63–1·32)	..
Employed				
Yes	1 (ref)	0·032	1 (ref)	0·078
No	0·35 (0·14–0·91)	..	0·58 (0·32–1·06)	..
Money to cover basic needs				
All of the time	1 (ref)	0·070¶	1 (ref)	0·12‖
Most of the time	1·04 (0·45–2·37)	..	0·83 (0·52–1·32)	..
Sometimes or no	0·57 (0·08–3·86)	..	0·52 (0·21–1·31)	..
Housing status				
Homeowner	1 (ref)	0·025	1 (ref)	0·031
Renting	0·56 (0·29–1·07)	..	0·71 (0·47–1·06)	..
Unstable or other	0·13 (0·02–0·95)	..	0·36 (0·18–0·73)	..
Ongoing relationship				
Yes	1 (ref)	0·88	1 (ref)	0·48
No	0·96 (0·57–1·61)	..	0·88 (0·63–1·24)	..
Recent HIV test				
No	1 (ref)	0·0010	1 (ref)	<0·0001
Yes	5·17 (1·89–14·08)**	..	2·73 (1·93–3·87)††	..
Condomless sex in the past 3 months				
No	1 (ref)	<0·0001	1 (ref)	<0·0001
Yes	5·01 (2·16–11·63)	..	4·57 (2·91–7·17)	..

(Table 2 continues on next page)

	Predictors of initiating PrEP (n=460)*		Factors associated with past 12-month use of PrEP (n=1162)†	
	Age-adjusted IRR (95% CI)	p value	Age-adjusted OR (95% CI)	p value
(Continued from previous page)				
Condomless sex with ≥2 partners in the past 3 months				
0 or 1	1 (ref)	<0·001	1 (ref)	<0·0001
≥2	5·43 (2·99–9·86)	..	5·64 (3·97–8·01)	..
Group sex in the past 3 months				
No	1 (ref)	0·045	1 (ref)	0·0010
Yes	1·69 (1·01–2·84)	..	1·77 (1·26–2·47)	..
PEP use in the previous 12 months				
No	1 (ref)	<0·0001	1 (ref)	0·0070
Yes	4·69 (2·83–7·79)	..	1·78 (1·17–2·71)	..
Recreational drug use				
None	1 (ref)	0·0020	1 (ref)	<0·0001
Drug use, non-injection, non-chemsex-related	0·39 (0·05–2·83)	..	0·82 (0·29–2·27)	..
Use of ≥1 chemsex-related drug, non-injection	2·86 (1·67–4·91)	..	2·70 (1·91–3·81)	
Injection drug use	1·00 (0·12–7·42)	..	1·76 (0·79–3·91)	
STI diagnoses				
No	1 (ref)	0·81	1 (ref)	0·73
Yes	1·07 (0·59–1·98)	..	1·07 (0·75–1·53)	..
Higher risk alcohol consumption				
No	1 (ref)	0·97	1 (ref)	0·12
Yes	1·01 (0·49–2·09)	..	0·63 (0·35–1·13)	..
Depressive symptoms				
No	1 (ref)	0·76	1 (ref)	0·11
Yes	0·87 (0·35–2·15)	..	0·62 (0·35–1·11)	..
Anxiety symptoms				
No	1 (ref)	..	1 (ref)	..
Yes	1·30 (0·52–3·24)	0·57	0·75 (0·39–1·41)	0·35
Calendar year	5·91 (3·68–9·49)	<0·0001	2·43 (2·12–2·79)	<0·0001
Calendar year category				
July 30, 2013–Dec 31, 2015	1 (ref)	<0·0001	1 (ref)	<0·0001
2016	6·69 (3·28–13·68)	..	2·80 (2·04–3·84)	..
Jan 1, 2017–March 31, 2018	21·19 (9·48–47·35)	..	7·44 (5·39–10·26)	..

Ethnicity, sexual identity, education, employment, money status, and housing status are fixed variables; age, lifestyle characteristics, and HIV-risk behaviour are time-varying variables. Condomless sex is condomless anal sex. IRR=incidence rate ratio. OR=odds ratio. PrEP=pre-exposure prophylaxis. PEP=postexposure prophylaxis. STI=sexually transmitted infection. *Total observations are from 875 questionnaires; total observations used: for age, country of birth and ethnicity, sexual identity, university education, employment status, relationship status, money status, recent HIV test, condomless sex in the past 3 months, condomless sex with ≥2 partners in the past 3 months, group sex in the past 3 months, STI diagnosis, recreational drug use, PEP use, alcohol use, depression, anxiety symptoms, and calendar year were from 868 questionnaires done by 457 men; and for housing status were from 860 questionnaires done by 453 men. †Total observations are from 2080 questionnaires; total observations used: for age, university education, employment status, money status, relationship status, recent HIV test, condomless sex in the past 3 months, condomless sex with ≥2 partners in the past 3 months, group sex in the past 3 months, STI diagnosis, recreational drug use, PEP use, alcohol use, depression, and anxiety symptoms were from 2062 questionnaires done by 1153 men; for country of birth and ethnicity were from 2061 questionnaires from 1152 men; for sexual identity were from 2050 questionnaires done by 1143 men; for housing status were from 2050 questionnaires done by 1149 men; and for calendar year were from 2061 questionnaires done by 1153 men. ‡IRRs and ORs for age are unadjusted, age is included as a continuous variable when adjusting effects of other variables for age. §Other ethnicity includes Black, Asian, Mixed, and other ethnic groups. ¶p_{trend}=0·54. ||p_{trend}=0·037. **Within the past 6 months. ††Within the past 3 months.

Table 2: **Longitudinal analysis of factors associated with initiating PrEP and cross-sectional analysis of factors associated with being on PrEP in the previous 12 months**

being a homeowner. We found some evidence of a trend between money status and reporting PrEP use (p_{trend}=0·037). Behavioural factors associated with reporting the use of PrEP were a recent HIV test, reporting condomless sex, condomless sex with two or more partners, group sex, non-injection chemsex-related drugs use, and PEP use. Country of birth and ethnicity, sexual identity, education, ongoing relationship, higher alcohol use, STI diagnosis, and symptoms of depression and anxiety were not associated with initiation of PrEP or use of PrEP (table 2).

In an additional analysis we looked at the association between health and behavioural factors and source of PrEP amongst those reporting use (190 questionnaires from 128 participants). We found that past 3-month STI diagnosis (unadjusted OR from GEE-logistic model 2·00, 95% CI 1·09–3·69; p=0·025), condomless sex (unadjusted OR 3·55, 95% CI 1·14–11·09; p=0·029), condomless sex with two or more partners (2·22, 1·01–4·85; p=0·045), group sex (2·32, 1·23–4·39; p=0·0090), use of non-injection chemsex-related drugs (3·69, 1·80–7·56; p<0·0001), and calendar year as a continuous variable (2·12, 1·43–3·15; p=0·028) were all associated with reported use of non-prescribed PrEP (data for other variables are not shown).

Discussion

To our knowledge, this Article is the first prospective study of PrEP use among MSM in England. In this study of MSM attending sexual health clinics in London and Brighton, UK, between 2013 and 2018, we found that use of PrEP increased substantially over the study period. The internet was the preferred source for obtaining PrEP, and online PrEP purchasing still continued even after the PrEP Impact trial started. Between January and March, 2018, about 48% of men who reported PrEP use obtained it from the internet, and paid for it using their own money. A substantial increase in PrEP use was also seen among men who self-reported engaging in condomless sex with two or more partners; in the period of January to March, 2018, the proportion was 78% compared with 0% in 2013.

The increased level of awareness, use, and rates of initiation of PrEP in this study coincided first with the PROUD study (Nov 29, 2012, to April 30, 2014),[3] and then the initiation of the PrEP Impact implementation trial in England, and the availability of PrEP through NHS sexual health clinics in Scotland and Wales, and through a pilot in Northern Ireland. The PrEP Impact trial started recruitment in 2017 and the rate of PrEP initiation among the men in our study, who at least at baseline had attended these study sites, increased by more than twenty times in 2017–18 compared with before 2015. The high proportion of men accessing PrEP online despite the PrEP Impact trial opening for enrolment might have been because available places were rapidly filled and recruitment was closed temporarily.[35] As a result, men in

need of PrEP were being turned away and had no choice but to purchase it via the internet (Clarke A and Nwokolo N, unpublished). Substantial advocacy efforts from community-based organisations have also contributed to some men accessing PrEP online.

In our analysis, older age was independently associated with being more likely to initiate PrEP, with the rate of initiation among men aged 40 years and older being four times higher than among those younger than 25 years. This finding was similar to that in a cohort in Amsterdam in which the median age among men initiating PrEP was 40 years,[14] and a cohort in Australia in which rates of PrEP initiation were highest among men aged 40 years and older.[15] We also found that indicators of socioeconomic disadvantage (eg, not being employed, having unstable housing status, and having less or no money for basic needs), were associated with a reduced rate of initiating PrEP or being on PrEP. Previous research in the UK has shown that lower socioeconomic situation is associated with worse HIV treatment outcomes among individuals living with HIV.[16] Efforts need to be made to ensure that socioeconomically disadvantaged individuals have equitable access to all effective HIV prevention strategies, including PrEP.

High-risk sexual behaviours such as condomless sex, condomless sex with two or more partners, group sex, and using non-injection chemsex-related drugs were also associated with PrEP use, indicating appropriate use of PrEP by these men. Similar to our findings, a recent national online prospective study in Australia reported that younger age, less use of illicit party or sex drugs, and lower engagement in HIV sexual risk behaviours such as group sex or any condomless sex, were independently associated with non-uptake of PrEP.[15] The study also reported an increase in the uptake of PrEP from baseline (2014–15) to 24 months of follow-up.

Qualitative data from the PROUD study[17] showed that MSM who were already having frequent condomless sex added PrEP as a prevention tool. MSM with a high risk of contracting HIV through condomless sex should be offered PrEP as a matter of urgency. In our study, more than 22% of respondents in 2018 were not using PrEP when having condomless sex with multiple partners and so were still at risk. These data would support the national roll-out of PrEP in England.

We did not find an association between STI diagnoses and taking PrEP, except among men who reported past 12-month non-prescribed PrEP use. A 2019 meta-analysis of 20 PrEP studies and trials among MSM found high incidences of STIs among MSM taking PrEP, ranging from 33·0 per 100 person-years to 99·8 per 100 person-years.[18] However, whether PrEP use leads to increased rates of STIs remains unknown. The meta-analysis generated estimates of STI incidence among MSM who engaged in high-risk sexual behaviours, rather than comparing the rates among MSM taking PrEP versus not taking PrEP. The PROUD study found extremely high levels of STI diagnoses, but detected no difference in the occurrence of STIs between the immediate and deferred PrEP groups;[1] while, the PrEPX study in Australia found the incidence of STIs increased during PrEP use, but that this finding was partly explained by increased testing frequency.[19] Additionally, in the PrEPX study, half of the participants were not diagnosed with an STI during follow-up and STIs were highly concentrated among PrEP users with repeat STIs, and associated with number of partners and group sex. Regular STI testing should continue alongside PrEP use to ensure patients' good sexual health.

Although in our study we found no significant association between anxiety or depression and reporting recent PrEP use or PrEP, in a 2020 Australian study, PrEP use was independently associated with lower levels of HIV-related anxiety among PrEP-eligible men (MSM at high risk of HIV infection) than among PrEP ineligible men (MSM at low risk).[20]

Alongside the increase in PrEP use, we found a substantial decreasing trend in PEP use between 2013 and 2018, and that the use of PEP was a predictor of future PrEP initiation. This finding suggests that transition from PEP use to PrEP use occurred in these men. Guidelines recommend transitioning MSM who are at continuous risk of HIV from use of PEP towards use of PrEP.[21] PrEP taken daily or on-demand before possible exposure is a highly effective strategy for reducing the risk of HIV acquisition among MSM who are at high and ongoing risk of infection.[22] PEP, on the other hand, is a short-term treatment and is to be used in emergency circumstances after recent HIV exposure (within 72 h).[22] Both PrEP and PEP should be a part of combination HIV prevention strategy.

Our study has some limitations. Men in this cohort were recruited from three sexual health clinics where the PROUD study was run and might have been better informed about PrEP than the general MSM population in England. Therefore, prevalence of PrEP and PEP use in this study might overestimate use in the MSM population nationwide. Men in this cohort were recruited from three sexual health clinics in urban areas in southeast England, and so the sample size was relatively small and these men might not be representative of the broader MSM population in England and the UK. Trends in use and predictors of PrEP initiation might also differ among MSM who are not engaged with sexual health clinics. Additionally, the sample comprised predominantly men who were highly educated, employed, in a stable economic situation, of white ethnicity, and with access to the internet (follow-up questionnaires were only available online, therefore to complete the questionnaires participants needed an internet connection), which might not allow generalisability to all MSM living in England. However, the Australian prospective cohort study that used a more diverse sample of MSM reached similar findings as were observed in our study.[15] Further research is needed to

For more on **PrEP in Scotland** see https://prep.scot/

For more on **PrEP in Wales** see https://www.friskywales.org/wales-prep-project.html

For more on **PrEP in Northern Ireland** see https://www.sexualhealthni.info/pre-exposure-prophylaxis-prep-hiv

For more on **buying PrEP online safely** see https://prepster.info/buying-prep-online/

investigate PrEP use among MSM who are more socioeconomically disadvantaged in England and the UK. Recall bias and social desirability bias might be evident in these self-reported data; however, the study collected sensitive and personal data through an online follow-up questionnaire, which might have reduced such bias.[23] Finally, the online retention of participants who initially registered in the study was lower than we hoped; however, more than 60% of participants who completed at least one online questionnaire (n=622) were followed-up until the end of the study (n=400).[24]

In summary, this study provides important data for PrEP implementation in England. PrEP use has increased substantially over the past 5 years, with a high proportion of PrEP being obtained via the internet. Our data suggest that men engaging in sexual behaviour related to high HIV risk, who are older, and those of higher socioeconomic status are significantly more likely to use PrEP. A fully commissioned programme for PrEP in England has been agreed; however, implementation has been delayed (Rodger AJ, unpublished). Due to the COVID-19 pandemic, the programme might not be fully operational across England by the end of the PrEP Impact trial in October, 2020. To transition participants of the PrEP Impact trial onto the nationally commissioned programme, an interim supply of PrEP will be made available by the trial for participants with an ongoing need for PrEP and who attend services where the national programme has not yet commenced. The results of our study can inform the implementation of the national programme by highlighted patient groups who might be at increased risk of HIV infection but less likely to be aware of or using PrEP and who could benefit most from public health outreach and advice. Improving access to PrEP via routine commissioning by NHS England could increase PrEP use among all eligible MSM and reduce socioeconomic disparities, if it is accompanied by an understanding of these disparities and tailoring of public health message and services to address them.

Contributors

AJR, ANP, FCL, JS, AS, NN, DA, RG, and AC conceived, designed, and managed the data collection in the AURAH2 study. NH, VC, JS, and ARM conducted data cleaning and variable derivation. SC contributed to the conception of the analysis, interpretation of data, and final approval of the manuscript. NH did all analyses and drafted the manuscript. All authors contributed to the conception of this analysis and participated in interpretation of data, revising, and final approval of the manuscript.

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Declaration of interests

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Data sharing

Any personally identifiable data cannot be made publicly available to protect participants privacy. All other relevant data are available upon request to the corresponding author.

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Use of HIV Pre-Exposure Prophylaxis among Gay, Bisexual, and Other Men Who Have Sex with Men in England: Data from the AURAH2 Prospective Study

N Hanum[1], V Cambiano[1], J Sewell[1], A Phillips[1], A Rodger[1], A Speakman[1], N Nwokolo[2], D Asboe[2], R Gilson[1,3], A Clarke[4], A Miltz[1], S Collins[5], and , F Lampe[1] for the AURAH2 Study Group

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Background

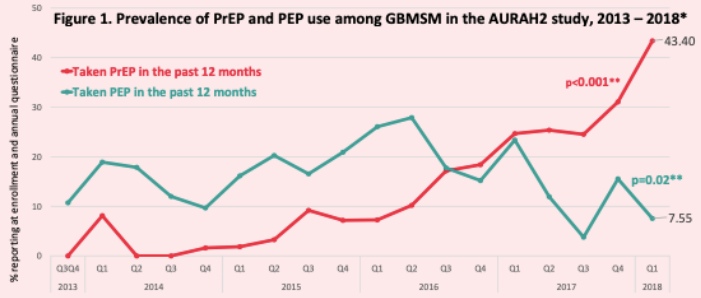
- A fully commissioned pre-exposure prophylaxis (PrEP) programme in England through the National Health Service (NHS) England has just been agreed in 2020. Before this, PrEP was only available through the PrEP Impact Trial (Public Health England) since October 2017, or by online purchasing.
- There is little information on trends in PrEP uptake and predictors of PrEP initiation among gay, bisexual, and other men who have sex with men (GBMSM) in England.
- We report changes from 2013 to 2018 in PrEP and post-exposure prophylaxis (PEP) use among HIV-negative GBMSM in AURAH2, a prospective cohort study, and assess predictors of PrEP initiation.

Methods

- The AURAH2 prospective study recruited 1167 HIV negative GBMSM from three large sexual health clinics in London and Brighton from June 2013 – April 2016 (table 1).
- Participants self-completed a baseline paper questionnaire at clinics and subsequent four-monthly and annual online questionnaires up to March 2018, including information on socio-demographics, HIV status, sexual behaviours, and PrEP and PEP use.
- We utilized GEE logistic models to examine longitudinal changes in past PrEP and PEP use (figure 1) and PrEP use among men who reported condomless sex (CLS) with ≥2 partners (figure 2).
- We used age-adjusted Poisson models to assess factors associated with PrEP initiation among men who reported never having used PrEP at baseline (table 2).
- We used data from annual follow-up questionnaires to describe the source for obtaining PrEP (figure 3).

Results

Figure 1. Prevalence of PrEP and PEP use among GBMSM in the AURAH2 study, 2013 – 2018*



*N=1166 participants provided 2084 baseline and annual questionnaires, one questionnaire was excluded due to missing data on year of enrolment
** p-value from GEE logistic model

- From Jul-Dec 2013 to Jan-Mar 2018, PrEP use in the past year increased overall (from 0% to 43·4 %).
- PEP use peaked in April-Jun 2016, but declined after 2016.

1167 men were enrolled in the study and included in the analysis.

Table 1. Baseline characteristics of participants (N=1167)

Mean age, years (SD)	34 (10.4)
Born in the UK and White ethnicity	49.4%
Gay	93.6%
University education	73.9%
Employed	90.9%
Money all the time to cover basic needs	77.4%
CLS with ≥2 partners	37%
Used PrEP	5%

- The prevalence of CLS with ≥2 partners increased from 46·4% in Jul-Dec 2013 to 50·9% in Jan-March 2018.
- The corresponding increase in PrEP use among men who reported CLS with ≥2 partners was from 0% to 78%.

Figure 2. Prevalence of PrEP use among men who reported CLS ≥2 partners

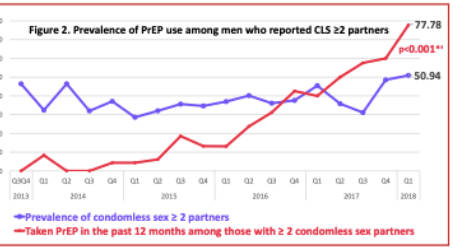
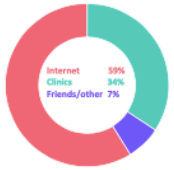


Figure 3. PrEP Source
(n=190 annual questionnaires)



About half of PrEP was obtained by purchasing online.

Table 2. Predictors of initiating PrEP

	Age-adjusted IRR (95% CI)	p-value
Age category (ref: <25)		
25 – 29	1.76 (0.47 – 6.56)	0.001
30 – 34	2.41 (0.69 – 8.45)	
35 – 39	1.92 (0.49 – 7.58)	
40 – 44	4.25 (1.14 – 15.79)	
>45	3.59 (1.07 – 11.97)	
Employed	2.84 (1.09 – 7.39)	0.032
Unstable housing vs. home owner	0.13 (0.02 – 0.95)	0.044
Recent HIV test	5.17 (1.89 – 14.08)	0.001
CLS in the past 3 month	5.01 (2.16 – 11.63)	<0.001
CLS with ≥2 partners	5.43 (2.99 – 9.86)	<0.001
Group sex in the past 3 months	1.69 (1.01 – 2.84)	0.045
PEP use in the previous 12 months	4.69 (2.83 – 7.79)	<0.001
Recreational drug use and chemsex	2.05 (1.21 – 3.47)	0.007
Calendar year category (ref: 2013 – 2015)		
2016	6.69 (3.28 – 13.68)	<0.001
2017 – 2018	21.19 (9.48 – 47.35)	<0.001

- Among men who had never used PrEP at baseline (n=460 men, 825 observations), predictors of initiating PrEP included: age ≥40 years; recent HIV test; CLS in previous 3 months; CLS with ≥2 partners; group sex; recreational drugs/chemsex use; PEP use; and calendar year.
- Non-employment and unstable housing were associated with lower rate of PrEP initiation.

Limitations

- Trends in use may differ among GBMSM who are not engaged with sexual health clinics.
- Prevalence of PrEP and PEP use may overestimate the use in the general UK GBMSM population, because men in this cohort were recruited from clinics where the PROUD study was conducted (Mc.Cormack et al., 2016).
- The sample characteristics may not allow generalisability to all GBMSM living in the UK.
- Self-report data may be subject to recall bias and social desirability bias.

Conclusions

- PrEP use increased significantly over time among a prospective cohort of GBMSM in England.
- Men who have high-risk HIV related sexual behaviour, older men, and men with better socioeconomic resources were significantly more likely to use PrEP.
- Improving access to PrEP by routine commissioning by NHS England could increase PrEP use among all eligible GBMSM and reduce socioeconomic disparities.

FUNDED BY NIHR | National Institute for Health Research

The AURAH2 study is funded by the National Institute for Health Research (NIHR under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-1212-20006). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Appendix 21. The AURAH2 study BHIVA 2020 Oral Presentation

UCL

Use of HIV pre-exposure prophylaxis among men who have sex with men in England: data from the AURAH2 prospective study

Nadia Hanum, Valentina Cambiano, Janey Sewell, Andrew N Phillips, Alison J Rodger, Andrew Speakman, Nneka Nwokolo, David Asboe, Richard Gilson, Amanda Clarke, Ada R Miltz, Simon Collins, and Fiona C Lampe, for the AURAH2 Study Group

aurah2

Background

2015

- PROUD study reported the efficacy of daily oral PrEP at 86%[1]
- PrEP available via the internet

2017

- Introduction of a PrEP programme for MSM in the UK is cost-effective and possibly cost-saving in the long term[2]
- PrEP Impact trial launched across England in October[3]

2018 – now

- BHIVA/BASHH PrEP guidelines: PrEP should be offered to HIV negative MSM at elevated risk[4]
- All PrEP impact trial participants will get National Health Service (NHS) England funded PrEP until 2020
- A nationally commissioned PrEP programme for England has been agreed

[1] McCormack et al., 2016; [2] Cambiano et al., 2017; [3] NHS England / PHE, 2017; [4] Brady et al., 2018

Background

- Combining PrEP scale-up with rapid ART initiation and a large increase in HIV testing volumes in London has led to steep falls in new infections largely in MSM[5]
- Similar decreases in HIV diagnoses among MSM in San Francisco,[6] New York City,[7] and New South Wales[8]
- Little information on past trends in PrEP uptake and predictors of PrEP initiation in England

[5] Nwokolo et al., 2017; [6] Scheer at al., 2018; [7] NYC Dept. of Health and Mental Hygiene, 2018; [8] The NSW HIV Strategy 2016 – 2020, 2018

Objectives

Among MSM participating in the AURAH2 study between 2013 – 2018:

- To provide longitudinal assessments of changes in use of PrEP and PEP;
- To assess the extent to which demographic, socio-economic, health and lifestyle factors are predictive of PrEP initiation;
- To determine factors associated with reporting the recent use of PrEP

Study design and participants

Prospective cohort study, three sexual health clinics in London and Brighton
Participants inclusion: HIV-negative gay, bisexual and other MSM, ≥18 years

aurah2

"Attitudes to and Understanding of Risk of Acquisition of HIV over time"

UCL | FUNDED BY NIHR | National Institute for Health Research

Mortimer Market Centre | Brighton & Hove Sexual Health & Contraception Service

The AURAH2 study is funded by the National Institute for Health Research (NIHR under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-1212-20006). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Period of study and data collection

Recruitment
July 30, 2013 – April 2016

Baseline paper questionnaire
- demographic
- socioeconomic
- general health and wellbeing
- knowledge and understanding of HIV
- sexual behavior, health and lifestyle
- PrEP and PEP

Online follow-up
March 2015 – March 2018

4-monthly questionnaire
- HIV status
- HIV testing
- sexual behaviour
- health and lifestyle

Annual questionnaire
PrEP and PEP

Analyses

- **Longitudinal changes in past 12-month PrEP and PEP use over time:**
  Generalized Estimation Equation (GEE) models with a logit link and robust standard errors
- **The rate of PrEP initiation and associated factors:**
  - Age-adjusted Poisson models with robust standard errors
  - PrEP initiation: the first report of PrEP in past 12 months from an annual questionnaire, following a No-PrEP use report at baseline
  - Time to initiation: the time from baseline to the date of completion of the questionnaire in which PrEP was first reported, or from baseline to the end of follow-up if PrEP was not initiated
- **Factors associated with being on PrEP (in the previous 12 months):**
  GEE models with a logit link function, adjusted for age

Study participants

1162 completed baseline questionnaire

622 subsequently completed at least an online follow-up questionnaire

483 completed at least one online annual questionnaire

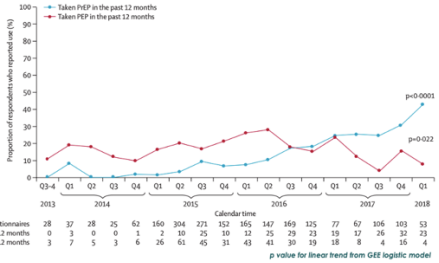
400 followed to end of study (March 2018)

Baseline socio-demographic characteristics of participants

	Completing baseline paper questionnaire on clinic (N=1162)	Completing at least one online follow-up questionnaire (N=622)	Completing at least one annual online questionnaire (N=483)
Mean age, years (SD) Median age, years (IQR)	34 (10.4) 31 (26 – 39)	34 (11.3) 33 (26 – 41)	35 (11.2) 33 (26 – 42)
Born in the UK and White ethnicity	49.4%	51.9%	54.7%
Gay	93.6%	94.5%	94.8%
University education	73.9%	76.1%	75.6%
Employed	90.9%	88.5%	89.2%
Money all the time to cover basic needs	77.4%	82.4%	84.0%
Housing status: Home owner Renting Unstable / other	 27.4% 59.3% 13.3%	 33.0% 54.0% 12.9%	 35.4% 52.6% 12.0%

Median number online questionnaire completed (IQR)	6 (3-7)
Total online follow-up questionnaire completed	3277

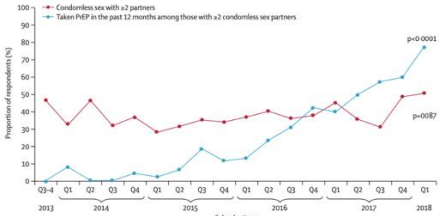
Prevalence of PrEP and PEP use in the past 12 months over time, 2013 – 2018



	Q3-4 2013	Q1	Q2	Q3	Q4	Q1 2014	Q2	Q3	Q4	Q1 2015	Q2	Q3	Q4	Q1 2016	Q2	Q3	Q4	Q1 2017	Q2	Q3	Q4	Q1 2018
Number of questionnaires	28	37	28	25	62	160	304	271	152	165	147	169	125	77	67	106	103	53				
Taken PrEP in the past 12 months	0	3	0	0	1	2	10	25	10	12	25	29	23	19	17	26	32	23				
Taken PEP in the past 12 months	3	7	5	3	6	26	61	45	31	43	41	30	19	18	8	4	16	4				

p value for linear trend from GEE logistic model

Prevalence of condomless sex with two or more partners and prevalence of PrEP use among these men, 2013 – 2018

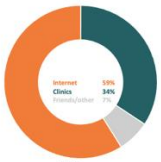


Number of questionnaires reporting condomless sex with ≥2 partners	13	12	13	8	23	45	96	96	52	61	59	61	47	35	24	33	50	27
Taken PrEP in the past 12 months and condomless sex with ≥2 partners	0	1	0	0	1	1	6	18	6	8	14	19	20	14	12	19	30	21

p value for linear trend from GEE logistic model

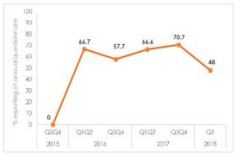
PrEP source

About half of PrEP was obtained by online purchasing



PrEP source
(n=190 annual questionnaires)

Prevalence of sourcing PrEP from internet over time



Longitudinal analysis of factors associated with initiating PrEP

	Predictors of initiating PrEP (N=460 participants, 875 questionnaires)	
	Age-adjusted IRR (95% CI)	p-value
Age category (ref: <25)		0.005
25-29	1.76 (0.47 – 6.56)	
30-34	2.42 (0.69 – 8.45)	
35-39	1.92 (0.49 – 7.58)	
40-44	4.25 (1.14 – 15.79)	
≥45	3.59 (1.07 – 11.97)	
Not employed	0.35 (0.14 – 0.91)	0.032
Unstable housing vs. home owner	0.13 (0.02 – 0.95)	0.025
Recent HIV test	5.17 (1.89 – 14.08)	0.001
CLS in the past 3 month	5.01 (2.16 – 11.63)	<0.001
CLS with ≥2 partners	5.43 (2.99 – 9.86)	<0.001
Group sex in the past 3 months	1.69 (1.01 – 2.84)	0.045
PEP use in the previous 12 months	4.69 (2.83 – 7.79)	<0.001
Use of ≥1 chemsex-related drug	2.86 (1.67 – 4.91)	0.002
Calendar year category		
2016 (ref: 2013 – 2015)	6.69 (3.28 – 13.68)	<0.001
2017 – 2018	21.19 (9.48 – 47.35)	

Longitudinal analysis of factors associated with initiating PrEP vs. Cross-sectional analysis of factors associated with being on PrEP

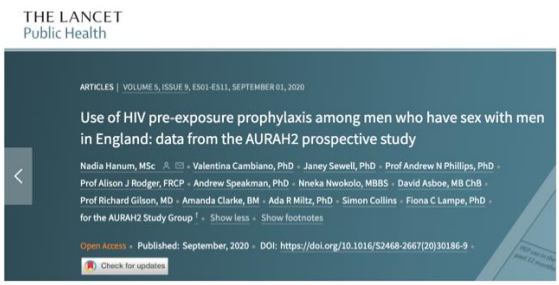
	Predictors of initiating PrEP (N=460 participants, 875 questionnaires)		Factors associated with being on PrEP (N=1162 participants, 2080 questionnaires)	
	Age-adjusted IRR (95% CI)	p-value	Age-adjusted OR (95% CI)	p-value
Age category (ref: <25)		0.005		<0.0001
25-29	1.76 (0.47 – 6.56)		1.13 (0.40 – 3.67)	
30-34	2.41 (0.69 – 8.45)		2.84 (1.43 – 5.49)	
35-39	1.92 (0.49 – 7.58)		3.12 (1.47 – 6.29)	
40-44	4.25 (1.14 – 15.79)		3.89 (1.80 – 8.36)	
≥45	3.59 (1.07 – 11.97)		3.54 (1.77 – 7.09)	
Not employed	0.35 (0.14 – 0.91)	0.032	0.58 (0.32 – 1.06)	0.078
Unstable housing vs. home owner	0.13 (0.02 – 0.95)	0.044	0.34 (0.18 – 0.73)	0.003
Money to cover basic needs				
Most of the time (ref: all of the time)	1.03 (0.45 – 2.37)	0.070	0.83 (0.51 – 1.31)	0.120
Sometimes / No	0.57 (0.08 – 3.86)		0.52 (0.21 – 1.29)	0.037 (p trend)
Recent HIV test	5.17 (1.89 – 14.08)	0.001	2.73 (1.93 – 3.87)	<0.001
CLS in the past 3 month	5.01 (2.16 – 11.63)	<0.001	4.57 (2.91 – 7.17)	<0.001
CLS with ≥2 partners	5.43 (2.99 – 9.86)	<0.001	5.64 (3.97 – 8.01)	<0.001
Group sex in the past 3 months	1.69 (1.01 – 2.84)	0.045	1.77 (1.26 – 2.47)	0.001
PEP use in the previous 12 months	4.69 (2.83 – 7.79)	<0.001	1.78 (1.17 – 2.71)	0.007
Use of ≥1 chemsex-related drug	2.05 (1.21 – 3.47)	0.007	2.70 (1.91 – 3.81)	<0.001
Calendar year category				
2016 (ref: 2013 – 2015)	6.69 (3.28 – 13.68)	<0.001	2.80 (2.04 – 3.84)	<0.001
2017 – 2018	21.19 (9.48 – 47.35)	<0.001	7.44 (5.39 – 10.26)	<0.001

Limitations

- The sample characteristics may not allow generalisability to all MSM living in England and in the UK
- Trends in use and predictors of PrEP initiation might differ among MSM who are not engaged with sexual health clinics
- Self-report data may be subject to recall bias and social desirability bias
- The online retention was lower than we hoped

Conclusions

- Use of PrEP increased substantially from 2013 to 2018 among MSM attending sexual health clinics in London and Brighton
- A substantial proportion of men accessing PrEP obtained it via the internet
- By 2018, PrEP use was almost 80% among men with multiple condomless sex partners
- Men engaging in sexual behaviour related to high HIV risk, who are older, and those of higher economic status are significantly more likely to use PrEP
- Improving access to PrEP via routine commissioning by NHS England could increase PrEP use among all eligible MSM and reduce socioeconomic disparities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Use of HIV pre-exposure prophylaxis among men who have sex with men in England: data from the AURAH2 prospective study

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Thank you!

Appendix 22. The AURAH2 study results paper "Trends in HIV incidence between 2013 – 2019 and association of baseline factors with subsequent incident HIV among gay, bisexual, and other men who have sex with men attending sexual health clinics in England: A prospective cohort study

PLOS MEDICINE

RESEARCH ARTICLE

Trends in HIV incidence between 2013–2019 and association of baseline factors with subsequent incident HIV among gay, bisexual, and other men who have sex with men attending sexual health clinics in England: A prospective cohort study

Nadia Hanum[1]*, Valentina Cambiano[1], Janey Sewell[1], Alison J. Rodger[1], Nneka Nwokolo[2], David Asboe[2], Richard Gilson[1,3], Amanda Clarke[4], Ada R. Miltz[1], Simon Collins[5], Valerie Delpech[6], Sara Croxford[6], Andrew N. Phillips[1], Fiona C. Lampe[1], for the AURAH2 Study Group[¶]

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¶ Membership of the AURAH2 Study Group is provided in the Acknowledgements.
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Abstract

Background

Prospective cohort studies of incident HIV and associated factors among gay, bisexual, and other men who have sex with men (GBMSM) in the United Kingdom are lacking. We report time trends in and factors associated with HIV incidence between 2013 and 2019 among a cohort of GBMSM: the AURAH2 prospective study.

Methods and findings

Participants were recruited through 1 of 3 sexual health clinics in London and Brighton (July 2013 to April 2016) and self-completed a baseline paper questionnaire and subsequent 4-monthly and annual online questionnaires (March 2015 to March 2018), including information on sociodemographics, lifestyle, health and well-being, HIV status, sexual/HIV-related behaviours, and preexposure prophylaxis and postexposure prophylaxis (PrEP/PEP). Incident HIV was ascertained by linkage with national HIV surveillance data from Public Health England (PHE). We investigated the associations of HIV incidence with (1) baseline factors using mixed-effects Weibull proportional hazard models, unadjusted and adjusted for age, country of birth and ethnicity, sexuality, and education level; and (2) time-updated factors, using mixed-effects Poisson regression models.

In total, 1,162 men (mean age 34 years, 82% white, 94% gay, 74% university-educated) were enrolled in the study. Thirty-three HIV seroconversions occurred over 4,618.9 person-

Data Availability Statement: Any personally identifiable data cannot be made publicly available, because this study was conducted with approval from The National Research Ethics Service (NRES) committee, which requires that to protect participants' privacy data from the studies are released only after they have provided written approval. A de-identified dataset sufficient to reproduce the study findings will be made available upon written request after approval from NRES committee. To request these data, please contact: nres.queries@nhs.net or through www.nres.nhs/contacts/nres-committe-directory/.

Funding: The AURAH2 study was funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (RP-PG-1212-20006). URL funder: https://www.nihr.ac.uk/. AJR holds the grant from the National Institute for Health Research. NH receives funding from the Indonesian Endowment Fund for Education (LPDP Indonesia Scholarship) during the conduct of the study. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: I have read the journal's policy and the authors of this manuscript have the following competing interests: AC reports personal fees from Gilead Sciences for advisory board attendance & conference sponsorship, personal fees from ViiV for advisory board attendance, outside the submitted work. FCL reports grants from National Institute for Health Research (NIHR) during the conduct of the study. NN has been a full-time employee of ViiV Healthcare since March 2019 and reports personal fees, and support for conference attendance from ViiV Healthcare, and Gilead Sciences outside the submitted work. All other authors have declared that no competing interests exist.

Abbreviations: ART, antiretroviral therapy; AURAH2, The Attitudes to and Understanding of Risk of Acquisition of HIV 2; CI, confidence interval; CLS, condomless anal sex; GAD-7, Generalised Anxiety Disorder-7; GBMSM, gay, bisexual, and other men who have sex with men; GEE, generalised estimation equation; GP, general practitioner; GUM, genitourinary medicine; HR, hazard ratio; IQR, interquartile range; IR, incidence rate; IRR, incidence rate ratio; LGV, lymphogranuloma venereum; NHS, National Health Service; NRES, National Research Ethics Service; PEP, postexposure prophylaxis; PHE, Public Health England; PHQ-9, Patient Health Questionnaire; PrEP, preexposure prophylaxis; PY, person-years; SD, standard deviation; STI, sexually transmitted

years (PY) of follow-up: an overall HIV incidence rate (IR) of 0.71 (95% confidence interval (CI) 0.51 to 1.00) per 100 PY. Incidence declined from 1.47 (95% CI 0.48 to 4.57) per 100 PY in 2013/2014 to 0.25 (95% CI 0.08 to 0.78) per 100 PY in 2018/2019; average annual decline was 0.85-fold ($p < 0.001$). Baseline factors associated with HIV acquisition included the following: injection drug use (6/38 men who reported injection drug-acquired HIV; unadjusted conditional hazard ratio (HR) 27.96, 95% CI 6.99 to 111.85, $p < 0.001$), noninjection chemsex-related drug use (13/321; HR 6.45, 95% CI 1.84 to 22.64, $p < 0.001$), condomless anal sex (CLS) (26/741; HR 3.75, 95% CI 1.31 to 10-74, $p = 0.014$); higher number of CLS partners (HRs >10 partners [7/57]; 5 to 10 partners [5/60]; and 2 to 4 partners [11/293]: 14.04, 95% CI 4.11 to 47.98; 9.60, 95% CI 2.58 to 35.76; and 4.05, 95% CI 1.29 to 12.72, respectively, $p < 0.001$); CLS with HIV–positive partners (14/147; HR 6.45, 95% CI 3.15 to 13.22, $p < 0.001$), versatile CLS role (21/362; HR 6.35, 95% CI 2.18 to 18.51, $p < 0.001$), group sex (64/500; HR 8.81, 95% CI 3.07 to 25.24, $p < 0.001$), sex for drugs/money (4/55, HR 3.27, 95% CI 1.14 to 9.38, $p = 0.027$) (all in previous 3 months); previous 12-month report of a bacterial sexually transmitted infection (STI) diagnoses (21/440; HR 3.95, 95% CI 1.81 to 8.63, $p < 0.001$), and more than 10 new sexual partners (21/471, HRs 11 to 49, 50 to 99, and >100 new partners: 3.17, 95% CI 1.39 to 7.26; 4.40, 95% CI 1.35 to 14.29; and 4.84, 95% CI 1.05 to 22.4, respectively, $p < 0.001$). Results were broadly consistent for time-updated analysis ($n = 622$ men). The study's main limitation is that men may not be representative of the broader GBMSM population in England.

Conclusions

We observed a substantial decline in HIV incidence from 2013 to 2019 among GBMSM attending sexual health clinics. Injection drug use, chemsex use, and measures of high-risk sexual behaviour were strongly associated with incident HIV. Progress towards zero new infections could be achieved if combination HIV prevention including Test and Treat strategies and routine commissioning of a PrEP programme continues across the UK and reaches all at-risk populations.

Author summary

Why was the study done?

- A decline has been observed in new HIV diagnoses among gay, bisexual, and other men who have sex with men (GBMSM) in the United Kingdom.
- Internationally, an overall decline in HIV diagnoses and incidence among GBMSM has also been reported in several cities in developed countries such as Australia, the United States, the Netherlands, and some other European countries between 2013 and 2019.
- To our knowledge, no prospectively followed cohort studies of GBMSM in England have reported trends in HIV incidence in recent years or on factors associated with incident HIV.

infection; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

What did the researches do and find?

- We estimated trends in HIV incidence between 2013 and 2019 among a cohort of GBMSM attending sexual health clinics, and we found a declining trend.
- We also assessed factors associated with HIV incidence, and our findings emphasise the importance of awareness of high-risk sexual behaviours and recreational drug use (particularly injection drug use and chemsex-associated drug use) as factors associated with HIV acquisition.
- Despite observing significant declines in HIV incidence, incidence rates (IRs) remained high among men who reported injection drugs use, chemsex drug use, condomless sex with multiple partners, and group sex.

What do these findings mean?

- Growing evidence shows that the HIV transmission declines may potentially be attributed to the comprehensive control and HIV treatment efforts in the UK.
- The continuation of intensification of HIV testing, immediate antiretroviral therapy (ART) initiation, the use of condoms, and routine commissioning of a preexposure prophylaxis (PrEP) programme could potentially ensure that the decline in HIV incidence is felt across all groups impacted by the epidemic.

Introduction

To bring the HIV epidemic under control, there has been a massive scale-up in the treatment and prevention of HIV over the past decade that has led to a gradual decline in new HIV infections globally [1]. In the United Kingdom (UK), modelling of HIV surveillance data suggests that the underlying incidence of new HIV infections has been falling steadily for more than 5 years (since 2012) [2]. The decline has been particularly marked among gay, bisexual, and other men who have sex with men (GBMSM), among whom 51% of all new HIV diagnoses occurred in the UK in 2018 [3]. In England, the modelled number of incident infections among GBMSM has declined by 65% since 2014, with the most rapid fall after 2016 [3]. The steep declines coincide with a period when increasing numbers of men accessed preexposure prophylaxis (PrEP) [4]. In addition, during this period, there were efforts to increase uptake and frequency of HIV testing, and HIV treatment guidelines changed to recommend prompt initiation of antiretroviral therapy (ART) for people newly diagnosed with HIV. Declines in new HIV diagnoses among GBMSM have also been reported in New South Wales in Australia [5] and San Francisco and New York City in the United States [6,7].

There remains, however, limited data from UK prospective studies assessing HIV acquisition risk, associated factors, and temporal trends for incident HIV [8,9]. Such data could be helpful in providing insight regarding the risk factors driving the HIV epidemic among GBMSM in England. The Attitudes to and Understanding of Risk of Acquisition of HIV 2 (AURAH2) study is among the first prospective observational cohort studies of initially HIV–negative GBMSM in England. We sought to evaluate trends in HIV incidence between 2013 and 2019 and the association of baseline and time-updated demographic, socioeconomic,

health, lifestyle, and behavioural factors with HIV incidence among GBMSM participating in AURAH2.

Methods

Study design and participants

Methodological details of the study have been published previously [10]. The AURAH2 study was a prospective cohort study that recruited GBMSM who were HIV negative or of unknown HIV status from 3 large sexual health clinics in London and Brighton (56 Dean Street, London; Mortimer Market Centre, London; and Claude Nicol Clinic, Brighton) from July 2013 to April 2016. Participants were eligible if they were aged 18 years or older and had attended the study clinics for routine testing for sexually transmitted infections (STIs) or HIV. Men were classified as GBMSM for the purposes of the analysis if they met at least one of the following criteria: (i) reported being gay or bisexual; (ii) reported anal sex with a man in the past 3 months; or (iii) reported having disclosed to their family, friends, or workmates as being gay, bisexual, and/or attracted to men. Participants who consented to the study completed a confidential baseline paper questionnaire in the clinic. During the follow-up period, participants self-completed subsequent 4-monthly and annual questionnaires that were available online from March 2015 until March 2018. The baseline questionnaire gathered information on demographic, socioeconomic, lifestyle, health and well-being–related factors, knowledge and understanding of HIV, sexual behaviours, STI diagnoses, and PrEP and postexposure prophylaxis (PEP) use. The 4-monthly questionnaires assessed information on HIV status, HIV testing history, sexual behaviours, and lifestyle factors. Annual questionnaires captured the same information as the 4-monthly questionnaire and additional information on PrEP and PEP use in the past year, relationship status, and health and well-being factors as assessed on the baseline questionnaire. This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline (**S1 Checklist**).

Ethics approval and participant consent

All participants provided written, informed consent before taking part. Consent to participate in the study included consent for linkage to Public Health England (PHE)'s datasets at the end of the study using limited participant identifiers. The AURAH2 study was approved by the designated research ethics committee, The National Research Ethics Service (NRES) committee London-Hampstead, ref: 14/LO/1881 in November 2014 [10]. Based on the research protocol and all versions of study documents, the AURAH2 study subsequently received permission for clinical research at the 3 participating National Health Service (NHS) sites: Chelsea and Westminster NHS Foundation Trust, Central and North West London NHS Foundation Trust, and the Brighton and Sussex University Hospitals NHS Trust. The AURAH2 study was registered on the NIHR clinical research network portfolio.

Completion of online follow-up questionnaires

Participants who completed a first online follow-up questionnaire in March 2015 had the option to complete up to 9 online questionnaires, as the follow-up finished in March 2018. When participants were due to complete a questionnaire, 2 remainder emails were sent after 2 and 4 weeks followed by a text message. If participants missed a questionnaire at any time during follow-up, they were still invited to complete subsequent questionnaires. At each online follow-up, participants were asked about the most recent date of HIV test and the result.

Baseline measures

All baseline measures were self-reported in the participant baseline questionnaire. Sociodemographic variables included age group (<25; 25 to 29; 30 to 34; 35 to 39; 40 to 44; ≥45 years), country of birth and ethnicity (white UK born; other ethnicity UK born; white non-UK born; other ethnicity non-UK born), self-reported sexual identity (gay; bisexual/other plurisexual identities), education (university degree; other qualification; no qualification), ongoing relationship (yes, living with partner; yes, not living with partner; no), employment status (employed; not employed), sufficient money for basic needs (yes; mostly; sometimes or no), and housing status (homeowner; renting including private, housing association, and council; unstable or other).

We considered the following measures of sexual/HIV-related behaviour in the preceding 3 months (classified as "yes" or "no" unless otherwise indicated): condomless anal sex (CLS), number of CLS partners (none; 1; 2 to 4; 5 to 10; >10), CLS with partners known to be HIV positive, sexual CLS role (no CLS; always insertive; always receptive; insertive and receptive [versatile]), group sex, sex for drugs or money, fisting, or sex toys use. We also considered HIV test in the previous 6 months, and bacterial STI diagnosis, number of new sexual partners (0 to 10; 11 to 49; 50 to 99; ≥100), and PrEP and PEP use in the previous 12 months. Bacterial STIs included gonorrhoea, syphilis, and chlamydia, including lymphogranuloma venereum (LGV).

Lifestyle factors included recreational drug use (injection drug use; noninjection use of 1 or more of the 3 chemsex-associated drugs [mephedrone, GHB/GBL, crystal methampethamine]; non-injection use of other drugs; no drug use), smoking status (never smoked; ex-smoker; current smoker) and alcohol consumption (higher-risk alcohol consumption: a score of ≥6 on a modified version the AUDIT-C WHO alcohol screening tool questionnaire, first 2 questions only) [11]. A total score of 6 was chosen given that AURAH2 participants were only asked the first 2 questions of the WHO AUDIT-C questionnaire rather than the full AUDIT-C. Mental health included symptoms of depression (defined as a score of ≥10 on the Patient Health Questionnaire [PHQ-9], which is the standard cutoff score used to define clinically significant depressive symptoms) [12], and anxiety symptoms (defined as a score of ≥10 on the Generalised Anxiety Disorder Scale [GAD-7], which represents the standard cutoff to define anxiety disorder) [13].

For sexual/HIV-related behaviour, mental health, and alcohol consumption measures, missing responses were considered to indicate the absence of the event or condition, because our outcome of interests was "past report of behaviours." Where there was no report of these measures, including missing, we classified answers as "no." For all other variables that were not classified as "yes" or "no," missing values were excluded from the analyses.

Time-updated measures

Age, recent HIV test, CLS, CLS with 2 or more partners, sexual CLS role, group sex, chemsex (a different variable from recreational drug use variable at baseline questionnaire; "have you used drugs before or during sex (chemsex) in the last three months?", classified as "yes" or "no"), and bacterial STI diagnosis were also used as time-varying variables derived from baseline, 4-monthly, and annual questionnaires. Relationship status, PrEP use, PEP use, recreational drug use, injection drug use, depressive symptoms, anxiety symptoms, and alcohol use were time-varying variables derived from baseline and annual questionnaires. All other variables were fixed variables that were only ascertained at baseline.

Ascertainment of incident HIV

There were 2 methods of ascertainment of incident HIV diagnosis during follow-up. First, records of all GBMSM enrolled in the AURAH2 study were linked to national HIV surveillance data by PHE [14,15]. The databases collect information on new HIV diagnoses from

laboratories, genitourinary medicine (GUM) clinics, general practitioners (GPs), and other services where HIV testing takes place in England. The data linkage process was carried out using a deterministic and hierarchical algorithm, based on gender identity, date of birth, year of birth, country of birth, ethnicity, originating clinic, years in the UK, and first initial and Soundex code (a 4-character coding of an adult surname). All data collected as part of the national HIV surveillance programme in the UK is pseudo-anonymised; no names are collected. The data matching process was completed in November 2019. For each study participant that matched to the HIV surveillance dataset, PHE data were provided on date and region of HIV diagnosis, CD4 and viral load at HIV diagnosis, and if relevant, time from diagnosis to linkage to care, time from diagnosis to treatment initiation, and death.

The second method of ascertainment of new HIV diagnoses was through the online follow-up questionnaires; participants were asked about the date and results of most recent HIV test. All the participants who reported being newly diagnosed with HIV in a follow-up questionnaire were also identified as having a new HIV diagnosis in the PHE surveillance databases. Linkage with PHE databases also identified a small number of participants who were positive at entry to the study ($n = 3$); these men were excluded from analysis.

Statistical analysis

For the analyses of HIV incidence and baseline-associated factors, all men enrolled in AURAH2 were included. Incident HIV infection was defined as seroconversion from HIV–negative status at baseline to HIV–positive during follow-up, confirmed by PHE. Person-years (PY) of follow-up were calculated from the date of completing the baseline questionnaire until (1) the date of HIV diagnosis from PHE for men who seroconverted or (2) 3 months before the date of data linkage with PHE datasets was completed (June 30, 2019) for men who did not seroconvert. Due to the linkage with PHE data for ascertainment of the endpoint, all men could be considered as remaining under follow-up over the entire period, even if follow-up questionnaires were not completed.

HIV incidence rates (IRs) were calculated as the number of new HIV infections divided by the number of PY of follow-up, reported with 95% confidence intervals (95% CIs). IRs were calculated per 100 PY, overall and according to calendar year from 2013 until 2019. As the study started on July 30, 2013 and ended on June 30, 2019, the first 2 years (2013 to 2014) and the last 2 years (2018 to 2019) were combined. The associations of baseline factors and current calendar year as a continuous variable with HIV incidence were analysed by calculating HIV IRs and using 2-level random-intercept proportional hazard models with sexual health clinic sites defining the second level to estimate conditional hazard ratios (HRs). The conditional distribution of the response given the random effects was assumed to be a Weibull distribution. HRs with 95% CI are presented unadjusted, and adjusted for sociodemographic factors that were less likely to be influenced by HIV and sexual behaviour: age at baseline, country of birth and ethnicity, sexual identity, and education.

Changes in the annual prevalence of sexual/HIV-related risk behaviours over time were also examined. The prevalence of CLS with 2 or more partners, group sex, bacterial STI, any recreational drug use, injection drug use, noninjection chemsex-related drug use (all in the previous 3 months), and PrEP and PEP use in the previous 12 months was calculated for each year from 2013/14 to 2018/19, using all available baseline and follow-up questionnaires from all participants at each time point. Trends over calendar time during the AURAH2 study period were assessed using univariate generalised estimation equation (GEE) models with a logit link and robust standard errors, accounting for multiple questionnaires responses from individual participants.

We also performed an additional longitudinal analysis among men who completed at least 1 online follow-up questionnaire to examine time-updated factors associated with HIV incidence. We used 2-level random-intercept Poisson regression models, unadjusted and adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and education, using all available baseline and follow-up questionnaires. We present these results as incidence rate ratios (IRRs) with their corresponding 95% CI. In the multivariable analyses, the whole statistical unit for a single individual with missing values was excluded from the analyses if a value for one of the covariates was missing (complete case analysis).

All analyses were planned prior to analysing final datasets from PHE in November 2019 (S1 Analyses Plan), and no data-driven changes took place to these analyses, except that we used mixed-effects modelling instead of Cox proportional hazard modelling (indicated in the analyses plan), in response to peer review comments. The use of hierarchical models was chosen to take into account of clustering according to clinic. All analyses were conducted using Stata statistical software (version 15.1).

Results

Characteristics of the participants

Between July 2013 and April 2016, a total of 1,162 HIV–negative men were enrolled in the study (Table 1). At baseline, the mean age of participants was 34 years (standard deviation [SD]: 10.4; interquartile range [IQR]: 26 to 39), 81.9% were of white ethnicity, 93.6% self-reported being gay, 74.4% had a university degree, 82.9% reported being employed, and 77.4% always had money to cover basic needs. In the previous 3 months, 63.9% reported having had CLS, 35.4% reported CLS with 2 or more partners, 12.7% reported CLS with HIV–positive partners, 43.1% reported group sex, 60.0% reported the use of at least 1 recreational drug, and 3.3% reported injection drug use. The type of drug injected was not ascertained in the baseline questionnaire, but all 38 people who injected drugs reported having taken at least 1 chemsex-related drug in the past 3 months. Overall, 38.0% of men reported having been diagnosed with a bacterial STI in the past year, and 5.0% and 20.7% reported ever having taken PrEP and PEP, respectively, in the past year. Three individuals did not complete the baseline questionnaire. The proportion of missing responses was low (<5% for all variables) (see footnotes in Table 1).

Of the 1,162 men enrolled, all were included in the PHE linkage for ascertainment of new HIV diagnosis. Of the 1,162 men, 622 completed at least 1 online follow-up questionnaire (54%), of whom 483 (78% of 622) completed at least 1 annual follow-up questionnaire, and 400 men (64% of 622) were followed until the end of the study. Men who were older, had greater financial security, with more stable housing, with university level education, and were employed were more likely to continue on the study (622 men versus 540 men who completed only the baseline questionnaire) (S1 Table). The number of follow-up questionnaires (4-monthly and annual) completed by the end of the study period was 3,277. Participants completed a median of 6 (IQR: 3 to 7) online questionnaires.

Trends in HIV incidence

In total, 33 of 1,162 men (2.8%) were newly diagnosed with HIV during the period from the date of completion of their baseline questionnaire until June 2019. Of all 33 diagnoses identified by the PHE linkage, 15 were self-reported by the participant on one of the AURAH2 online follow-up questionnaires. There were no additional unconfirmed self-reported HIV diagnoses. The 3 men who did not complete a baseline questionnaire were included in the incidence analysis as data on their age, HIV status, and PY of follow-up time were available from PHE. There were no deaths recorded among the 33 men diagnosed with HIV.

Table 1. Baseline characteristics and association with incident HIV among 1,162 GBMSM participating in the AURAH2 prospective study, 2013–2019*.

Baseline characteristics	Participants *N* (%)	HIV infections from baseline– 2019 *n* (%)	PY at risk	HIV IR per 100 PY (95% CI)	Unadjusted conditional HR (95% CI)	*p*-value
Demographic characteristics						
Age at baseline category, years						0.421 0.417[t]
<25	275 (23.9)	8 (2.9)	1087.61	0.74 (0.37–1.47)	1 (Ref)	
25–29	207 (17.9)	3 (1.5)	839.50	0.36 (0.11–1.10)	0.49 (0.13–1.85)	
30–34	227 (19.7)	5 (2.2)	896.65	0.56 (0.23–1.34)	0.76 (0.25–2.32)	
35–39	156 (13.5)	8 (5.1)	605.63	1.32 (0.66–2.64)	1.79 (0.67–4.76)	
40–44	121 (10.5)	4 (3.3)	480.92	0.83 (0.31–2.22)	1.13 (0.34–3.77)	
≥45	167 (14.5)	5 (2.9)	674.09	0.74 (0.31–1.78)	1.02 (0.33–3.12)	
Mean age (SD)	**34 (10.4)**					
Median age (IQR)	**31 (26–39)**					
Country of birth and ethnicity[$]						0.176
Born in the UK, white	568 (49.4)	10 (1.8)	2,296.31	0.44 (0.23–0.81)	1 (Ref)	
Born in the UK, other ethnicity	60 (5.2)	1 (1.7)	242.16	0.41 (0.06–2.93)	0.94 (0.12–7.38)	
Non-UK born, white	374 (32.5)	17 (4.5)	1,463.62	1.16 (0.23–1.34)	2.63 (1.21–5.76)	
Non-UK born, other ethnicity	148 (12.9)	2 (1.4)	581.72	0.34 (0.66–2.64)	0.78 (0.17–3.54)	
Sexual identity						0.128
Gay	1,076 (93.6)	26 (2.4)	4,291.83	0.61 (0.41–0.89)	1 (Ref)	
Bisexual/other	74 (6.4)	4 (5.4)	291.26	1.37 (0.52–3.66)	2.26 (0.79–6.49)	
Socioeconomic characteristics and partnership status						
Education						**0.014** **0.013[t]**
University degree	853 (74.4)	17 (1.9)	3,413.05	0.49 (0.31–0.80)	1 (Ref)	
Other qualification	272 (23.8)	11 (4.4)	1,108.62	1.02 (0.56–1.84)	2.01 (0.94–4.28)	
No qualification	21 (1.8)	2 (9.5)	75.83	2.64 (0.66–10.55)	**4.65 (1.07–20.14)**	
Employed[†]						0.074
Yes	952 (82.9)	29 (3.1)	3,767.14	0.77 (0.53–1.10)	1 (Ref)	
No	197 (17.1)	1 (0.5)	812.17	0.12 (0.01–0.87)	0.16 (0.02–1.19)	
Money to cover basic needs						0.627 0.613[t]
All of the time	896 (77.4)	24 (2.7)	3,581.41	0.67 (0.45–1.00)	1 (Ref)	
Most of the time	194 (16.8)	5 (2.6)	768.90	0.65 (0.27–1.56)	0.97 (0.37–2.54)	
Sometimes/No	68 (5.9)	1 (1.5)	264.84	0.38 (0.05–2.68)	0.55 (0.07–4.09)	
Housing status[@]						0.342 0.330[t]
Renting	680 (59.3)	13 (1.9)	2,707.24	0.48 (0.28–8.27)	1 (Ref)	
Home owner	314 (27.4)	14 (4.5)	1,252.75	1.11 (0.66–1.89)	2.34 (1.10–4.97)	
Unstable or other	153 (13.3)	3 (1.9)	611.33	0.49 (0.16–1.52)	1.02 (0.29–3.58)	
Ongoing relationship						0.200 0.191[t]
Yes, living with partner	272 (23.5)	11 (4.0)	1,080.22	1.01 (0.56–1.84)	1 (Ref)	
Yes, not living with partner	193 (16.7)	3 (1.6)	783.15	0.38 (0.12–1.19)	0.38 (0.10–1.35)	
No	693 (59.8)	16 (2.3)	2,755.05	0.58 (0.36–0.95)	0.57 (0.26–1.22)	
Sexual/HIV-related behaviour characteristics						
HIV test in the past 6 months						0.325
No	322 (27.8)	6 (1.9)	1,324.99	0.45 (0.20–1.01)	1 (Ref)	

(*Continued*)

Table 1. (Continued)

Baseline characteristics	Participants *N* (%)	HIV infections from baseline– 2019 *n* (%)	PY at risk	HIV IR per 100 PY (95% CI)	Unadjusted conditional HR (95% CI)	*p*-value
Yes	837 (72.2)	24 (2.9)	3,293.42	0.73 (0.49–1.09)	1.57 (0.64–3.85)	
CLS in the past 3 months‡						**0.014**
No	418 (36.1)	4 (0.9)	1,704.76	0.23 (0.09–0.63)	**1 (Ref)**	
Yes	741 (63.9)	26 (3.5)	2,913.66	0.89 (0.61–1.31)	**3.75 (1.31–10.74)**	
Number of CLS partners in the past 3 months‡						**<0.001 <0.001 [t]**
No CLS partners	424 (36.6)	4 (0.9)	1,727.09	0.23 (0.09–0.62)	1 (Ref)	
One CLS partner	325 (28.0)	3 (0.9)	1,306.35	0.23 (0.07–0.71)	0.98 (0.22–4.40)	
2–4 CLS partners	293 (25.3)	11 (3.8)	1,163.99	0.95 (0.52–1.71)	**4.05 (1.29–12.72)**	
5–10 CLS partners	60 (5.2)	5 (8.3)	212.67	2.36 (0.98–5.64)	**9.60 (2.58–35.76)**	
More than 10 CLS partners	57 (4.9)	7 (12.3)	208.30	3.36 (1.60–7.05)	**14.04 (4.11–47.98)**	
CLS with partners known to be HIV positive in the past 3 months‡						**<0.001**
No	1,012 (87.3)	16 (1.6)	4,086.01	0.39 (0.24–0.64)	**1 (Ref)**	
Yes	147 (12.7)	14 (9.5)	532.41	2.63 (1.56–4.44)	**6.45 (3.15–13.22)**	
Sexual role CLS in the past 3 months						**<0.001**
No CLS/did not state which partner	423 (36.5)	4 (0.9)	1,724.83	0.23 (0.08–0.62)	1 (Ref)	
Always insertive	217 (18.7)	2 (0.9)	877.05	0.22 (0.05–0.91)	0.98 (0.18–5.35)	
Always receptive	157 (13.6)	3 (1.9)	623.35	0.48 (0.15–1.49)	2.06 (0.46–9.19)	
Versatile (sometimes insertive, sometimes receptive)	362 (31.2)	21 (5.8)	1,393.19	1.51 (0.9–2.31)	**6.35 (2.18–18.51)**	
Number of new sexual partners in the past 12 months‾						**0.001 0.001[t]**
0–10 new partners	688 (59.4)	9 (1.3)	2,772.34	0.32 (0.17–0.62)	1 (Ref)	
11–49 new partners	367 (31.6)	15 (4.1)	1,446.30	1.04 (0.63–1.72)	**3.17 (1.39–7.26)**	
50–99 new partners	72 (6.2)	4 (5.6)	272.66	1.47 (0.55–3.91)	**4.40 (1.35–14.29)**	
100 or more new partners	32 (2.8)	2 (6.3)	127.12	1.57 (0.39–6.29)	**4.84 (1.05–22.41)**	
Group sex in the past 3 months						**<0.001**
No	659 (56.9)	4 (0.6) 64	2,670.75	0.15 (0.06–0.39)	1 (Ref)	
Yes	500 (43.1)	64 (12.8)	1,947.67	1.33 (0.91–1.96)	**8.81 (3.07–25.24)**	
Fisting or sex toys use in the past 3 months						0.202
No	745 (64.3)	16 (2.2)	2,982.81	0.54 (0.33–0.88)	1 (Ref)	
Yes	414 (35.7)	14 (3.4)	1,635.61	0.86 (0.51–1.45)	1.59 (0.77–3.25)	
Sex for drugs or money in the past 3 months						**0.027**
No	1,104 (95.2)	26 (2.4)	4,418.16	0.59 (0.40–0.86)	1 (Ref)	
Yes	55 (4.8)	4 (7.3)	200.26	1.99 (0.75–5.32)	**3.27 (1.14–9.38)**	
PEP use in the past 12 months						**0.029**
No	919 (79.3)	19 (2.1)	3,709.52	0.51 (0.33–0.80)	1 (Ref)	
Yes	240 (20.7)	11 (4.6)	908.89	1.21 (0.67–2.18)	**2.29 (1.09–4.81)**	
PrEP use in the past 12 months						0.190
No	1,101 (95)	27 (2.7)	4,408.52	0.61 (0.42–0.89)	1 (Ref)	
Yes	58 (5.0)	3 (5.2)	209.49	1.43 (0.46–4.44)	2.21 (0.67–7.30)	
Bacterial STI diagnoses in the past 12 months						**0.001**
No	719 (62.0)	9 (1.3)	2,936.07	0.31 (0.16–0.59)	1 (Ref)	

(*Continued*)

Table 1. (Continued)

Baseline characteristics	Participants *N* (%)	HIV infections from baseline– 2019 *n* (%)	PY at risk	HIV IR per 100 PY (95% CI)	Unadjusted conditional HR (95% CI)	*p*-value
Yes	440 (38.0)	21 (4.8)	1,682.35	1.25 (0.81–1.91)	**3.95 (1.81–8.63)**	
Health and lifestyle characteristics						
Smoking status						0.735
Never smoked	612 (53.1)	14 (2.3)	2,452.23	0.57 (0.34–0.96)	1 (Ref)	
Ex-smoker	290 (25.2)	8 (2.8)	1,163.82	0.69 (0.34–1.37)	1.20 (0.50–2.87)	
Regular smoker	250 (21.7)	8 (3.2)	977.79	0.82 (0.41–1.64)	1.41 (0.59–3.37)	
Recreational drug use in the past 3 months						**<0.001 <0.001 [t]**
No	464 (40.0)	3 (0.7)	1,895.32	0.16 (0.05–0.49)	1 (Ref)	
Noninjection drug and non-chemsex use	336 (29.0)	8 (2.4)	1,350.96	0.59 (0.29–1.18)	3.73 (0.99–14.05)	
Chemsex-related drug use (no injection)	321 (27.7)	13 (4.1)	1,254.47	0.97 (0.61–1.79)	**6.45 (1.84–22.64)**	
Injection drug use	38 (3.3)	6 (15.8)	126.67	4.74 (2.13–10.54)	**27.96 (6.99–111.85)**	
Higher-risk alcohol consumption (modified WHO AUDIT-C score of ≥6)						0.714
No	935 (80.1)	25 (2.7)	3,721.68	0.67 (0.45–0.99)	1 (Ref)	
Yes	224 (19.3)	5 (2.2)	896.74	0.56 (0.23–1.34)	0.83 (0.32–2.17)	
Depressive symptoms (PHQ-9 score ≥10)						0.844
No	1,018 (87.8)	26 (2.6)	4,064.75	0.64 (0.43–0.93)	1 (Ref)	
Yes	141 (12.2)	4 (2.8)	553.67	0.72 (0.27–1.92)	1.12 (0.39–3.20)	
Anxiety symptoms (GAD-7 score ≥10)						0.462
No	1,033 (89.1)	28 (2.7)	4,118.39	0.68 (0.47–0.98)	1 (Ref)	
Yes	126 (10.9)	2 (1.6)	500.03	0.39 (0.10–1.59)	0.58 (0.14–2.45)	
Year of enrolment						0.430
2013	28 (2.4)	2 (7.1)	149.98	1.33 (0.33–5.33)	1 (Ref)	
2014	152 (13.1)	3 (1.9)	735.62	0.4 (0.13–1.26)	0.29 (0.05–1.94)	
2015	788 (67.8)	21 (2.7)	3,115.90	0.67 (0.44–1.03)	0.43 (0.09–1.93)	
2016	194 (16.7)	7 (3.6)	617.36	1.13 (0.54–2.38)	0.67 (0.11–4.09)	

*All measures were self-reported, missing data, or missing questionnaire for:

Age: 9 (all HIV negative); Country of birth and ethnicity, Sexuality: 12 (9 HIV negative, 3 HIV positive); University education: 16 (13 HIV negative, 3 HIV positive); Relationship status, Money status: 4 (1 HIV negative, 3 HIV positive); Employment: 13 (10 HIV negative, 3 HIV positive); Housing status: 15 (12 HIV negative, 3 HIV positive); Smoking status: 10 (7 HIV negative, 3 HIV positive); HIV test, CLS, Number of CLS partners, New sexual partners, Sexual CLS role, Group sex, Fisting or sex toys use, PEP use, PrEP use, Recreational drug use, STI diagnoses, Alcohol consumption, Depressive symptoms, and Anxiety symptoms: 3 (all HIV positive).

[t] *p*-value for trend.

§Other ethnicity includes black, Asian, mixed, and other ethnic group.

†Employed group includes full-time ($n = 845$) and part-time ($n = 107$) employment/self-employment; No employment group includes unemployed registered or not registered for benefits ($n = 60$), sick or disabled ($n = 6$), retired ($n = 24$), and other (student or training or looking after home or dependents or other) ($n = 107$).

#Renting housing includes private renting and renting from council or housing association; unstable or other housing includes temporary accommodation, staying with friends or family, other accommodation, and homeless.

‡CLS with men only.

¯New partners include men and women.

AURAH2, The Attitudes to and Understanding of Risk of Acquisition of HIV 2; CI, confidence interval; CLS, condomless anal sex; GAD-7, generalised anxiety disorder-7; GBMSM, gay, bisexual, and other men who have sex with men; HR, hazard ratio; IQR, interquartile range; IR, incidence rate; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; PY, person-years; PHQ-9, patient health questionnaire-9; SD, standard deviation; STI, sexually transmitted infection; WHO-AUDIT, World Health Organization–Alcohol Use Disorders Identification Test.

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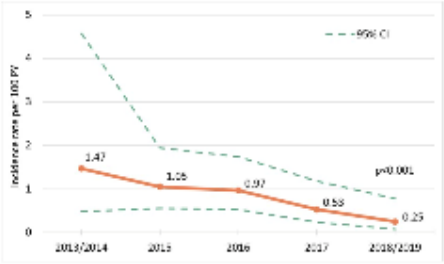

Fig 1. HIV incidence among GBMSM in the AURAH2 study, 2013–2019. AURAH2, The Attitudes to and Understanding of Risk of Acquisition of HIV 2; CI, confidence interval; GBMSM, gay, bisexual, and other men who have sex with men; PY, person-years.

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The overall HIV IR in this cohort with 4,618.9 PY of follow-up time was 0.71 (95% CI 0.51 to 1.00) per 100 PY (Fig 1 **and** Table 2). HIV incidence fell progressively from 2013 until 2019; from 1.47 (95% CI 0.48 to 4.57) per 100 PY in 2013/2014 to 0.25 (95% CI 0.08 to 0.78) per 100 PY in 2018/2019. The incidence declined on average by 0.85-fold per year from 2013 to 2019 ($p < 0{\cdot}001$, modelled using mixed-effects Weibull proportional hazard).

The most common age category at the time of new HIV diagnoses was between 35 and 44 years, with a total of 13 men (39.4%) in this age range being diagnosed with HIV, followed by men in the age category of 25 to 34 years (8 men, 24.2%), <25 years (7 men, 21.2%), and ≥45 years (5 men, 15.2%). The median (IQR) age at time of new HIV diagnosis was 35 years (26 to 40).

Association of baseline factors with incident HIV

Table 1 presents the association of baseline factors with incident HIV diagnosis. In univariable mixed-effects Weibull proportional hazard models, the factor most strongly associated with HIV acquisition was reporting injection drug use in the past 3 months, with an almost 28-fold higher rate compared to men who did not report recreational drug use (HR 27.96, 95% CI 6.99 to 111.85, global $p < 0.001$). The HIV IR among people who injected drugs was 4.74 (95% CI 2.13 to 10.54) per 100 PY. Having used at least 1 noninjection chemsex-related drug was also strongly associated with HIV acquisition (HR 6.45, 95% CI 1.84 to 22.64, compared to no drug use); the association with non-chemsex–related drugs was weaker (HR 3.73, 95% CI 0.99 to 14.05).

Other sexual/HIV-related behaviour risk factors were strongly associated with increased risk of HIV infection: CLS (HR 3.75, 95% CI 1.31 to 10·74, $p = 0.014$), greater number of CLS

Table 2. HIV incidence among GBMSM participating in the AURAH2 prospective study, 2013–2019.

Calendar year	PY	No. of HIV infections	IR (per 100 PY)	95% CI
2013/2014	203.55	3	1.47	0.48–4.57
2015	953.53	10	1.05	0.56–1.95
2016	1,139.29	11	0.97	0.53–1.74
2017	1,134.80	6	0.53	0.24–1.18
2018/2019	1,187.69	3	0.25	0.08–0.78
Overall	**4,618.86**	**33**	**0.71**	**0.51–1.00**

AURAH2, The Attitudes to and Understanding of Risk of Acquisition of HIV 2; CI, confidence interval; GBMSM, gay, bisexual, and other men who have sex with men; IR, incidence rate; PY, person-years.

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partners, with increased risk for those having at least 2 partners (HR for 2 to 4 partners 4.05, 95% CI 1.29 to 12.72; HR for 5 to 10 partners 9.60, 95% CI 2.58 to 35.76, HR for more than 10 partners 14.05, 95% CI 4.11 to 47.98, compared with no CLS, global $p < 0.001$), CLS with HIV–positive partners (HR 6.45, 95% CI 3.15 to 13.22, $p < 0.001$), versatile CLS role (HR 6.35, 95% CI 2.18 to 18.51, $p < 0.001$), group sex (HR 8.81, 95% CI 3.07 to 25.24, $p < 0.001$), and sex for drugs or money (HR 3.27, 95% CI 1.14 to 9.38, $p = 0.027$) in the past 3 months; reporting a bacterial STI diagnosis in the past 12 months (HR 3.95, 95% CI 1.81 to 8.63, $p = 0.001$), reporting more than 10 new sexual partners in the past 12 months (HR for 11 to 49 new partners 3.17, 95% CI 1.39 to 7.26, HR for 50 to 99 new partners 4.40, 95% CI 1.35 to 14.29, HR for 100 or more new partners 4.84, 95% CI 1.05 to 22.41, compared to 0 to 10 new partners, global $p = 0.001$) and having used PEP in the past 12 months (HR 2.29, 95% CI 1.09 to 4.81, $p = 0.029$).

For socioeconomic and demographic characteristics, lower level of education was associated with increased risk of HIV infection (HR for no qualification 4.65, 95% CI 1.07 to 20.14 compared to university degree, global $p = 0.014$). There was some evidence that nonemployed men were at lower risk of infection than employed men (HR 0.16, 95% CI 0.02 to 1.19, $p = 0.074$).

Adjustment for age at baseline, country of birth and ethnicity, sexual identity, and education did not materially change the associations between incident HIV and baseline factors (S2 Table). There were no significant associations of age group, housing status, financial status, relationship status, HIV test in the past 6 months, fisting or sex toys use in the past 3 months, PrEP use in the past 12 months, smoking status, alcohol consumption, country of birth and ethnicity, sexual identity, year of enrolment, depressive symptoms, and anxiety symptoms at baseline with risk of HIV infection (Table 1).

Prevalence of sexual risk behaviours over time

Fig 2 shows the trends in reported sexual risk behaviours, drug use, and the use of PrEP and PEP by calendar year, based on all available baseline and follow-up questionnaires from all 1,162 participants enrolled (total 4,439 questionnaires). Fig 2A shows that the annual prevalence of CLS with 2 or more partners in the past 3 months increased somewhat from 38.3% to 41.0% (p-value for linear trend from GEE logistic model = 0.006) between 2013/2014 and 2018, while group sex declined substantially from 46.7% to 24.2% ($p < 0.001$), as did bacterial

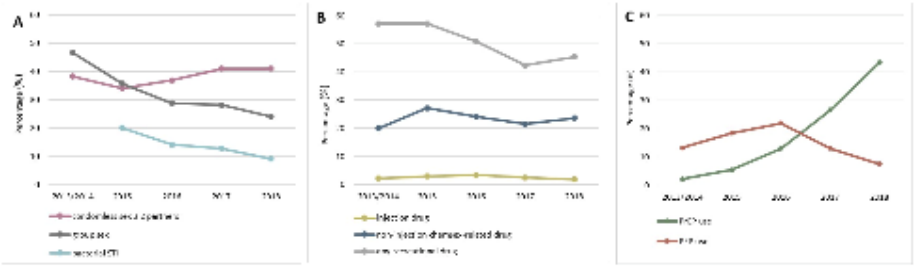

Fig 2. Annual prevalence of sexual/HIV-related behaviours among GBMSM in the AURAH2 study, 2013–2018*. *Annual reports of (A) sexual risk behaviours in the previous 3 months, data from all available baseline, 4-monthly, and annual questionnaires (N = 4,439 questionnaires), bacterial STI in the previous 3 months, data from 4-monthly and annual questionnaires (N = 3,277 questionnaires); (B) recreational drug use in the past 3 months, data from baseline and annual questionnaires (N = 2,104 questionnaires); (C) PrEP and PEP use in the last 12 months, data from baseline and annual questionnaires (N = 2,085 questionnaires). AURAH2, The Attitudes to and Understanding of Risk of Acquisition of HIV 2; GBMSM, gay, bisexual, and other men who have sex with men; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection.

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STI diagnoses in the last 3 months from 20.1% to 9.2% ($p < 0.001$) between 2015 and 2018. For bacterial STIs, data were not included from the baseline questionnaire (since 2013) as it asked about diagnoses in the previous 12 months rather than in the last 3 months. Any recreational drug use in the past 3 months decreased from 57.2% to 45.5% ($p < 0.001$), while injection drug use (prevalence around 2%, $p = 0.903$) and the use of at least 1 chemsex-related drug (prevalence between 20% and 30%, $p = 0.232$) were stable (Fig 2B). Past 12-month PrEP use increased significantly from 2.22% to 43.4% ($p < 0.001$); on the other hand, PEP use peaked at 21.9% in 2016, then declined to 7.6% in 2018 ($p = 0.07$) (Fig 2C).

Association of time-updated factors with incidence HIV among men who completed at least one online follow-up questionnaire

Among the 622 men who completed an online follow-up questionnaire, 19 were diagnosed with HIV during the period from the date of completion of their baseline questionnaire until June 30, 2019. With a total of 2,495 PY of follow-up time, the overall HIV IR in this subgroup of men was 0.76 (95% CI 0.49 to 1.19) per 100 PY, similar to the overall IR among all men enrolled in the AURAH2 cohort (0.71, 95% CI 0.51 to 1.00 per 100 PY). Table 3 shows unadjusted and adjusted IRRs from mixed-effects Poisson models for factors associated with HIV incidence among these men (total complete observations 3,821 questionnaires). In this analysis, age, partnership status, sexual/HIV-related behaviours, PrEP and PEP use, and health and lifestyle variables were time updated, whereas ethnicity and country of birth, education, employment, sexual identity, financial status, and housing status were fixed variables that were only asked at baseline questionnaires. Longitudinal factors associated with HIV incidence among these men were quite similar to those among the 1,162 men, in particular, injection drug use (unadjusted IRR 21.67, 95% CI 3.96 to 118.30, $p < 0.001$), chemsex (3.89, 95% CI 1.35 to 11.22, $p = 0.012$), CLS with 2 or more partners, versatile CLS role, group sex (all in the previous 3 months), bacterial STI diagnosis (in the previous 12 months at the baseline questionnaire and in the past 3 months at the 4-monthly and annual questionnaires), and calendar year.

Discussion

Using a prospectively followed cohort of initially HIV–negative GBMSM in London and Brighton, we demonstrate a substantial decline in HIV incidence, from 1.47 per 100 PY to 0.25 per 100 PY between 2013 and 2019. The results of an earlier report from England's national STI surveillance system also estimated that the annual HIV incidence among men who have sex with men attending English sexual health clinics decreased from 1.90 per 100 PY in 2012/2013 to 0.79 per 100 PY in 2016/2017 [4]. Based on the CD4 back-calculation model that is used to estimate HIV incidence among GBMSM living in England based on data on new HIV diagnoses, incidence begun to fall in 2012 [2,16].

The substantial decline in HIV incidence in our cohort was also described in some other countries [5–7,17,18]. It may be attributed to important behavioural changes within GBMSM populations. The dramatic decline in HIV infection rates in AURAH2 coincides with declines in the proportion of individuals reporting group sex and any recreational drug use since 2013, and diagnosis of bacterial STIs since 2015. The declining trends in group sex and diagnosis of bacterial STIs have been reported previously among men in AURAH2 who completed at least an online follow-up ($n = 622$), during the online follow-up period (2015 to 2018) [19]. This decline could be a feature of the fact that the study recruited GBMSM attending sexual health clinics for STI testing. Engagement in care for STI monitoring may have had a preventive impact on subsequent STI occurrence, or a

Table 3. Association of time-updated factors with incident HIV among 622 GBMSM who completed at least 1 online follow-up questionnaire, 2013–2018*.

	Unadjusted IRR (95% CI)	*p*-value	Adjusted[€] IRR (95% CI)	*p*-value
Demographic characteristics				
Age (time-updated) per year	3,785 obs	0.843	3,770 obs	0.4
	1.00 (0.96–1.05)		1.02 (0.97–1.06)	
Age (time-updated) category	3,785 obs	0.676	3,770 obs	0.325
<25	Ref		Ref	
25–29	0.22 (0.02–1.93)		0.65 (0.21–1.92)	
30–34	0.41 (0.07–2.23)		0.61 (0.22–1.97)	
35–39	0.72 (0.16–3.23)		0.99 (0.19–5.17)	
40–44	0.35 (0.04–3.14)		0.49 (0.05–4.92)	
≥45	0.86 (0.23–3.21)		1.21 (0.28–5.21)	
Country of birth and ethnicity	3,782 obs	0.953	3,770 obs	0.905
Born in the UK, white	Ref		Ref	
Born in the UK, other ethnicity	1.63 (0.20–13.29)		1.77 (0.21–15.04)	
Non-UK born, white	0.97 (0.28–3.31)		1.00 (0.29–3.46)	
Non-UK born, other ethnicity	0.74 (0.09–6.03)		0.79 (0.09–6.54)	
Sexual identity	3,793 obs	0.639	3,770 obs	0.569
Gay	Ref		Ref	
Bisexual/other	1.63 (0.21–12.54)		1.82 (0.23–14.34)	
Socioeconomic characteristics and partnership status				
University education	3,805 obs	0.923	3,770 obs	0.932
Yes	Ref		Ref	
No	0.94 (0.29–3.06)		0.95 (0.29–3.09)	
Employed	3,772 obs	0.305	3,760 obs	0.243
Yes	Ref		Ref	
No	0.34 (0.04–2.64)		0.29 (0.03–2.32)	
Money to cover basic needs	3,805 obs	0.744	3,770 obs	0.829
All of the time	Ref		Ref	
Most of the time	1.29 (0.29–5.83)		1.43 (0.30–7.06)	
Sometimes/No	0.10 (0.05–0.18)		0.12 (0.05–0.25)	
Housing status	3,750 obs	0.611	3,738 obs	0.701
Home owner	Ref		Ref	
Renting	0.56 (0.17–1.85)		0.66 (0.16–2.71)	
Unstable/other	0.97 (0.19–4.82)		1.12 (0.18–6.81)	
Ongoing relationship**	1,536 obs	0.094	1,522 obs	0.148
Yes	Ref		Ref	
No	0.63 (0.36–1.08)		0.65 (0.36–1.17)	
Sexual/HIV-related behaviour characteristics				
Recent HIV test[†]**	3,699 obs	0.34	3,651 obs	0.329
No	Ref		Ref	
Yes	1.87 (0.51–6.80)		1.90 (0.52–6.92)	
CLS in the past 3 months	3,821 obs	0.871	3,770 obs	0.196
No	Ref		Ref	
Yes	1.09 (0.38–3.14)		2.71 (0.60–12.23)	
CLS with 2 or more partners	3,819 obs	**0.005**	3,770 obs	**0.004**
One/none	Ref		Ref	

(*Continued*)

Table 3. (Continued)

	Unadjusted IRR (95% CI)	*p*-value	Adjusted[€] IRR (95% CI)	*p*-value
2 or more	**6.19 (1.72–22.17)**		**9.39 (2.07–42.66)**	
Sexual role CLS in the past 3 months	3,803 obs	0.705	3,752 obs	**0.016**
No CLS/did not state which partner	Ref		Ref	
Always insertive	-		-	
Always receptive	0.95 (0.18–4.88)		2.47 (0.35–17.67)	
Versatile (sometimes insertive, sometimes receptive)	1.79 (0.60–5.32)		**4.55 (1.01–21.11)**	
Group sex in the past 3 months	3,819 obs		3,770 obs	
No	Ref	**0.043**	Ref	**0.029**
Yes	**2.98 (1.03–8.61)**		**3.51 (1.14–10.77)**	
PEP use in the past 12 months[**]	1,530 obs	0.971	1,512 obs	0.888
No	Ref		Ref	
Yes	1.04 (0.12–8.90)		1.16 (0.13–10.11)	
PrEP use in the past 12 months[**]	1,532 obs	0.97	1,512 obs	0.999
No	Ref		Ref	
Yes	0.96 (0.12–7.81)		0.99 (0.13–7.51)	
Bacterial STI diagnoses[‡]	3,819 obs	**0.005**	3,770 obs	**0.002**
No	Ref		Ref	
Yes	**4.46 (1.57–12.68)**		**5.93 (1.95–18.03)**	
Health and lifestyle characteristics				
Recreational drug use in the past 3 months[**]	1,536 obs	0.152	1,518 obs	0.111
No	Ref		Ref	
Yes	4.81 (0.56–41.26)		5.83 (0.66–50.97)	
Chemsex in the past 3 months	3,819 obs	**0.012**	3,770 obs	**0.006**
No	Ref		Ref	
Yes	**3.89 (1.35–11.22)**		**4.81 (1.57–14.74)**	
Injection drug use in the past 3 months[**]	1,536 obs	**<0.001**	1,518 obs	**0.001**
No	Ref		Ref	
Yes	**21.67 (3.96–118.30)**		**18.99 (3.39–106.14)**	
Higher-risk alcohol consumption[**] **(modified WHO AUDIT-C equals ≥6)**	1,536 obs	0.26	1,521 obs	0.335
No	Ref		Ref	
Yes	2.10 (0.58–7.63)		1.91 (0.51–7.08)	
Depressive symptoms[**] **(PHQ-9 score ≥10)**	1,536 obs	0.818	1,521 obs	0.701
No	Ref		Ref	
Yes	1.28 (0.15–10.64)		1.53 (0.17–13.31)	
Anxiety symptoms[**] **(GAD-7 score ≥10)**	1,537 obs	0.559	1,526 obs	0.681
No	Ref		Ref	
Yes	1.88 (0.23–15.60)		2.06 (0.23–18.30)	
Calendar year as a continuous variable	3,821 obs	**<0.001**	3,769 obs	**0.004**
	0.52 (0.45–0.59)		**0.47 (0.28–0.78)**	
Calendar year category	3,821 obs	0.053	3,769 obs	**0.01**
2013–2014	Ref		Ref	
2015	0.26 (0.07–1.05)		**0.17 (0.04–0.82)**	
2016	0.35 (0.10–1.19)		**0.20 (0.05–0.83)**	

(*Continued*)

Table 3. (Continued)

	Unadjusted IRR (95% CI)	*p*-value	Adjusted[€] IRR (95% CI)	*p*-value
2017–2018	0.06 (0.01–0.54)		0.05 (0.01–0.44)	

[*]Total complete observations: 3,821 questionnaires; sexual/HIV-related behaviour data were based on the last time man asked; number of new sexual partners, fisting or sex toys, sex for drugs or money, and smoking status were not included in the analysis because they were only asked at the baseline questionnaire.

[€]Adjusted for age (time-updated), country of birth and ethnicity, sexual identity, and university education.

[**]Data were not collected at the 4-monthly questionnaire (only baseline and annual questionnaires).

[†]In the past 6 months at the baseline questionnaire and in the past 3 months at the 4-monthly and annual questionnaires.

[‡]In the past 12 months at the baseline questionnaire and in the past 3 months at the 4-monthly and annual questionnaires.

CI, confidence interval; CLS, condomless anal sex; GAD-7, generalised anxiety disorder-7; GBMSM, gay, bisexual, and other men who have sex with men; IRR, incidence rate ratio; PEP, postexposure prophylaxis; PHQ-9, patient health questionnaire-9; PrEP, preexposure prophylaxis; STI, sexually transmitted infection; WHO-AUDIT, World Health Organization–Alcohol Use Disorders Identification Test.

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"regression to the mean" effect may have operated because the men were recruited at a time of particularly high STI risk [19]. In contrast to these trends in STIs, group sex, and drug use overall, we observed in this study that the prevalence of CLS with 2 or more partners slightly increased, and the prevalence of injection drug use and noninjection chemsex-related drug use remained relatively stable, between 2013 and 2018 (baseline–the end of follow-up). The decline in HIV incidence is, therefore, unlikely to be solely explained by changes in sexual behaviour during this period.

Lower levels of infectious HIV in the community due to more timely HIV diagnosis and earlier treatment among those accessing HIV care are likely to have had a role in declining incidence, in line with previous prediction [20,21]. A recent study in Australia, the TAIPAN study, has demonstrated that the decrease in community-level HIV viraemia (≥200 copies/mL) from 28.6% in 2012 to 12.8% in 2017 among HIV–positive gay and bisexual men was significantly associated with decreasing HIV incidence in New South Wales and Victoria (from 0.88 per 100 PY in 2012 to 0.22 per 100 PY in 2017) [5].

PrEP use during follow-up may also have impacted on declining HIV incidence. An important finding in our study was that the fall in HIV incidence coincided with a major increase in the proportion of men reporting past 12-month PrEP use over time [22], which could indicate an association. In our study, baseline and longitudinal reported PrEP use was not associated with reduced HIV incidence. At baseline, only 5% of men reported PrEP use in the past 12 months, and possibly, these men were early PrEP takers having high-risk sexual behaviour putting them at particularly high risk of HIV infection. It is possible that no clear association was observed due to opposing factors operating—PrEP use decreasing the risk of HIV acquisition on the one hand, and PrEP use acting as an indicator of very high-risk behaviour (similar to the other markers of CLS) on the other. Moreover, in this study, past 12-month PrEP use was only asked at baseline and annual questionnaires; therefore, we do not have a complete picture of PrEP use during follow-up, or of adherence or consistency in using PrEP. Taken together, our results are consistent with the hypothesis that the benefits of ART in reducing HIV transmission in combination with increased uptake of PrEP has had a substantial impact in reducing HIV incidence in the GBMSM population.

Recreational drug use was one of the strongest factors associated with HIV incidence in this cohort. HIV incidence was especially high among men who reported the use of injection drugs, 4.8 per 100 PY, almost 28-fold higher than the incidence among men who did not report any recreational drugs. The use of noninjection chemsex-related drugs also increased the risk of HIV incidence more than 6-fold. A systematic review investigating recreational

drug use in GBMSM has demonstrated that chemsex use is associated with increased risky behaviour such as CLS and group sex, as well as with an increase in STIs and poor mental health symptoms [23]. Polydrug use has also been reported to be associated with condomless sex and higher partner numbers in HIV–negative and HIV–diagnosed GBMSM in the UK [24,25]. There are limited data on injection drug use among GBMSM in the UK and Europe. Findings from the 2014 Gay Men's Sex Survey, an online survey of 14,464 GBMSM living in the UK, suggest that injection drug use (amphetamine, crystal methamphetamine, heroin, mephedrone, GHB/GBL, and ketamine) is significantly associated with CLS with multiple partners [26]. The survey also found that injecting was most common among those who were of age 30 to 59 years, lived in London, and were HIV seropositive. Data from Australian and Canadian GBMSM cohorts have also observed strong associations between injecting drugs and sexual risk behaviours [27,28]. Further research into the barriers to accessing HIV prevention services among GBMSM who inject drugs, despite the availability of harm reduction programmes in the UK, will be useful.

We also observed that the risk of acquiring HIV was higher among GBMSM who reported high-risk sexual behaviours (CLS with multiple or HIV–positive partners, group sex, greater number of new sexual partners, versatile CLS role, and sex for drugs or money) and bacterial STI diagnoses. Risk was particularly high for men reporting group sex and those with higher numbers of CLS partners in the past 3 months. This is consistent with findings from other cohort studies in the UK and other countries [8–9,29]. Routine inquiry and documentation of these factors could enable better direction of prevention efforts at both the individual and population level.

In the AURAH2 cohort, most demographic and socioeconomic factors were not associated with incident HIV. However, we observed a higher IR among men with nonuniversity level of education that might be explained by the higher prevalence of high-risk sexual behaviours in this subgroup of men. The prevalence of past 3-month CLS at baseline was significantly higher among men with no educational qualifications, at 86% ($p = 0.038$), compared to men with university-level education and other qualification (**S3 Table**). A lower educational level has been reported to be associated with risk-taking behaviours and with an increased risk of HIV seroconversion in European studies [30,31]. We did not find evidence that high alcohol use, smoking, or symptoms of depression or anxiety were associated with incident HIV in the baseline associated factors or time-updated analysis, although CIs were wide for some factors. It has previously been reported that the relationship of mental health symptoms with sexual behaviour may be complex and operate in both directions [32].

The strengths of this study include the prospective design and HIV status confirmation of all 1,162 participants enrolled in AURAH2 through linkage with national HIV surveillance data. This allows for optimum use of available information to estimate HIV incidence and trends for all men in the cohort. Prior to data linkage, we have presented our interim results restricted to men under follow-up with questionnaire [33–34], adopting the single random point method to decide HIV infection dates between self-reported first HIV positive test results and last HIV negative test results [35]. We also observed significant decline over time among these men; however, trends were only able to be calculated from 2015 until 2018 (online follow-up period), and we missed a number of diagnosis that were further identified after linking our data with PHE.

There are some limitations to this study. Men in this cohort were recruited from sexual health clinics in urban areas of London and Brighton and are predominantly highly educated, employed, in a stable economic situation, and of white ethnicity. These men may not be representative of the broader GBMSM population in England and the UK. It is possible that the incidence estimates and risk factors identified are not generalizable to GBMSM

who do not attend sexual health clinics. The small number of HIV infections in each calendar year among men in this study has resulted in relatively wide CIs of IRs; therefore, IRs and associations with factors must be interpreted carefully. In addition, assessment of trends over time in sexual behaviour may be subject to "regression to the mean" as the clinic visit at which recruitment occurred may have been specifically prompted by a recent period of higher risk. For risk factors analysis, we focused on baseline factors in order to include all data from the whole cohort, which may have underestimated the associations between sexual/HIV-related behaviours and HIV incidence, including the impact of PrEP. However, we observed similar results when analysis was restricted to 622 men using time-updated variables. In terms of the time-updated analysis, the online retention of participants who initially registered in the study was not optimal; however, 64% (400 of 622) of participants who completed at least an online questionnaire were engaged in the study throughout. Our results may be sensitive to specific recall bias and social desirability bias in men's responses in the baseline questionnaire. Data linkage to surveillance systems using pseudo-anonymised identifiers has potential for mismatches or missing seroconversions; however, this has been minimised by PHE data triangulation; all self-reported seroconversions were validated by PHE data. Lastly, this study would not include seroconversions that were not diagnosed or those that were diagnosed outside the UK.

In summary, this study provides evidence of a substantial decline in HIV incidence among a cohort of GBMSM attending sexual health clinics in England. Our data suggest that GBMSM reporting the use of recreational drugs, in particular injection drug use and chemsex drug use, high-risk sexual behaviours such as CLS with multiple partners, CLS with HIV–positive partners, group sex, and those with a bacterial STI, are at increased risk of HIV acquisition. HIV infections are also significantly higher among those with lower levels of education at baseline. Temporal trends in sexual risk behaviours and drug use in the cohort over the study period were mixed, but the marked decrease in incidence coincided with a substantial increase in PrEP use. Given similar findings from recent data among GBMSM in the UK and other countries, it is likely that the observed decline is largely related to the increase in testing and earlier ART initiation from 2013 onward and the scale-up of PrEP. Although efforts to end HIV epidemic are having a substantial effect, further improvements specially to increase HIV test coverage across all populations at risk remain very important. Sustainable and comprehensive HIV prevention and control efforts must continue in the UK to reach zero new infections by 2030.

Supporting information

S1 Checklist. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement The AURAH2 Study.
(DOC)

S1 Analyses Plan. Longitudinal analysis of new HIV infections and their predictors among MSM in England: The AURAH2 Study–Data Analysis Plan.
(PDF)

S1 Table. Baseline sociodemographic, health and lifestyle characteristics, sexual behaviour, and PrEP and PEP use among participants who completed the baseline, 4-monthly, and annual questionnaire in the AURAH2 study.
(DOCX)

S2 Table. Adjusted associations of baseline characteristics with incident HIV among 1,162 GBMSM participating in the AURAH2 study.
(DOCX)

S3 Table. Associations between ethnicity, education, and employment characteristics with sexual behaviour measures at baseline among 1,162 GBMSM in the AURAH2 study.
(DOCX)

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Disclaimer

The views expressed in this study are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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Appendix 23. The AURAH2 study AIDS Impact 2019 Oral Presentation

UCL

Substantial decline in HIV incidence between 2015 – 2018 among a prospective cohort of men who have sex with men in England

Nadia Hanum, Valentina Cambiano, Janey Sewell, Fiona C Lampe, Alison J Rodger, Andrew Speakman, Nneka Nwokolo, David Asboe, Richard Gilson, Amanda Clarke, Ada Miltz, Simon Collins, Valerie Delpech, Peter Kirwan and Andrew N Phillips for the AURAH2 Study Group

aurah2

Background

- Decline in new HIV diagnoses and incidence among gay, bisexual, and other men who have sex with men (MSM) in the UK[1]
  - New diagnoses decreased by 31% between 2015 and 2017
  - Estimated new infections more than halved between 2012 and 2017
- Factors for the decline:
  - Earlier ART initiation
  - Increase in HIV testing
  - Increase use of Pre-Exposure Prophylaxis (PrEP)
- MSM is still the group most at risk of acquiring HIV in the UK[2]
- Limited information from UK prospective studies assessing HIV acquisition risk and associated factors

[1] Nash et al., 2018 ; [2] Brown et al., 2017

Aim

- To estimate trends in HIV incidence between 2015 – 2018 in a prospective cohort study of initially HIV-negative MSM
- To assess whether changes in prevalence of condomless anal sex (CLS) and use of Pre-Exposure Prophylaxis (PrEP) explain any incidence trend

Methods: study design and setting

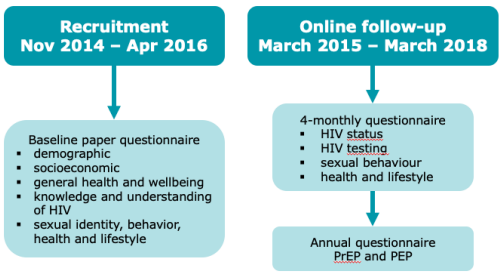
Prospective cohort study, 3 sexual health clinics in London and Brighton

aurah2
"Attitudes to and Understanding of Risk of Acquisition of HIV over time"

56 Dean Street | Mortimer Market Centre | Brighton & Hove Sexual Health & Contraception Service

Participants inclusion: HIV-negative gay, bisexual and other MSM, ≥18 years

Methods: period of study and data collection



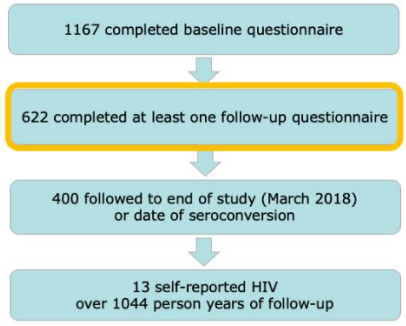
Sewell et al., 2016

Analyses

- Annual HIV incidence per 100 PY and 95% CI, 2015 – 2018
  - Periods of observation for each individual:
    - (1) First follow-up to HIV seroconversion
    - (2) First follow-up to last HIV negative follow-up
    - (3) First follow-up to censoring (March 2018)
  - MSM self-reported HIV
  - HIV infection date: single random-point imputation method between latest-negative and earliest-positive dates*
- Trends in HIV incidence and associations with CLS and PrEP use, 2015 - 2018
  - Poisson regression with robust standard errors
  - Adjustment for age
  - Additional adjustment for CLS with ≥ 2 partners and PrEP use using pooled data from all available follow-up questionnaires

*Vandormael, 2018

Results

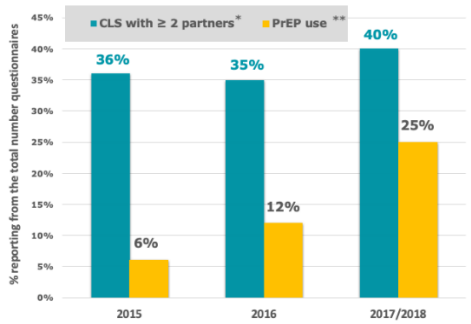


Results: Participants characteristics

Baseline characteristics of participants completing at least one follow-up questionnaire (n=622)	
Mean age, years (SD)	34 (11.3)
Gay	94%
White ethnicity	84%
University education	77%
Employed	89%
CLS with more than 2 partners	37%
used PrEP	5%

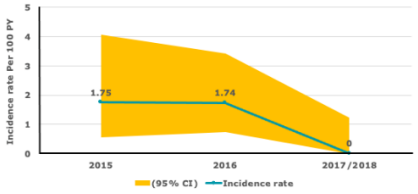
Median number online questionnaire completed (IQR)	6 (3 – 7)

Results: Prevalence of CLS and PrEP use over time



* proportion had CLS with more than 2 partners, in the last three months from the total number questionnaires
** proportion took PrEP in the past year, as reported in most recent annual questionnaire

Results: HIV Incidence 2015 - 2018



HIV incidence among MSM participating in the AURAH2 study, 2015 - 2018

Calendar year	PY of follow-up	No. of seroconversions	Incidence rate per 100 PY (95% CI)
2015	286	5	1.75 (0.57 – 4.07)
2016	460	8	1.74 (0.75 – 3.43)
2017 / 2018	298	0	0 (0 – 1.24)
Overall	1044	13	1.24 (0.66 – 2.12)

Results: Trends in HIV incidence and association with CLS and PrEP use

	Unadjusted IRR (95% CI)	p-value	Age-adjusted IRR (95% CI)	p-value	Adjusted IRR † (95% CI)	p-value
Calendar year	0.31 (0.14 – 0.67)†	0.004	0.30 (0.13 – 0.68)	0.004	0.31 (0.13 – 0.76)	0.01
CLS with ≥ 2 partners	2.87 (0.94 – 8.76)	0.065	3.59 (1.10 – 11.70)	0.03	3.84 (1.16 – 12.63)	0.03
PrEP use*	1.19 (0.27 – 5.39)	0.81	0.58 (0.07 – 4.96)	0.62	0.64 (0.06 – 6.29)	0.7

† incidence rate ratio per calendar year
‡ adjusted for age and all other variables in the table
* used PrEP in the past year, as reported in most recent annual questionnaire

Used PrEP in the past year, as reported in most recent annual questionnaire:
- was reported by 1 of the 13 seroconverters
- was not necessarily current consistent or adherent PrEP

Future work

Linkage between the AURAH2 data and national HIV surveillance data by Public Health England (PHE) to all 1167 participants:

- to verify the number of HIV diagnoses reported by the participants
- to discover any diagnoses within cohort that have not been reported
- To repeat the incidence analysis in the full group who completed baseline questionnaire

Conclusions

- In a prospective cohort of MSM closely followed over time, we found evidence of a substantial decline in HIV incidence from 2015 - 2018.
- The decline was not explained by changes in prevalence of CLS.
- The prevalence of PrEP use increased substantially over the follow-up period. It was not possible to evaluate the effectiveness of PrEP.
- The decline in HIV incidence is likely to be partially driven by changes in prevalence of infectious HIV in the community.

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56 Dean Street: Ali Ogilvy, David Asboe, Nneka Nwokolo

Mortimer Market Centre: Ana Milinkovic, Fabienne Styles, Rosanna Laverick, Marzena Orzol, Emmi Suonpera, Richard Gilson

Brighton & Hove Sexual Health & Contraception Service: Celia Richardson, Elaney Youssef, Sarah Kirk, Marion Campbell, Lisa Barbour, Amanda Clarke

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Thank you

Appendix 24. The AURAH2 study BHIVA 2019 Poster Presentation

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Substantial decline in HIV incidence between 2015 – 2018 among a prospective cohort of men who have sex with men in England

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Background

- Recent data reveal that new HIV diagnoses in the UK have declined among men who have sex with men (MSM).
- There are no data from UK prospective studies assessing HIV acquisition risk and associated factors.
- We estimated trends in HIV incidence between 2015 and 2018 in a prospective cohort study of initially HIV undiagnosed MSM.

Methods

- The prospective cohort study, Attitudes to and Understanding Risk of Acquisition of HIV over Time (AURAH2), recruited HIV negative MSM from three large sexual health clinics in London and Brighton from Nov 2014 – April 2016.
- Participants self-completed a baseline paper questionnaire at clinics, and subsequent four-monthly and annual online questionnaires, including information on HIV status, sexual behaviors, and PrEP use to March 2018.
- We used Poisson regression with robust standard errors to evaluate trends in incident HIV infection, adjusted for age.
- We considered additional adjustment for condomless anal sex (CLS) with two or more partners in the last three months, and use of PrEP (took PrEP in the past year, as reported in most recent annual questionnaire), to assess whether these factors explained any incidence trend.

Results

- This analysis includes 622 participants completing one or more online questionnaire (Table 1).
- 13 HIV seroconversion were reported during follow-up; overall incidence rate was 1.24 (95% CI 0.66 – 2.12) per 100 person-years (PY), the total follow-up time at risk was 1044 PY (Figure 1, Table 2).
- HIV incidence rate declined significantly from 2015 to 2018; age-adjusted incidence rate ratio (IRR) was 0.30 per calendar year; 95% CI 0.13 – 0.68; p = 0.004 (table 3).
- Over time, there was a small increase in prevalence of CLS with ≥ 2 partners and a substantial increase in PrEP use (Table 1).
- CLS with ≥ 2 partners was associated with higher risk of HIV seroconversion.
- PrEP use (reported by 1 of 13 seroconverters) was not significantly associated with incidence risk.
- The decreasing trend over calendar time in HIV incidence remained similar after additional adjustment for CLS ≥ 2 partners and PrEP use.

Conclusions

- In a prospective cohort of MSM closely followed over time, we found evidence of a substantial decline in HIV incidence from 2015 - 2018.
- This was not explained by changes in self-reported condomless sex, and is likely to be partially driven by changes in prevalence of infectious HIV in the community.
- The contribution of PrEP was difficult to ascertain due to limited power.

Limitations

- The data on HIV infections may be underestimated at present as linkage with Public Health England (PHE) data not completed.
- The decreasing trend could in part be a cohort effect.

Table 1. Description of the participants in the AURAH2 study completing at least one online questionnaire, 2015 – 2018 (N=622)

	Overall
Mean age at baseline, years (SD)	34 (11.3)
Gay	94%
White Ethnicity	84%
University level education	77%
Median number online questionnaires completed (IQR)	6 (3 – 7)
CLS with ≥ 2 partners*	
2015	36%
2016	35%
2017/2018	40%
PrEP use**	
2015	6%
2016	12%
2017/2018	25%

* proportion reported CLS in the last three months from the total number questionnaires
** proportion took PrEP in the past year, as reported in most recent annual questionnaire

Figure 1: HIV incidence among MSM participating in the AURAH2 study, 2015 - 2018

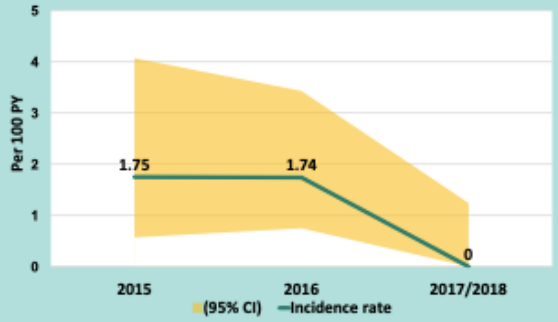

Table 2. HIV incidence among MSM participating in the AURAH2 study, 2015 - 2018

Calendar year	PY of follow-up	No. of seroconversions	Incidence rate per 100 PY (95% CI)
2015	286	5	1.75 (0.57 – 4.07)
2016	460	8	1.74 (0.75 – 3.43)
2017/2018	298	0	0 (0 – 1.24)
Overall	1044	13	1.24 (0.66 – 2.12)

Table 3. Factors associated with HIV seroconversion among MSM participating in the AURAH2 study, 2015 – 2018.

	unadjusted IRR (95% CI)	p-value	adjusted IRR (95% CI)	p-value
Calendar year	0.31 (0.14 – 0.67)†	0.004	0.30 (0.13 – 0.68)‡ 0.31 (0.13 – 0.76)§	0.004 0.01
CLS with ≥ 2 partners	2.87 (0.94 – 8.76)	0.065	3.59 (1.10 – 11.70)‡ 3.84 (1.16 – 12.63)§	0.03 0.03
PrEP use	1.19 (0.27 – 5.39)	0.81	0.58 (0.07 – 4.96)‡ 0.64 (0.06 – 6.29)§	0.62 0.7

† incidence rate per calendar year
‡ adjusted for age
§ adjusted for age and all other variables in the table

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