Sexual behaviour of HIV-diagnosed men who have sex with men in England in the era of effective antiretroviral therapy: results from the ASTRA study

THESIS

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DECLARATION

I, Marina Daskalopoulou 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.

MDaskalopoulou

ABSTRACT

Transmission of HIV among men who have sex with men (MSM) in the UK is ongoing. Among HIV-diagnosed MSM, condomless sex (CLS) with HIV-serodifferent partners (CLS-D) was considered the main HIV transmission risk before evidence of the favourable impact of antiretroviral treatment (ART).

Using data on HIV-diagnosed MSM from the ASTRA study (2011-2012), this thesis assessed: (i) prevalence of different types of CLS, including CLS-D with appreciable risk of HIV transmission (accounting for ART/viral load); (ii) associated co-factors (socio-demographic, lifestyle, psychological, HIV-related); (iii) prevalence and factors associated with other sexually transmitted infections (STIs), and subsequent risk of hepatitis C virus (HCV) co-infection.

Among 2189 HIV-diagnosed MSM, 38% had recent CLS; 16% had CLS-D; only 4% had CLS-D with appreciable HIV transmission risk. These CLS measures tended to be associated with younger age, more recent HIV diagnosis, and not being on ART, and were strongly associated with recreational drug and polydrug use (which were prevalent). When classifying MSM into mutually exclusive categories, 36% did not have sex in the past three months; 25% had condom-protected sex only; 22% had CLS with HIV-seroconcordant partners only ('CLS-C without CLS-D', which may indicate HIV-serosorting); 16% had CLS-D. Chemsex-associated drug use and disclosure of HIV-status to new sex partners were more common among MSM who had 'CLS-C without CLS-D' compared to CLS-D. Over 10% of MSM had recent STI co-infections. Recreational and injection drug use, CLS, and multiple partners were associated with pre-existing STIs, with initial evidence of association with incident HCV.

Consideration of different types of CLS among HIV-diagnosed MSM demonstrated differing implications for prevention of HIV versus other STI transmission. Expansion of ART use should further impact favourably on HIV transmission risk. There is a need for focus on harm reduction in recreational drug use and prevention of STI co-infections among HIV-diagnosed MSM.

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GLOSSARY OF TERMS

ACASI	Audio computer assisted self-interviewing
AIDS	Acquired Immune Deficiency Syndrome
Anti-HCV	Antibody to hepatitis C virus
aPR	Adjusted prevalence ratio
ART	Antiretroviral therapy
ASTRA	Antiretrovirals, Sexual Transmission Risk and Attitudes study
ATN	Adolescent Medicine Trials Network for HIV/AIDS Interventions
BASHH	British Association for Sexual Health and HIV
BHIVA	British HIV Association
bSTIs	Bacterial sexually transmitted infection
CASCADE	Concerted Action on SeroConversion to AIDS and Death in Europe
CASI	Computer assisted self-interviewing
CD4	Cluster of differentiation 4
CI	Confidence interval
CLS	Condomless sex
CLS-C	Condomless sex with HIV-seroconcordant partner(s)
CLS-D	Condomless sex with HIV-serodifferent partner(s)
CT	Chlamydia trachomatis
CYPs	Cytochorome proteins
DAA	Directly acting agents
DDI	Drug-drug interaction
DNA	Deoxyribonucleic acid
EDD	Erectile dysfunction drugs
EIA	Enzyme linked immunoassays
ELISA	Enzyme-linked immunoabsorbent assay
EMIS	European Men who have sex with men Internet study
FSSQ	Functional Social Support Questionnaire
FU	Follow-up
GAD-7	Generalised Anxiety Disorder 7-item scale
GBL	gamma-Butyrolactone
GCPS	Gay Community Periodic Surveys
GHB	gamma-Hydroxybutyric acid
GMSHS	Gay Men's Sexual Health Surveys
GMSS	Gay Men's Sex Survey
GUD	Genital ulcer disease
GUM	Genitourinary Medicine
GUMCAD	Genitourinary Medicine Activity Database
HAART	Highly active antiretroviral therapy
HARS	HIV and AIDS reporting system
HBV	Hepatitis B virus infection
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus infection
HIV	Humman Immunodeficiency Virus
HOPS	HIV Outpatient Study
HPV	Human papillomavirus
HSV	Herpes simplex virus
IDU	Injection drug use

INSTI	Integrase strand transfer inhibitor
IQR	Interquartile range
IR	Incidence rate
IRR	Incidence rate ratio
LGV	Lymphogranuloma venerum
LISA	Longitudinal Investigations into Supportive and Ancillary health services
LSD	lysergic acid diethylamide
MACS	Multicenter AIDS Cohort Study
MDMA	3,4-methylenedioxy-methamphetamine
MMP	Medical Monitoring Project
MNL	Multinomial logistic regression
MSM	Men who have sex with men
MTCT	Mother-to-child transmission
NATSAL	National Survey of Sexual Attitudes and Lifestyles
NG	Neisseria gonorrhoea
NGU	Non-gonococcal urethritis
NHBS	National HIV Behavioural Surveillance System
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NNRTI	Non-nucleoside reverse transcriptase inhibitors
NRTI	Nucleoside reverse transcriptase inhibitors
NSU	Non-specific urethritis
OCS	Ontario Cohort Study
OR	Odds ratio
PEP	Post-Exposure Prophylaxis
PHE	Public Health England
PHI	Primary HIV infection
PHQ-9	Patient Health Questionnaire
PI	Protease Inhibirot
POCT	Point-of-care test
PR	Prevalence ratio
PrEP	Pre-Exposure Prophylaxis
PY	Person-years at risk
RCT	Randomised controlled trial
RITA	Recent Infection Testing Algorithm
RNA	Ribonucleic acid
RT	Reverse transcriptase
SD	Standard deviation
SHCS	Swiss HIV Cohort Study
SMART	Strategies for Management of Antiretroviral Therapy
SOPHID	Survey of Prevalent HIV Infections Diagnosed
START	Strategic Timing of Antiretroviral Treatment
STI	sexually transmitted infection
SUMIT	Seropositive Urban Men's Intervention Trial
SVR	Sustained virological response
TV	Trichomonas vaginalis
UAI	Unprotected anal intercourse
UK	United Kingdom
UK CHIC	UK Collaborative HIV Cohort Study
VL	HIV-RNA viral load
WHO	World Health Organization

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1 Introduction

1.1 Thesis aims

In order better inform HIV prevention strategies and clinical care in the current era of effective antiretroviral therapy (ART), there is a need for greater understanding of the sexual behaviour of HIV-diagnosed men who have sex with men (MSM), as well as the factors associated with sex that may pose a risk of transmission of human immunodeficiency virus (HIV) or other sexually transmitted infections (STIs). This thesis aims to ascertain the prevalence of specific sexual behaviours in HIV-diagnosed MSM in the United Kingdom (UK), with a particular focus on measures of condomless sex, including condomless sex with appreciable risk of transmission of HIV. The thesis aims to investigate factors associated with different types of condomless sex, including socio-demographic, psychological, HIV-related, and lifestyle factors. Prevalence of non-disclosure of HIV-serostatus to the social circle and to sexual partners is also investigated; the association of sexual non-disclosure with condomless sex is additionally examined. This thesis also aims to investigate the prevalence of, and factors associated with, other STIs (including hepatitis C virus, HCV) and the subsequent risk of incident HCV co-infection among HIV-diagnosed MSM. To address these aims, data from the Antiretrovirals, Sexual Transmission Risk and Attitudes (ASTRA) study is used, a cross-sectional UK study of HIV-diagnosed individuals attending HIV clinics (2011-2012), with an additional longitudinal component.

1.2 Thesis overview

Chapter 1 states the thesis aims and provides a background on HIV treatment and transmission. Evidence relating to HIV transmission risk is reviewed and an overview of the HIV epidemic in the UK is presented, with a focus on MSM.

Chapter 2 provides a literature review of studies examining the prevalence and correlates of condomless sex among HIV-diagnosed MSM since the introduction of widespread ART (1995-2016) in high-income countries.

Chapter 3 describes the methodology of the ASTRA study, on which thesis analyses are based, as well as the main statistical methods used. The characteristics of HIV-diagnosed MSM participating in ASTRA are described in detail and compared to the HIV-diagnosed population under care in the UK during 2011-2012.

Chapter 4 defines the main measures of sexual behaviour used in the thesis for HIV-diagnosed MSM from ASTRA (including different measures of condomless sex), and assesses their prevalence, inter-

relationships, and cross-sectional associations with socio-demographic, psychological, HIV- and ART-related factors.

Chapter 5 explores definitions of higher HIV risk condomless sex with HIV-serodifferent partners (CLS-D) by incorporating clinical criteria that could affect HIV infectiousness. The resulting prevalence of higher HIV risk CLS-D is assessed among ASTRA MSM.

Chapter 6 investigates the prevalence and co-factors associated with of recreational drug use and polydrug use among HIV-diagnosed MSM in ASTRA. The association of recreational drug use with condomless sex and other measures of sexual behaviour is examined.

Chapter 7 examines the prevalence of HIV serostatus non-disclosure within the social context, to a stable partner, and to new sexual partners among HIV-diagnosed MSM in ASTRA. Cross-sectional associations of non-disclosure with socio-demographic, psychological, and HIV-related factors are determined. The association of non-disclosure with measures of sexual behaviour is also evaluated.

Chapter 8 assesses the prevalence and factors associated with self-reported STI co-infections. In the subgroup of HIV-diagnosed MSM with clinical data linked to the ASTRA questionnaire, prevalence and incidence of hepatitis C virus (HCV) is examined. Cross-sectional and prospective associations of sexual behaviour and other factors with prevalent and incident HCV are assessed.

The literature review presented in chapter 2 provides background to the thesis aims, and in particular serves as a review for results chapter 4. Results chapters 5 to 8 each include additional literature reviews relevant to the objectives of the specific chapter, and end with a discussion of results in the context of other literature.

Chapter 9 summarises the findings and conclusions from each chapter and discusses limitations and implications of these findings.

1.3 Background

Since the beginning of the HIV epidemic in 1981, a total of 78 million individuals (95%CI 71-87 million) have acquired HIV, and 39 million (35-43) have died of AIDS-related diseases.[1] Thirty-five years after the isolation of HIV, antiretroviral therapy (ART), technological and research advances in the understanding of transmission dynamics and determinants have transformed HIV from a 'death sentence' to a treatable chronic condition.[2] The life expectancy of people living with HIV in the UK has dramatically increased since the introduction of effective ART, increasing by about 10 years during the ART era. Modelling studies now show that the life expectancy of HIV-positive MSM in high-income countries with extensive access to ART and HIV care is 75 years.[3,4]

HIV circulates in body fluids of an HIV-positive person not on suppressive ART, including blood, cerebrospinal fluid, semen, rectal and cervical/vaginal fluids, and breastmilk. Therefore, transmission of HIV may occur through anal or vaginal sex, from a mother to child during pregnancy, birth, or breastfeeding, by sharing needles, syringes, or receiving blood transfusions/products contaminated with HIV, and by occupational exposure to HIV (needlestick injuries in healthcare workers).[41] The virus is not spread by casual or social contact (sharing utensils, toilets, air space, swimming pools) with HIV-positive people). Risk of transmission varies by mode of exposure and is dependent upon the concentration of HIV in body fluids.[2,8,42]A detailed overview of the origins, biology, and natural history of HIV is provided in Appendix V. The following sections (1.3.1-1.3.5) provide a historical background to the use of ART for treatment and prevention of HIV.

1.3.1 Aims of antiretroviral therapy (ART)

The principal aim of life-long continuous ART is to prevent mortality and morbidity associated with chronic HIV infection. This is attained by achieving and maintaining continuous suppression of HIV viral replication, referred to as 'undetectable viral load' (VL), meaning a lack of HIV-1 RNA detection below the lower limit, usually <50c/mL. This allows recovery of immune function, measured by the number of CD4 T-cells in a cubic millimetre of blood (CD4 count). Normal CD4 count ranges between 500 and 1200cells/mm^3, and opportunistic infections most prevalent below 200cells/mm^3. Recent evidence from cohort studies in the UK[5] and the USA[6] shows that individuals who started ART during 2008–2010 with CD4 counts above 350cells/mm^3 one year after ART initiation have estimated life expectancy approaching that of the general population.[6]

A further aim of ART is the prevention of onward sexual transmission of HIV through the reduction of plasma HIV-RNA (viral load) levels, referred to as Treatment as Prevention (TasP). Longitudinal studies and randomised controlled trials (RCTs) have estimated the risk of transmission to be extremely low

among heterosexual[7,8], and more recently, among MSM[9,10] serodifferent couples (in which one partner is HIV-positive and the other is HIV-negative) when the HIV-positive partner is on effective ART. In addition, HIV-negative partners can use antiretroviral drugs in order to prevent acquisition of HIV either before exposure to the virus (pre-exposure prophylaxis, PrEP) or after (post-exposure prophylaxis, PEP).

1.3.2 Initiation of ART for clinical benefit

The correct timing of start of ART for a person diagnosed with HIV has been a major point of debate. The clinical decision of when to initiate ART in people who have not undergone previous ART (were ART-naïve) has traditionally been guided by CD4 count levels, with recommended CD4 thresholds tending to increase as new guidelines were introduced over time.

From 2008, the British HIV Association (BHIVA) recommended that individuals with chronic HIV infection start ART at or below CD4 count of 350cells/mm^3.[11] This guideline was based on evidence from large-scale cohort studies carried out in the mid to late 2000's, demonstrating the higher risk of progression to AIDS and death among those who delayed ART initiation until their CD4 was below 350 cells/mm^3, compared to those who started ART at CD4 count above 350cells/mm^3.[12–14] In early 2015, the Tempano ANRS trial (2008-2015) disseminated results; a total of 2056 HIV-diagnosed people in the Ivory Coast were randomised to either immediate ART (provided CD4 count was below 800cells/mm^3) or deferred ART according to WHO criteria.[15] During the course of the study, WHO guidelines for ART initiation changed the CD4 count criteria multiple times, from 200cells/mm^3 in 2008-2009, to 350 in 2009-2012, and to 500 from 2012-2014. Tempano found that early initiation of ART at CD4 counts above 500cells/mm^3 independently resulted in a 44% reduction of severe HIV-related illnesses and 35% reduction in risk of death, compared to deferred ART.[15] The comparator group for much of the follow-up time, however, was the group deferred to ART initiation at or below 200cells/mm^3 as a limited number of people were randomised after the WHO raised the CD4 count criteria to 350cells/mm^3. The median CD4 count in the comparator group was thus much lower than the 2008 BHIVA guidelines.

In May 2015, interim results from the multi-national START randomised trial (2009-2013) offered definitive proof that initiation of ART at CD4 count higher than 500cells/mm^3 provided 57% reduced risk of developing AIDS, other serious non-AIDS event, or death over three years, when compared to deferring ART until CD4 count decreased to 350cells/mm^3.[16]As a result, treatment guidelines worldwide were amended to recommend ART initiation regardless of CD4 count, proposing the absolute risk be considered in individual decisions.[17]

1.3.3 Initiation of ART for prevention of HIV transmission: Evidence among heterosexual men and women

In the mid-2000's, longitudinal studies of heterosexual serodifferent couples estimated a reduction of 80% in risk of HIV transmission attributed to use of ART.[18,19] A meta-analysis of longitudinal studies on HIV transmission according to use of ART found that among 11 cohorts and 5021 heterosexual serodifferent couples the rate of overall transmission from the HIV-positive partner on ART was 0.46 per 100 person-years (95%CI 0.19-1.09) based on five seroconversions; there were no observed transmissions from individuals on treatment and with VL below 400c/mL.[20]

By 2011, robust evidence from RCTs indicated that ART could be beneficial in reducing HIV transmission if initiated immediately, irrespective of CD4 count.[7,21] The multinational HIV Prevention Trials Network (HPTN) RCT (2007-2010) demonstrated a benefit of early versus deferred ART initiation (at baseline with CD4 count ≥350cells/mm^3 or after two consecutive CD4 counts of ≤250cells/mm^3, respectively) in the reduction of sexual transmission of HIV.[7] Among 1763 serodifferent heterosexual couples in HPTN052, 28 genetically-linked HIV transmissions occurred, only one of which was in the early ART initiation arm. This represents a relative reduction in the risk of HIV transmission of 96%.[7]As the CD4 count threshold in the deferred arm was substantially lower than that in the 2008 BHIVA guidelines, it was considered that HPTN052 may overestimate the benefit of immediate treatment compared to initiation at CD4 count below 350cells/mm^3.

The risk of HIV transmission is greater for anal sex than for vaginal sex (further discussed in section 1.4.5).[22] Hence, the degree to which these results apply to anal sex (among MSM or heterosexuals) was uncertain. In addition, prevalence of condom use was high in HPTN-052, with 5% of HIV-diagnosed participants reporting condomless sex in the past week.[7]

1.3.4 Initiation of ART for prevention of HIV transmission: Evidence among men who have sex with men

The best available evidence for use of ART to prevent transmission of HIV among MSM derives from two cohort studies, PARTNER phase 1 (2010-2014) and *Opposites Attract* (2012-2015). PARTNER is an international study of serodifferent couples who report condomless anal sex and the HIV-positive partner is on ART.[23] The study aims to assess the risk of transmission from the HIV-positive partner on ART with when viral load (VL) is below 200c/mL.[9] At baseline and every six months, both partners complete questionnaires on sexual risk behaviour, the HIV-negative partner is tested for HIV, and the HIV-positive partner's VL is measured. By 2016, phase 1 of PARTNER had recruited 1166 couples, of whom 888 (38% MSM couples) contributed a total of 1238 couple-years follow-up (CYFU).[24] The interim results reported no phylogenetically linked transmissions of HIV, despite 22,000 CLS acts among MSM

and 36,000 vaginal or anal CLS acts among heterosexuals. PARTNER gave a rate of within-couple HIV transmission of 0/100 CYFU (95%CI 0.00-0.30). For MSM, the upper confidence limit of the estimated transmission risk for all sex was 0.84/100 CYFU; for anal CLS, the upper bound was 0.71/100 CYFU (combining heterosexual and MSM data) and 2.70/100 CYFU for MSM who had receptive anal CLS with ejaculation.[9] These results were extremely important, but included fewer receptive anal CLS acts compared to all other sex acts (approximately 7750 for receptive CLS vs 11700 for insertive CLS). For this reason, phase 2 of PARTNER (2014-2017) continues follow-up of MSM couples in order to accrue a larger sample size and increase precision for the estimate of transmission risk for receptive anal sex, especially with ejaculation. *Opposites Attract* is a prospective cohort study of serodifferent MSM partnerships in Australia, Thailand, and Brazil, who report regular condomless anal sex and the HIV-positive partner has VL< 200c/mL.[25] Unlike the PARTNER study, which required all HIV-positive partners to be on ART, 82.4% were on ART in *Opposites Attract*. Preliminary results (late 2014) among 88 MSM couples reporting condomless anal sex with 91 CYFU showed no linked HIV transmissions.[26] The upper bound of the 95%CI for the rate of transmission was 4.06/100 CYFU for all CLS, and 6.46/100 CYFU for receptive CLS. The study reported much higher upper risk bounds compared to PARTNER, likely because of less cumulative total person time at risk accrued. Data from both PARTNER and *Opposites Attract* has added substantial evidence that the rate of HIV transmission among MSM is extremely low when the HIV-positive partner is on ART with suppressed viral load (<200c/mL). Ongoing follow-up will be important in better defining the risk of transmission according to type of condomless anal sex.

1.3.5 Initiation of ART for prevention of HIV acquisition

The short-term use of antiretroviral drugs by HIV-negative individuals following high-risk exposure to HIV (post-exposure prophylaxis) has been recommended since 1990. Randomised trials of antiretroviral drug use prior to sexual exposure to HIV (pre-exposure prophylaxis) have recently demonstrated the protective effect against HIV acquisition.

1.3.5.1 Post-exposure Prophylaxis (PEP)

Post-exposure prophylaxis (PEP) is now accepted as a standard of care for both occupational and non-occupational exposures (via condomless sex or sharing of needles).[27] This is based on limited evidence from one case-control study of healthcare workers, which demonstrated that ART can prevent chronic HIV infection if administered within a short time following exposure to the virus.[28] The WHO recommends PEP initiation with a three-drug ART regimen within 72 hours of exposure, for a period of 28 days.[29]

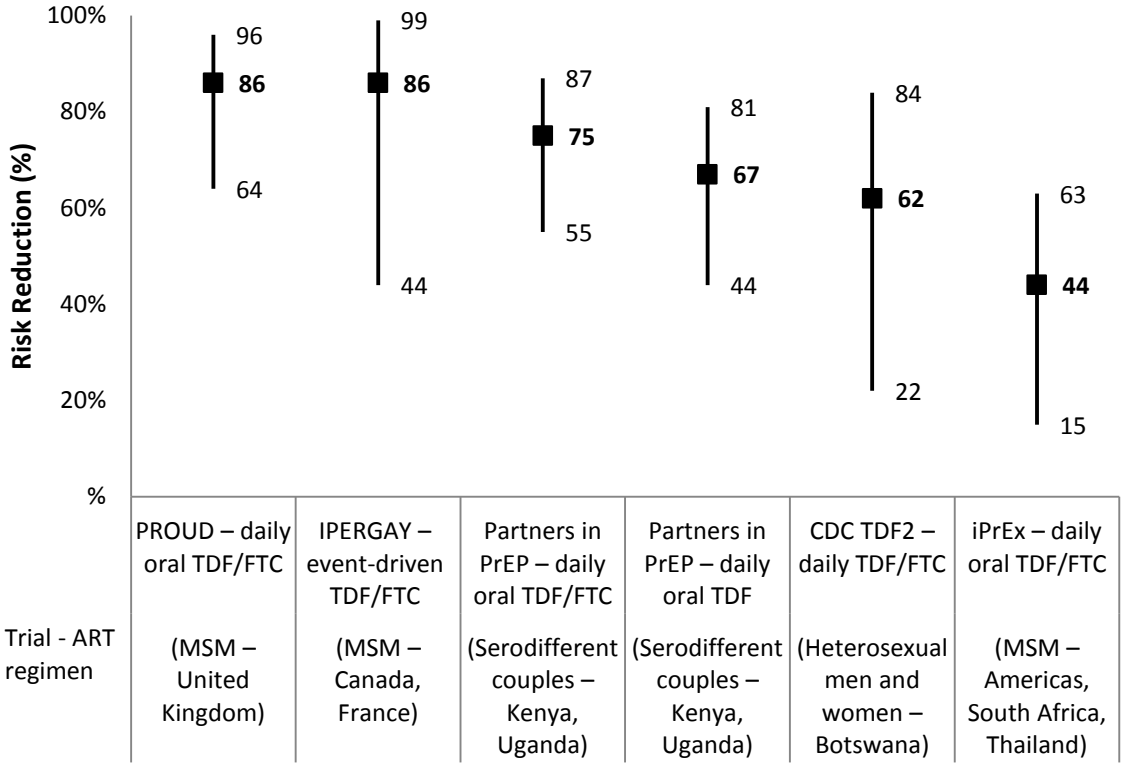
1.3.5.2 Pre-Exposure Prophylaxis (PrEP)

The provision of antiretroviral drugs to HIV-negative individuals before exposure to HIV (pre-exposure prophylaxis, PrEP) has been shown to reduce the risk of acquiring HIV. A number of trials of PrEP have been conducted, with differing strategies, including: oral PrEP taken before sex as a pill, topical PrEP as a

vaginal gel or ring or rectal gel impregnated with ART, or long-acting injection PrEP. Randomised trials carried out in sub-Saharan Africa in the late 2000's showed that topical PrEP has a small protective effect (from 6-39%) against HIV acquisition. The modest benefit shown is likely due in part to low adherence but may also be due to other biological factors.[30–33] Five large RCTs have provided evidence for the substantial protective effect conferred by oral PrEP and are summarised in Figure 1.1.[34–37] On the basis of these studies, the WHO and the US Centers for Disease Control and Prevention approved the use of Truvada (emtricitabine/tenofovir) among "high risk" groups in July 2012.[38] The PROUD trial (2012-2016) randomised HIV-negative MSM attending sexual health clinics in England to immediate versus deferred Truvada (at enrolment versus after 12 months). Early results showing high efficacy of immediate PrEP (86%, 95%CI 64-96%) lead to early discontinuation of the trial in 2014, and participants in the deferred arm were offered immediate PrEP.[36] Coupled with similar efficacy reported in the French IPERGAY trial (86%) which used intermittent as opposed to continuous dosing in PROUD, these results supported early access to PrEP among those at high risk of acquiring HIV.[37]

A recent modelling study estimated that the provision of PrEP along with expanded testing coverage among HIV-negative MSM in the UK could prevent more than 7000 new HIV infections before 2020.[39] Ongoing randomised trials, such as the PREP-5 in Canada and EPIC-NSW in Australia, will explore implementation of PrEP in real-world settings among MSM, with relation to its effectiveness, acceptability, and impact on STIs. Further strategies for PrEP, including daily versus intermittent use, are examined in ongoing randomised trials, such as IPERGAY in France and AMPrEP in the Netherlands.[40] A summary of the current status of PrEP in the UK is provided in section 1.5.4.1.

Figure 1.1: Summary of oral PrEP efficacy (95%CI) from randomised trials of among populations including MSM.[34–37]



CDC: Centers for Disease Control; TDF/FTC: Emtricitabine/tenofovir

1.4 Sexual transmission of HIV

HIV transmission by sexual intercourse accounts for nearly 90% of infections worldwide.[43] A discussion of other modes of HIV transmission is provided in Appendix V. The probability of infection through sex depends on a multitude of biological and behavioural factors.[8,44–49] These are discussed below and include (in addition to use of ART discussed in sections 1.3.2-1.3.5): stage of HIV infection and associated viremia, physiological susceptibility to HIV, presence of ulcerative STIs in both HIV-negative and HIV-positive partners, whether condoms are used, type of sex act and positioning.

1.4.1 Effect of HIV-RNA on transmission

Viral load (VL) is the strongest predictor of the risk of HIV transmission. The first evidence to emerge on the role of VL was in the landmark Rakai Project cohort study (1994-1999), which followed 415 serodifferent heterosexual couples for 30 months; the couples were not on ART (ART-naïve) and none reported consistent condom use during vaginal sex (none of the partners reported anal sex during follow-up).[8] The incidence of HIV infection in the HIV-negative partners (seroconversion) was 11.8 per 100 person-years based on 90 new infections and did not differ by gender of the index partner (male-to-female or female-to-male transmission).[8] HIV-positive participants whose partners seroconverted were found to have higher serum VL compared to those whose partners did not seroconvert. A dose-response

relationship was also found between higher VL (≥1500c/mL) and increased risk of transmission.[8] Although transmissions in this study were not genetically confirmed, the data presented were crucial in assessing transmission risk by VL concentration.[50] Subsequent studies further corroborated these findings among serodifferent heterosexual ART-naïve couples in Africa.[51,52] The Partners in Prevention Transmission Study (2004-2008) modelled the relationship of plasma VL and risk of heterosexual transmission in genetically-linked transmission events.[52] This study found the incidence of HIV to be 2.3 per 100 person-years based on 108 genetically linked seroconversions. In addition, a linear relationship was observed between log risk of HIV transmission and $\log_{10}$ plasma HIV RNA concentrations (log-linear relationship); an average decrease in plasma VL of 0.74$\log_{10}$c/mL (95%CI 0.60-0.97 $\log_{10}$c/mL) was associated with a reduction in heterosexual transmission risk by 50%. [52]

1.4.2 Effect of stage of HIV infection on transmission

Primary HIV infection (PHI) is the first stage of HIV disease, characterised by active viral replication and CD4 cell depletion; it is a major driver of the HIV epidemic, estimated to cause a large proportion of new infections.[53,54] AIDS refers to the point in disease progression when CD4 counts decline to critical levels (<200 cells/mm^3) resulting in opportunistic infections and clinical immunodeficiency. The risk of sexual transmission of HIV is highest during PHI and AIDS, as sustained viral replication and ensuing high-level viremia boost the host's infectiousness.[55] As most HIV infections are not diagnosed during the acute stage, the HIV-positive person, being unaware of their seropositive status, may continue to have condomless sex. This may result in clusters of HIV transmissions, especially if there is high level of concurrent sexual partnerships.[56]

A stochastic modelling study from the UK found that in 2010 a median of 48% (90%CI 34-62%) of new infections among MSM were derived from MSM with undiagnosed PHI and 34% (22-46%) from MSM with undiagnosed asymptomatic infection (clinical latency).[57] Later studies among MSM from Switzerland and Denmark also reported similar findings.[4,58]

1.4.3 Effect of host susceptibility on transmission

Langerhans cells express CD4 co-receptors on their membrane, and have thus been identified as a primary target for HIV infection during sexual transmission. These cells are accumulated in mucous membranes (cervix, sperm and seminal plasma, as well as the foreskin and frenulum of the penis[44,59]) which allow contact with free virus from secretions, rather than requiring HIV to cross epithelia to infect them.[60] The host's degree of infectivity depends on immune system activation, which may increase the number and receptivity of susceptible Langerhans cells, or affect viral replication within infected cells.[44] Male circumcision also substantially reduces the risk of acquiring HIV, by up to 53%,[61–63] due to removal of foreskin tissue on the penis, which is rich in Langerhans cells.

1.4.4 Effect of other sexually transmitted infections on transmission (STIs)

A detailed review and discussion of the role of STIs in increasing the risk of HIV transmission is provided in Chapter 8. Briefly, STIs increase the risk of both HIV acquisition (in HIV-negative individuals) and transmission (from ART-naïve HIV-positive individuals) through a number of biological mechanisms (discussed in section 8.2). Much of the evidence on STI/HIV co-infection comes from studies performed prior to the era of widespread ART. It remains unclear whether co-infection with HIV and other STIs carries higher risk of HIV transmission if the HIV-positive partner is on virally suppressive ART.[64,65]

Hepatitis C virus (HCV) remains of particular concern for HIV-positive individuals. HCV is most efficiently transmitted through blood contact, primarily by injection drug use (IDU) (section 8.2.7.1). However, sexual transmission of HCV is ongoing among HIV-positive MSM (not reporting IDU) in North America and Europe.[66,67] The reasons for this increase are multifactorial (further discussed in Chapter 8) and most likely associated with sexual practices which lead to mucosal trauma and bleeding.[68] The effect of HCV co-infection on onwards transmission of HIV remains unclear, particularly in the context of HIV suppression.

1.4.5 Effect of type of sex on transmission

The risk of HIV transmission varies according to the type of sex (anal or vaginal), position during sex (insertive versus receptive partner), and specific sexual practices.

Consistent condom use is recognised as one of the safest, most cost-effective, and readily available methods of reducing the risk of HIV transmission.[69,70] This section refers to condomless anal or vaginal sex (CLS), in other words sex during which condoms are not used. Anal CLS is associated with a greater risk of HIV transmission compared to vaginal CLS (1.69% per act versus 0.18% respectively).[71] This difference is due to greater susceptibility of rectal mucosal membranes to HIV as well as to traumatic abrasions when compared to cervicovaginal membranes.[22] Oropharyngeal membranes are considerably less susceptible to HIV infection compared to cervicovaginal or rectal membranes (due to thicker epithelial layers and low CD4 cell concentrations); no HIV transmissions have been recorded via oral CLS to date.[72] For this reason, oral CLS is not discussed in this thesis (and was not a part of the ASTRA study questionnaire).

Partner positioning during condomless anal sex is also associated with risk of HIV transmission. Receptive anal sex (when the HIV-negative partner is in receptive or 'bottom' position and the HIV-positive partner is in the insertive or 'top' position) carries a greater risk of HIV acquisition compared to insertive anal sex (when the HIV-positive partner is in bottom position and the HIV-negative partner is the top position). Pooled meta-analysis data from 16 studies shows that the risk of HIV acquisition is highest during CLS when the HIV-negative partner is receptive rather than insertive, among

heterosexuals and MSM alike. Specifically, the per-partner transmission probability for receptive CLS has been estimated to be 40.4% (95%CI 6.0-74.9%) compared to 21.7%(0.2-43.3) for insertive CLS.[22] In addition, risk of transmission is increased when the HIV-positive partner is in insertive position and ejaculates inside the receptive HIV-negative partner.[73]

In addition to anal CLS, other sexual practices may also facilitate transmission of HIV; those associated with mucosal trauma, such as the manual insertion of digits in the rectum ('fisting') or use of sex toys, may lead to bleeding, which can increase risk of transmission of HIV and other STIs. In addition, frequency and duration of sex acts as well as high number of sexual partners are associated with greater transmission risk, although the relative contribution of each factor remains unclear.[43]

1.5 HIV epidemiology

1.5.1 The global HIV epidemic

A total of 36.7 million (95%CI 34.0-39.8 million) people were living with HIV globally in 2015, of whom 46% (43-50%) had access to ART.[74] New infections have decreased by 38% since 2001, with 2.1 million (1.8-2.4 million) people becoming newly infected with HIV in 2015. Since 2010, there have been no declines in the number of new HIV infections among adults. AIDS-related deaths have also decreased by 45% since the peak in 2005. In western and central Europe and North America there were 2.4 million people (2.2-2.7 million) living with HIV, and 91,000 (89,000-97,000) new infections in 2015.

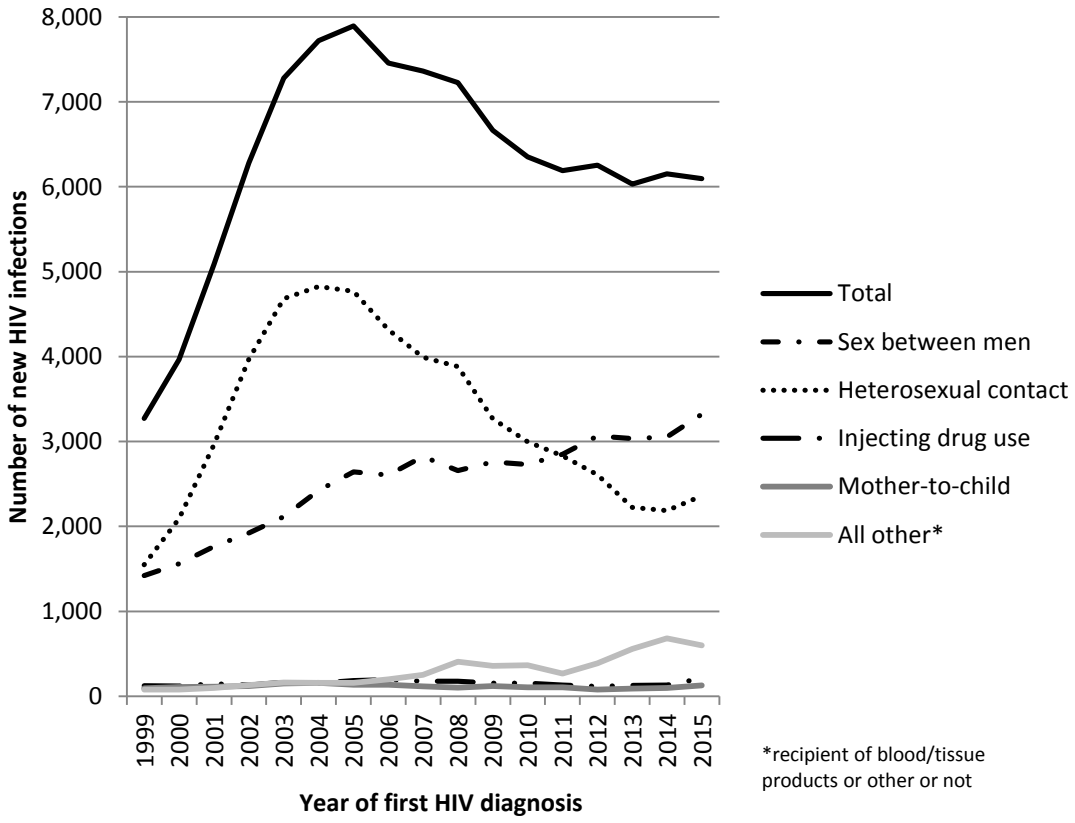
1.5.2 The UK HIV epidemic (until 2015)

The number of people living with HIV in the UK had been steadily increasing between 2010 and 2015. This was due to effective ART leading to longer life expectancy of people living with HIV, together with ongoing HIV transmission. In 2015, there were an estimated 101,200 (95%CI 97,500-105,700) people living with HIV in the UK, with an overall HIV prevalence of 1.6 per 1000 population (and 2.1 per 1000 among people aged 15 to 74 years).[75] Among people living with HIV, 47,000 men (44,200-50,900) had acquired HIV through sex with other men, 19,600 men (18,600-21,500) and 29,900 women (28,900-31,000) had acquired HIV through heterosexual sex. The majority of HIV-positive heterosexuals (60%) were of black African ethnicity, while the majority of MSM (86%) are white. These estimates include individuals who are unaware of their HIV infection (are undiagnosed) and are thus at risk of unknowingly transmitting HIV. Through a multi-parameter statistical model fitted to unlinked anonymous sero-surveillance and behavioural survey data, Public Health England estimates the proportion of undiagnosed individuals to be 13% (10-17%) in 2015, a decline from 25% (19-31%) in 2010.[76] As HIV develops into a chronic condition, the age of people accessing care for HIV has been increasing, with almost 17% now aged 50 years or over.

HIV treatment coverage in the UK is high and in line with the UNAIDS "90-90-90" goals,[77] whose target is that 90% of people living with HIV know their HIV status, 90% of diagnosed are on ART, and 90% of those on ART are virally suppressed by 2020. In 2015, among all people living with diagnosed HIV, 96% were on ART, of whom 94% were virally suppressed (VL<200c/mL).[75]

The overall trend of new HIV diagnoses in the UK declined between 2005 and 2010, and has since stabilised at around 6,000 newly diagnosed individuals annually.[78] This corresponds to a new diagnosis rate of 0.10 per 1,000 population. (Figure 1.2) The number of new diagnoses among heterosexuals has declined by almost half since 2005; among MSM, the number of new diagnoses increased from 2006 until 2014 and has remained high in 2015. During 2015, 6,095 people were newly diagnosed with HIV in the UK; 3,320 men acquired HIV through sex with other men and 2,360 men and women acquired HIV through heterosexual contact. Among newly diagnosed individuals, the prevalence of a late stage HIV diagnosis (with CD4 count <350 cells/mm^3 within three months of diagnosis) has steadily declined from 56% in 2005 to 29% in 2015. Late stage HIV is associated with ten-fold higher risk of death within a year of diagnosis,[79] making timely diagnosis critical in ART initiation and prevention of onward HIV transmission.

Figure 1.2: Number of new HIV infections by exposure category, sex, and year of diagnosis
Adapted from [80]



1.5.3 The UK HIV epidemic among men who have sex with men (until 2015)

The HIV epidemic in the UK remains concentrated among gay, bisexual, and other men who have sex with men. As effective ART has led to a reduction in premature deaths from HIV and transmission of HIV is ongoing among MSM, the number of MSM living with HIV had been increasing from 38,400 (34,300-43,800) in 2010 to 47,040 (44,219-50,860) in 2015.[75] HIV prevalence was one in 17 among MSM aged 15-44 years in 2015, a rate of 58.7 (51.2-68.0) per 1,000. Prevalence differs substantially by UK region, being higher in London compared to the rest of England and Wales (one in seven vs one in 25 respectively).[76] In 2015, 12% (7-19%) of MSM living with HIV were undiagnosed.[81] Although the prevalence of undiagnosed HIV infection among MSM has followed a decreasing trend since 2010, there was no evidence of a significant decline between 2013 and 2015.

Linkage and retention to HIV care following diagnosis is high among MSM in the UK, who accounted for 45% (n=38,432) of all individuals accessing HIV care in 2014.[78] Over 94% of all MSM living with HIV were receiving ART. Among MSM accessing care, almost 89% were receiving ART and 77% of those had an undetectable viral load. The median age at diagnosis among MSM was 33 years in 2015; over 80% of MSM newly diagnosed were of white ethnicity, 4% of black African or Caribbean ethnicity and 60% were born in the UK.

Despite high rates of HIV testing coverage in STI clinics and high prevalence of effective ART for HIV-diagnosed MSM, HIV transmission remained ongoing among MSM. The trend of new HIV diagnoses among MSM in the UK increased steadily from 1999 to 2015.(Figure 1.2) Even though the proportion of MSM newly diagnosed with late stage HIV has declined in the past decade, from 42% (n/N=948/2,255) in 2005 to 30% (777/2,628) in 2015, this remains high.[80] Similarly, almost 4% (121/3,055) of new diagnoses observed among MSM were reported as first AIDS diagnoses, and 7% (209/3,055) were reported among MSM who died.[81] Timely diagnosis of HIV infection among MSM thus remains a major challenge.

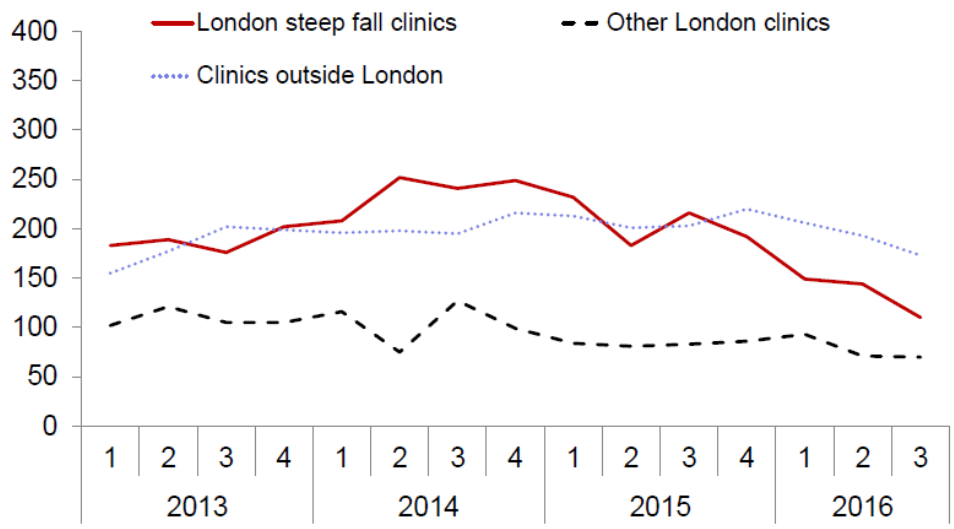
Individuals newly diagnosed with HIV may also receive blood testing by Recent Infection Testing Algorithm (RITA), which distinguishes between recent or established infection. Among 2,823 individuals tested by RITA in 2015, 1,589 were MSM, of whom, 429 (27%; 95%CI 25-29%) had been recently infected.[78] The high proportion of recently infected MSM may be attributable to more frequent HIV testing patterns compared to heterosexuals,[82] however, findings from RITA further highlight the issue of ongoing HIV transmission among MSM in the UK.

1.5.4 Changing epidemiology of HIV among MSM in the UK (2016 onwards)

1.5.4.1 Reduction in HIV diagnoses among MSM

In late 2016, five HIV clinics in London ('steep fall' clinics) observed a substantial fall in the number of new HIV diagnoses among MSM. (Figure 1.2)[85] In parallel, in London, there has been an extensive increase in the number of HIV tests conducted among both individuals attending for a new test as well as those attending for a repeat test at the at the same clinic in the last two years. The downturn in new HIV diagnoses among repeat testers also has an impact on the number of new diagnoses among new testers in these five HIV clinics. In other London clinics and in the rest of England, smaller declines in the number of HIV diagnoses have been observed. This may be due to the smaller scale of HIV testing conducted in these clinics, which is still not as effective in reducing the number of new HIV diagnoses, despite increases in HIV testing overall. By October 2017, an 18% decline in new HIV diagnoses was documented in the UK (between 2015 and 2016).[86] This decrease was concentrated among MSM and particularly in London, and was driven both by increased HIV testing and increased uptake of early ART.

Figure 1.3: New HIV diagnoses among MSM attending GUM clinics in England (2013-2016). From *'Towards Elimination of HIV amongst gay and bisexual men in the United Kingdom'*[85]



GUM: Genitourinary Medicine clinic; Steep fall clinics: >20% decrease in HIV diagnoses between October 2014 to September 2015 and October 2015 to September 2016, and >40 diagnoses during this period.

1.5.4.2 PrEP

In March 2016, NHS England announced that it would not commission PrEP for HIV prevention, considering "local authorities as the responsible commissioner for HIV prevention services". The National AIDS Trust (NAT) challenged the legality of this decision in the High Court and the Court of

Appeal, arguing that there is no legal impediment to NHS England funding PrEP. In November 2016 the Court of Appeal ruled in favour of NAT, confirming that NHS is obliged to give due consideration to commissioning PrEP. As a result, NHS England announced funding for a clinical trial evaluating real-world PrEP implementation among 10,000 participants at "high risk of HIV" across 70 GenitoUrinary Medicine (GUM) clinics over three years. The IMPACT trial began enrolment in October 2017 among eligible groups: HIV-negative individuals who report condomless sex, a recent STI, and/or use of recreational drugs and HIV-negative partners of an HIV-diagnosed person not virally suppressed. The trial aims to measure PrEP eligibility, uptake, and use among eligible GUM attendees, and to assess the impact of PrEP on new HIV diagnoses and STIs. Results are expected from 2020 onwards.

During this period, Scotland was making headway in provision of PrEP. In October 2016 an expert group of clinicians, public health practitioners, community representatives, and academics produced a report recommending PrEP to the Scottish Medicines Consortium (SMC), responsible for evaluating the cost-effectiveness of new licensed medications and advising NHS Boards accordingly.[83] In April 2017 the SMC licensed use of PrEP, making Scotland the first UK country to offer full PrEP provision through the NHS. An estimated 1700 individuals are eligible for PrEP in Scotland, of whom 58% are expected to present for use.

In April 2017, the All Wales Medicines Strategy Group advised the Welsh government against funding PrEP on the grounds of cost-effectiveness. Nevertheless, the Welsh government approved PrEP provision through the NHS, as part of a three year trial.[84] The PrEPARE trial aims to begin enrolling participants in all six GUM clinics in Wales by 2018.

1.6 Conclusion

This thesis uses data from the Antiretrovirals Sexual Transmission Risk and Attitudes (ASTRA) study, which was planned and conducted during a period of ongoing HIV transmission among MSM and changing HIV prevention messages (2008 onwards). The study was completed in 2012, prior to emergence of results from PARTNER, PrEP trials, the change in guidelines on ART initiation, and the first observed decline in HIV diagnoses in MSM in 2016. Nevertheless, the extent to which these advances in HIV treatment and prevention affect sexual behaviours of HIV-diagnosed MSM in the UK remains unclear. Findings from the ASTRA study (and this thesis) are important informing HIV clinical care and prevention effors and in planning and conducting future epidemiological research of sexual behaviours among HIV-diagnosed MSM.

2 Literature review of sexual behaviour among HIV-diagnosed men who have sex with men

2.1 Chapter aims

This chapter provides a context to the evolving concept of 'high risk sex' for HIV transmission among MSM living with HIV since the introduction of antiretroviral therapy (ART) in 1995. The overall aim is to review quantitative studies of sexual behaviour among HIV-diagnosed MSM in high income countries. A historical overview is first provided on the trends in prevalence of condomless sex (CLS) in the context of widespread ART use and the 2008 Swiss Statement. A literature review is then undertaken of studies carried out from 1995 to 2016 that have assessed the prevalence of and factors associated with condomless sex (including with HIV-serodifferent and HIV-seroconcordant partners) among MSM living with HIV in high income countries. Evidence is summarised according to study recruitment location; firstly, from studies of HIV-diagnosed clinic attendees (with a laboratory-confirmed positive HIV diagnosis), and secondly, from convenience samples including both HIV-diagnosed and/or HIV-positive MSM (either self-reported HIV-positive or tested HIV-positive as part of the study but were undiagnosed/unaware of their serostatus).

2.2 Terminology used

Condomless anal sex (CLS) has been the key indicator of HIV transmission risk in HIV behavioural research and surveillance, and as such, is considered a 'risky' sexual practice often referred to as 'unprotected intercourse' (UAI) in the literature.[87] Among people living with HIV the definition of 'high risk sex' is usually restricted to condomless anal or vaginal sex with an individual who does not have HIV (HIV-negative) or does not know their HIV status (CLS with an HIV-serodifferent partner, CLS-D). However, over recent years evidence has accumulated on the extremely low risk of HIV transmission during CLS-D when the HIV-positive partner is on ART with an undetectable HIV viral load (VL).[8,88] There is now understanding that condom use is not the only method of 'protection' against transmission of HIV infection, and that referring to condomless sex as 'unprotected' may be inappropriate. Hence, this thesis uses the more specific term CLS instead of UAI.

2.3 Condomless sex – historical overview of an evolving concept of transmission risk behaviour

2.3.1 Rationale

HIV incidence is driven by patterns of sexual risk behaviour between HIV-diagnosed, HIV-undiagnosed, and HIV-negative MSM.[89] Given the increase in uptake of HIV testing and ART use in the past decade, sustained HIV incidence among MSM points to increasing sexual risk behaviours during this period.[90] While the majority of HIV transmissions among MSM in the UK derive from HIV-undiagnosed MSM,[57,91,92] a sizeable proportion of transmissions is estimated to originate from HIV-diagnosed individuals; modelling studies have estimated the this to be up to 18% in the UK[57] and up to 29% in the Netherlands.[4] The prevalence of CLS may be continuously evolving in response to changes in HIV treatment and prevention. A number of important co-factors may also impact on levels of CLS (with HIV-negative/unknown and other HIV-positive partners) among HIV-diagnosed MSM: sociodemographic factors (for example, level of educational attainment, employment, financial status), lifestyle characteristics (use of recreational drugs and alcohol), HIV-related factors (time since HIV diagnosis, use of ART, beliefs regarding infectiousness), mental health issues (symptoms of depression and anxiety), and sexual partner characteristics. Understanding the drivers of various types of CLS among HIV-diagnosed MSM is important for targeting and informing prevention strategies and thus warrants further study.

2.3.2 Trends in prevalence of condomless sex in the context of introduction of combination ART (1996-2008)

The introduction of ART in 1995/1996 was accompanied by reported increases in prevalence of 'high-risk sexual behaviours' (such as CLS) among all MSM (HIV-negative and HIV-diagnosed or HIV-positive) in Europe and North America.[93–97] This raised concern about a possible causal effect, whereby HIV optimism among MSM (raised hope or optimism about HIV being readily treatable due to ART), may prompt complacency around 'safe sex' practices, and thus lead to increases in 'risky' sexual behaviours.[98] While a number of cross-sectional studies showed an association between HIV optimism (assessed using attitudinal questions on a questionnaire) and 'high-risk' sexual behaviours (defined as CLS) among HIV-negative and HIV-diagnosed MSM at the time,[95,99–101] they were unable to establish causality, or examine longitudinal trends. In the 'London Gyms' study of 455 HIV-positive (and 1776 HIV-negative) MSM surveyed annually in gyms and HIV outpatient clinics (1998-2001), there was evidence of a substantial increase, among HIV-diagnosed MSM, in prevalence of CLS and CLS-D.[98] (Further discussed in section 2.5.1) This increase, however, was unlikely to be explained by increases in HIV optimism, as there were no differences in prevalence of CLS between those reporting and those not reporting HIV optimism.[98] In addition, no interaction was found between year, HIV optimism, and CLS. The authors

hypothesize that other factors may account for the increasing trend in CLS, such as widespread access to the internet and sex-on-premises venues, and 'habituation to the risk of HIV' after two decades since the first AIDS reports. Levels of HIV optimism also remained stable despite the increasing evidence of the benefits of ART, which appears to indicate the absence of a causal dose-response relationship between HIV optimism and 'high-risk'.[102] During the early 2000's, evidence from studies of HIV-outpatients in Western Europe and USA found either no association between HIV optimism, ART use, and sexual risk behaviours,[98,103–107] or found that MSM on ART had lower prevalence of sexual risk behaviours compared to MSM not on ART.[108–110]

2.3.3 Use of ART and condomless sex among HIV-diagnosed MSM

With the introduction and widespread use of combination ART for treatment of HIV, many studies aimed to investigate whether ART use impacted on levels of CLS among people diagnosed with HIV. These studies showed that MSM on ART had lower prevalence of sexual risk behaviours compared to MSM not on ART.[100,103,104,108–116] A meta-analysis of 25 studies of HIV-diagnosed people recruited from HIV clinical settings in Western Europe, North America, and Australia (1996-2003) reported that the prevalence of CLS was not higher among HIV-positive people receiving ART (versus not receiving ART) or among HIV-positive people with an undetectable VL on ART (versus with detectable VL on ART).[117] Coupled with evidence from this meta-analytic review, results from the Strategies for Management of Antiretroviral Therapy (SMART) study (2002-2006) also showed no support for the hypothesis that receiving ART or having undetectable VL leads to 'risky' sexual behaviours (such as CLS and CLS-D) among MSM. The SMART trial was the first of its kind to compare continuous versus intermittent CD4-guided ART.[79] A USA sub-study of 875 HIV-diagnosed SMART participants (heterosexuals and MSM) found that those on ART at baseline had 30% lower odds of having CLS-D in the past two months compared to those not on ART.[112] Over two years of follow-up, the proportion of SMART participants reporting CLS and CLS-D in the past two months was similar in the two study arms, at about 13% and 5% respectively, and did not differ by gender or sexual orientation.[112]

2.3.4 Prevalence of condomless sex in the era following the Swiss Statement (2008 onwards)

Following the evidence that ART use was not associated with sexual behaviours with 'higher risk' of HIV transmission, the late 2000's saw fundamental changes in the awareness and understanding of HIV transmission risk.[118] Evidence continued to accumulate on the profound protective effect of virological suppression on ART on reducing an individual's HIV infectiousness, mostly from observational studies of heterosexual HIV-serodifferent couples.[8,19,119](Section 1.3) In 2008 an internationally renowned panel of Swiss HIV clinicians and scientists from the National HIV/AIDS Commission convened to summarise this information by issuing the "Swiss statement", which states that condom use can be discontinued in a stable HIV-serodifferent partnership if the following three conditions are met: (i.) the HIV-positive

partner is receiving ART with excellent adherence, (ii.) plasma HIV VL has been undetectable(<40 copies/mL) for six months or longer, and (iii.) both partners do not have another STI.[120] An HIV-diagnosed person who met these conditions was deemed "not sexually infectious (i.e. cannot transmit HIV through sexual contact.)"[121] The statement referred to monogamous heterosexual HIV-serodifferent partners having vaginal CLS. It attracted worldwide attention and was initially extremely controversial and not unanimously accepted by experts and health professionals, due to lack of evidence from randomised trials and concern about the potential impact on sexual behaviour among people with HIV.[122,123] Debate arose on whether condom use was necessary to prevent transmission of HIV if HIV replication was suppressed. It was hypothesized that the prevalence and patterns of 'risky' sexual behaviours among HIV-positive people (vaginal or anal CLS-D) could change as a result of raised awareness of the Swiss statement.[124] The only study finding evidence of the impact of the "Swiss statement" on changes in prevalence of CLS among HIV-diagnosed people is the Swiss HIV Cohort study (SHCS), which has enrolled HIV-diagnosed clinic attendees since 1988.[125] Retrospective analyses of over 2000 MSM in the SHCS indicate an increase in prevalence of CLS-D with stable and occasional partners (comparing periods 2000-2007 and 2008-2013).[124,126] In addition, among MSM with stable HIV-negative or HIV-unknown status partners, there was a significant association between having undetectable VL on ART and reporting higher prevalence of CLS-D. This indicates that HIV-diagnosed MSM may have adopted the belief that ART can be used to prevent sexual transmission of HIV. The "Swiss statement" may have elicited changes in the acceptability of CLS in Switzerland by making MSM more aware of the conditions for lower infectiousness. However, the increase in CLS-D prevalence may have also been due to a real change in sexual behaviours and liberalisation of attitudes towards CLS; hence it is difficult to disentangle whether the increase in CLS after the introduction of ART or after the "Swiss Statement" may have been a period or a cohort effect, or a mixture of both. [127]

In this context, the ASTRA study (discussed in Chapter 3) was designed as part of a program of research aiming to investigate whether a policy of early ART for all HIV-diagnosed people in the UK would be associated with a decline in HIV transmissions through a reduction in infectiousness of HIV-diagnosed people.(Section 1.3) There was concern that increased awareness of the protective effect of undetectable VL on HIV infectiousness may adversely impact on levels of CLS among MSM with HIV, and that increases in CLS may compromise or undermine the full potential impact of early treatment in reducing transmission. The ASTRA study aimed to understand the association between use of ART, perceived (self-reported) VL suppression, and sexual behaviours, in order to inform assessment of the public health impact of a possible strategy of early ART initiation.[89]

2.4 Literature review methods

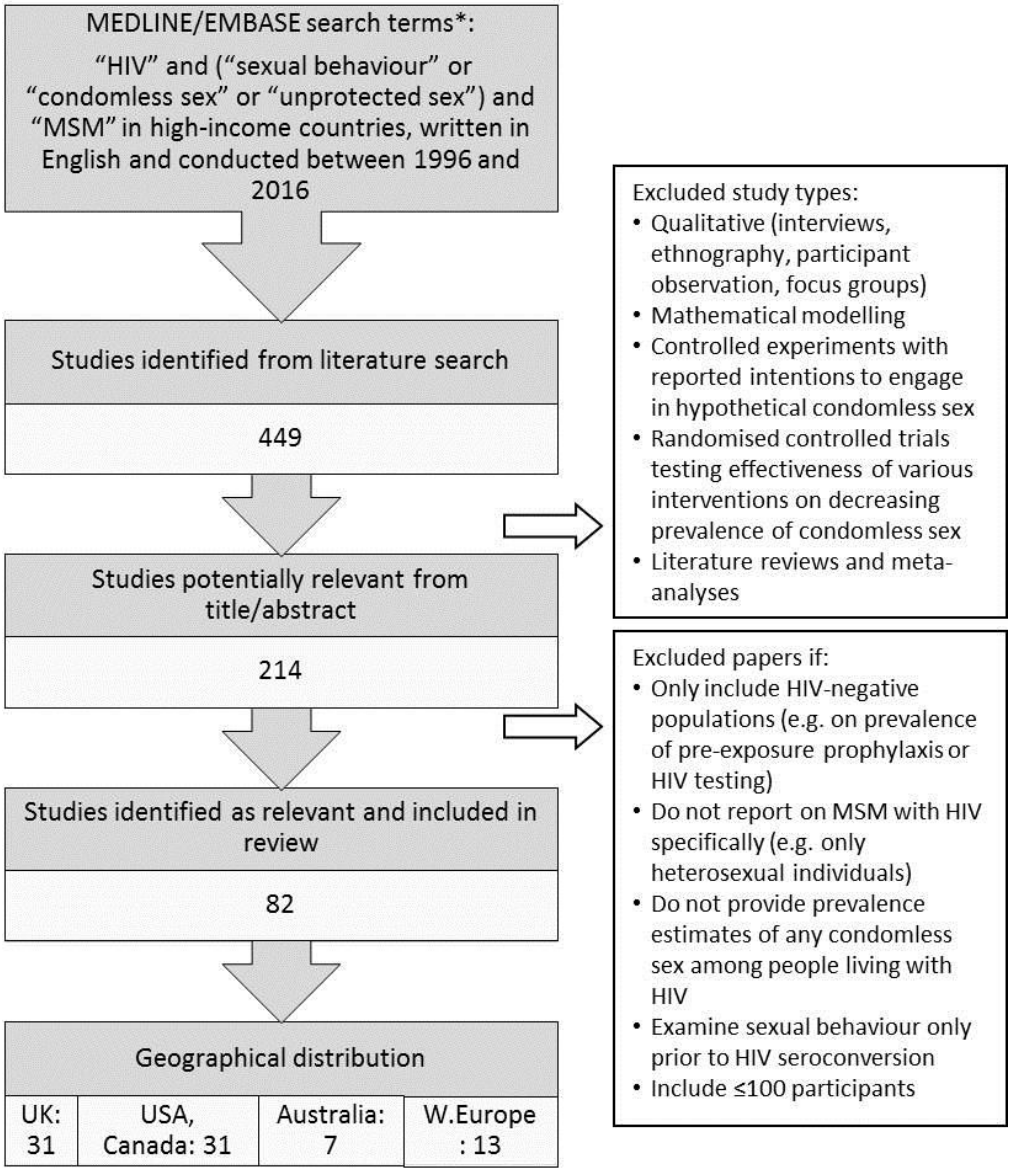
The aim of this literature review was to locate peer-reviewed research on the prevalence of and/or factors associated with CLS (any CLS, CLS with HIV-serodifferent or HIV-seroconcordant partners) among

MSM living with HIV in high-income countries. A search on MEDLINE and EMBASE (OvidSP version) was conducted in December 2014 and repeated in September 2016. (Search strategy shown in Appendix II and search results in Appendix III.) Specific inclusion criteria for this review were (Figure 2.1):

- Original research studies (cross-sectional, cohort, case-control studies, and randomised controlled trials),
- Reporting on the prevalence of and/or factors associated with CLS among MSM who are living with HIV,
- Conducted in North America (United States and Canada), Western Europe (including the United Kingdom), or Australia,
- Conducted between 1996 and 2016 (recruitment to have commenced no earlier than 1996),
- Have at least 100 HIV-diagnosed participants,
- Written in English

Exclusion criteria were: published systematic reviews and studies that *only* included: heterosexual individuals or transgender men living with HIV, HIV-negative or HIV-unknown status MSM, prison, sex worker, or paediatric/adolescent populations (under 18 years). A sequential search was conducted using thesaurus searching (medical subject headings, MeSH, and all items indexed with that heading) and textword searching (in titles, abstracts, article bodies, and keywords).(Figure 2.1) A manual assessment of retrieved publications (by reading the abstract or if needed, the full paper) was then conducted using inclusion and exclusion criteria.(Details in Appendix III) The methodological quality of each paper was assessed with regards to research design, study sample (response rate, representativeness of the study population), data collection (ascertainment of the dependent and independent variables), sources of bias (respondent bias, confounders), and data analysis. While a formal assessment of study quality was not conducted, studies were excluded if they did not meet eligibility and/or quality assessment criteria (and the reasoning was provided for each study in Table of Appendix III). An additional search was carried out on the Sigma Research website (http://sigmaresearch.org.uk/) in order to identify relevant reports which may not be published in peer-reviewed journals. Following this search strategy, a total of 82 papers (representing approximately 40 unique studies) were identified as relevant and included in the literature review.

Figure 2.1: Literature review diagram



See Appendices II and III for detailed search term strategy and results

2.5 Overview of evidence on prevalence of condomless sex among HIV-diagnosed MSM

2.5.1 Studies of HIV-outpatient clinics

Table 2.1 summarises evidence from 10 studies which have recruited HIV-diagnosed MSM in clinical settings (attending for HIV care in hospitals, clinics, or enrolled in clinical trials) in Western Europe or the USA since 1996, and have assessed the prevalence of various types of CLS.

The 'London Gyms' study (1998-2008) was one of the first to examine trends in sexual behaviour of HIV-diagnosed MSM in the UK.[128] This annual questionnaire survey of gym-attending MSM in London was part of a behavioural surveillance programme enrolling over 6000 MSM, of whom 16.5% were HIV-diagnosed and recruited from HIV outpatient clinics (remaining 63.8% were HIV-negative and 19.7% never tested, not discussed here).[129–131] Over the study period, there was a significant increase in prevalence of any CLS in the previous three months among 1001 HIV-diagnosed MSM in the clinic sample, however this masked more complex underlying trends; as shown in Figure 2.2, the prevalence of CLS-D (with HIV-negative of HIV-unknown status partners) in the past three months increased rapidly between 1998 and 2002 ($p<0.001$), and declined between 2003 and 2005 ($p<0.05$) returning to the level reported in 1998.[131] Other UK clinic-based questionnaire studies of HIV-diagnosed MSM that have incorporated measures of CLS-D include the 'Internet and HIV' and 'East London' studies, which found the prevalence of CLS-D in the previous three months to be 18.0% and 20.2% respectively.(Table 2.1)[103,132] A smaller cross-sectional study from HIV-outpatient clinics in London and South East England ('Switching study', 2005) examined the association between ART switching and psychological, clinical variables, and CLS; among 451 HIV-diagnosed MSM, 15% reported having CLS with a partner of unknown HIV-serostatus in the previous three months.[133]

During the late 2000's evidence from cross-sectional studies and probability samples from HIV-diagnosed MSM in the clinic setting in high-income countries suggested a plateau in the prevalence of CLS-D and an increase in the prevalence of condomless sex with other HIV-positive partners (CLS-C).[73,90,128,134–137](Table 2.2) In the 'London Gyms' study, for example, the prevalence of CLS-C in the previous three months (CLS only with other HIV-positive partners and not with HIV-serodifferent partners) doubled significantly over the study period.[131](Figure 2.2) Point estimates for prevalence of CLS-C in the past three months were similar among HIV-diagnosed MSM in the clinic samples of the 'Internet and HIV' and 'East London' studies (15% and 14% respectively).[103,138,139]

These trends were further observed in a systematic review of 30 cross-sectional studies conducted between 2000 and 2007 of over 18,000 HIV-diagnosed MSM recruited from HIV clinics and gay social venues in the USA.[111] There was marked heterogeneity of CLS prevalence estimates across study recruitment settings and time periods, sampling methods, and sexual behaviour recall windows (from last sex to the past 12 months). The aggregate estimates (with any recall window) were: CLS 43% (95%CI 37-48%), CLS-C 30% (25-36%), and CLS-D 26% (21-30%).[111] No significant difference was observed by the length of the recall window; the prevalence of CLS-D in the previous three months ranged from 25% to 68%. In addition, CLS with HIV-unknown status partners was found to be more prevalent than CLS with HIV-negative partners (16 vs 13% respectively). As the review was based on studies conducted in the USA, however, results could not be extrapolated to HIV-diagnosed MSM in the UK.

2.5.2 **Studies of HIV-positive or HIV-diagnosed MSM from convenience samples**

Results from studies using convenience sampling of HIV-diagnosed MSM (attending social or community venues, using specific websites) during the same period in the UK and the USA show diverse trends in the prevalence of CLS.(Table 2.2) The UK behavioural surveillance system was an annual survey of MSM recruited from gay venues and GUM clinics between 1996 and 2004, with oral fluid HIV antibody tests.[97,105,140,141] During the study period, approximately 5.3% of MSM recruited were HIV-diagnosed (aware of their serostatus) and within this group levels of CLS in the past 12 months remained stable (between 31.1% and 43.9%).[97,105,140,141] However, there was evidence of a significant increase in the overall prevalence of CLS in the past twelve months between 2005 and 2013 among over 1500 HIV-diagnosed MSM participating in the London and Scotland Gay Men's Sexual Health Surveys (GMSHS).[142,143] This was also observed in the US National HIV Behavioural Surveillance (NHBS) of 1586 HIV-positive MSM recruited from venue-based, time-space sampling between 2011 and 2014 (Table 2.2).[136] However, no statistically significant increase in CLS was observed in the UK Gay Men's Sex Survey (GMSS) of 243 internet-recruited HIV-positive MSM in England between 2001 and 2008.[134,144]

Prevalence of CLS-C increased significantly between 2000 and 2014, as evidenced in the GMSS, London GMSHS, and the NHBS studies.[134,136,143,144] (Table 2.2) While CLS-C (when HIV-seropositive status is known with certainty) poses no risk of HIV transmission it contributes to transmission of other sexually transmitted infections (STIs). The rise in prevalence of CLS-C in the UK mirrors the trend of increasing diagnoses of STIs observed in the past decade (further discussed in Chapter 8).[145–147] These epidemics are overlapping and disproportionately affect HIV-diagnosed MSM in the UK, suggesting that CLS-C may play a key role in continued transmission of other STIs.[148,149] The prevalence of, and factors associated with CLS with HIV-seroconcordant versus HIV-serodifferent partners, are not well studied among HIV-diagnosed MSM in the UK.

Table 2.1: Summary of studies recruiting HIV-diagnosed MSM from clinical settings in high-income countries (1996-2016)

Study / Data collection period / Country		Recruitment, study type	Sample	On ART (%)	CLS recall window	Type of partner	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
London Gyms [128,131,150]	1998-2008 UK	Cross-sectional annual self-completed questionnaire study of HIV-negative and HIV-positive MSM using gyms in central London and of HIV-diagnosed MSM attending for HIV care in NHS hospitals. Here showing data for HIV-diagnosed MSM only.	• N total =6064 • N HIV-diagnosed MSM from clinics=1001 (16.5%)	*Not shown*	Past 3 months	Stable, casual, combined	1998: 31.4% 2008: 51.4% (p<0.001)‡ (see Figure 2.2 for full details)	1998: 19.5% 2008: 27.0% (p=0.65)‡	1998: 11.9% 2008: 24.3% (p<0.001)‡	CLS-D: CLS with HIV-negative or HIV-unknown status partners. CLS-C: CLS with other HIV-positive partners only (CLS-D and CLS-C are mutually exclusive categories)
Internet and HIV [132,151]	2002-2003 UK	Cross-sectional self-completed questionnaire study of HIV-diagnosed MSM receiving HIV care at a London NHS hospital. (Not shown here: additional samples of HIV-positive and HIV-negative MSM from gay website, GUM clinic, gyms)	• N total= 4015 • N HIV-diagnosed MSM from clinics= 506 (12.6%)	66%	Past 3 months	Casual	*Not shown*	18.0%	15.0%	CLS-D: CLS with HIV-negative or HIV-unknown status partners.

Study / Data collection period / Country		Recruitment, study type	Sample	On ART (%)	CLS recall window	Type of partner	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
Southern California Acute Infection and Early Disease Research Program [152]	2002-2006 USA	Cohort study of recently HIV-diagnosed individuals (≤12 months) with self-interview questionnaires on sex behaviours at baseline (enrolment) and every 3 months during in 1st year enrolled. Here showing data for HIV-diagnosed MSM only.	• N HIV-diagnosed MSM at baseline: 225 • N HIV-diagnosed MSM with ≥1 follow-up visit: 193	32%	• at baseline : last sex • at follow-up: past 3 months	Last partner	47.5%	At baseline: 42% At follow-up (month 12): 50%	At baseline: 78.6% At follow-up: 73.3%	CLS-D: CLS with HIV-negative or HIV-unknown last partner
Positive STEPS [113]	2004 USA	Baseline questionnaire of a behavioural intervention among randomly selected HIV-diagnosed men and women attending for care in 7 clinics. Results here are from MSM HIV-diagnosed for ≥6 months, either planning on or already receiving care in clinic, and reporting any anal sex or IDU in past 3 months.	• N total=1050 • N HIV-diagnosed MSM=496 (47.0%)	69%	Past 3 months	*Not shown*	*Not shown*	• Total: 23.0% • with HIV-negative partners: 14.5% • with HIV-unknown partners: 12.7%	35.8%	CLS-D includes HIV-negative and unknown status partners

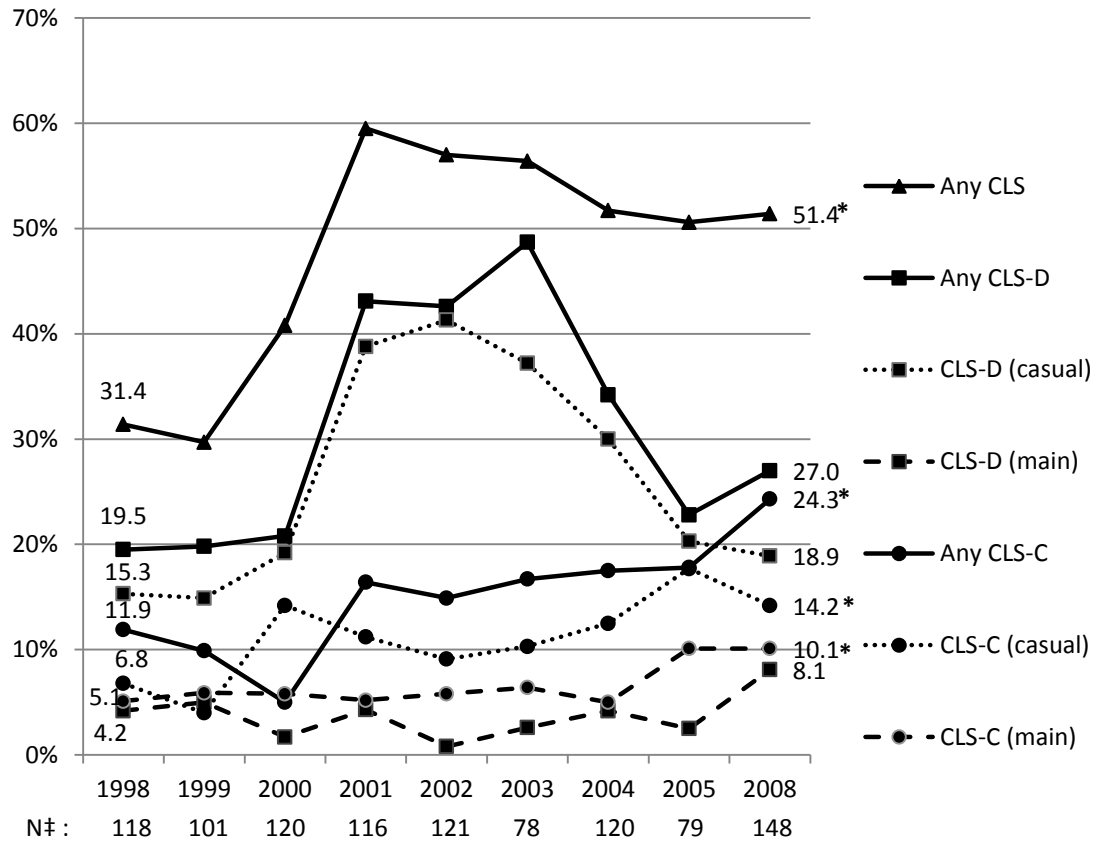
Study / Data collection period / Country		Recruitment, study type	Sample	On ART (%)	CLS recall window	Type of partner	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
East London [103,153]	2004-2005 UK	Cross-sectional self-completed questionnaire study of HIV-diagnosed men and women attending for HIV care in six East London NHS hospitals. Results here for HIV-diagnosed MSM only.	• N total =1687 • N HIV-diagnosed MSM=758 (44.9%)	71%	Past 3 months	Any (stable or casual)	37.8%	• Total: 20.2% • with HIV-negative partners: 3.8% • with HIV-unknown partners: 16.4%	14.0%	Hierarchical classification (mutually exclusive): 1.CLS-C only, 2.CLS-D (with ≥1 HIV-negative partner), 3.CLS with HIV-unknown partner (not with HIV-negative: incl. MSM with HIV-unknown and HIV-positive partners)
Switching Study [114,154]	2005-2006 UK	Cross-sectional self-completed questionnaire study in 5 HIV outpatient clinics in London and Brighton. Here showing results for HIV-diagnosed MSM only.	• N total = 666 • N HIV-diagnosed MSM=451 (67.7%)	68%	Past 3 months	Any	*Not shown*	15.30%	*Not shown*	CLS-D includes HIV-negative and unknown status partners

Study / Data collection period / Country		Recruitment, study type	Sample	On ART (%)	CLS recall window	Type of partner	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
ANRS-VESPA1 and VESPA2 [155]	2003 and 2011 France	National cross-sectional, interviewer-administered surveys. Random location-stratified sample of HIV-diagnosed people attending for HIV care in 102 hospitals, diagnosed for ≥6 months. Showing results for MSM only.	VESPA1: • N total=2932 • N HIV-diagnosed MSM=1117 (35.6%) VESPA2: • N total=3022 • N HIV-diagnosed MSM=1337 (39.1%)	>80%	Past 12 months and most recent partner	Stable and Casual	Most recent casual partner: 2003: 22.9% 2011: 17.5% (p=0.07)†	Stable partner: 2003: 22.9% 2011: 25.1% (p=0.64)†	*Not shown*	CLS-D with stable partner: CLS with a HIV-negative or HIV-unknown status stable partner. Most recent CLS: no condom use at last sex with a casual partner.
START trial (baseline) [156]	2009-2013 International	RCT of HIV-diagnosed people allocated to early or deferred ART initiation. Results from ART-naïve HIV-diagnosed MSM on sexual behaviour questionnaire at baseline (prior to randomisation) from Europe/Israel only	• N total=4601 • N HIV-diagnosed MSM= 2559 (55.6%) Europe/Israel: • N total = 1518 • N HIV-diagnosed MSM=1173 (77.2%)	0%	Past 2 months	*Not shown*	*Not shown*	• Overall MSM in Europe/Israel : 15.1% • MSM diagnosed ≥3 months ago: 13.7% • MSM diagnosed <3 months ago: 25.4%	*Not shown*	CLS-D defined as CLS with HIV-negative or HIV-unknown status partners

Study / Data collection period / Country		Recruitment, study type	Sample	On ART (%)	CLS recall window	Type of partner	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
Medical Monitoring Project (MMP) [157,158]	2009-2010 USA	HIV surveillance system producing nationally representative estimates of behavioural and clinical characteristics of HIV-diagnosed adults receiving care. Cross-sectional random sample survey (face-to-face interviews) of black or white non-Hispanic HIV-diagnosed MSM reporting sex with a man in past 12 months, with ≥1 medical visit.	• N total = 4217 • N HIV-diagnosed MSM=1010 (23.9%)	>80%	Past 12 months	*Not shown*	*Not shown*	20.0% (95%CI 17.0-23.0%)	*Not shown*	CLS-D: 'unprotected anal sex' with a male partner of HIV-negative or HIV-unknown status
Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN070)[159]	2011 USA	Cross-sectional questionnaire survey of young (16-24) HIV-diagnosed MSM receiving care in clinics in 14 US cities. Restricted to those who reported ≥1 episode of anal sex with a male partner in past 12 months.	• N HIV-diagnosed MSM= 200 (100%)	47%	Past 3 months	*Not shown*	43.0%	• 20.5% insertive • 22.5% receptive	• 21.5% insertive CLS-C • 21.0% receptive CLS-C	CLS-D: CLS with HIV-negative or unknown status partners

95%CI: confidence interval; ‡: test for trend p-value for period shown; †: p-value for difference between two periods shown; ART: Antiretroviral Therapy; NHS: National Health Service; CLS: condomless sex; CLS-D: condomless sex with HIV-serodifferent partners; CLS-C: condomless sex with HIV-seroconcordant (HIV-positive) partners; GUM: Genito-Urinary Medicine (sexual health clinic); IDU: injection drug use; RCT: randomised controlled trial; START: Strategic Timing of AntiRetroviral Treatment trial; 'Not shown': study did not provide relevant information.

Figure 2.2: Prevalence of condomless sex (CLS) in the previous three months among HIV-diagnosed MSM recruited from HIV outpatient clinics in the London Gyms study (1998-2008)[131]



‡ N HIV-diagnosed MSM surveyed each respective year
No data for 2006 and 2007 as survey was carried out annually between 1998 and 2005 and again in 2008.
** p-value<0.05 for trend for period 1998-2008 (2006-2007 data imputed).*

2.5.3 HIV transmission risk reduction during condomless sex with HIV-serodifferent partners (CLS-D)

HIV-risk reduction strategies in the context of CLS-D include sexual positioning and withdrawal before ejaculation.(section 1.4.5) Insertive anal sex (when the HIV-positive partner is in the insertive or 'top' position and the HIV-negative partner is in receptive or 'bottom' position) with ejaculation inside the HIV-negative partner carries a greater risk of HIV transmission compared to receptive anal sex (when the HIV-positive partner is in receptive position).[22,73] HIV-positive MSM may have developed understanding of the relative risks of insertive versus receptive CLS-D, and thus adopted the receptive position as a risk reduction measure. However, there have been few studies examining trends in seropositioning and withdrawal before ejaculation among HIV-diagnosed MSM in Europe.

The earliest evidence of patterns in sexual positioning based on partner's HIV-serostatus emerged from ten cross-sectional surveys of MSM recruited from gay community and sexual health settings in Sydney between 1996 and 2000.[160] Among 2695 HIV-positive MSM recruited, , the vast majority were the receptive partner only in the past 6 months (69.0%), and a minority reported CLS with ejaculation inside their HIV-serodifferent stable partner (2.7%).

Conversely, results from HIV-positive MSM recruited from community-based venues in New York City and San Francisco in 2000-2001 showed that while some men in San Francisco were more likely to report being the receptive than the insertive partner (with HIV-unknown and HIV-negative partners), this pattern was not observed among men in New York.[73] A meta-analysis of 30 cross-sectional USA studies (2000-2007), found that a higher proportion of HIV-diagnosed MSM reported taking the receptive rather than the insertive position during CLS with HIV-negative partners (9% vs 5%).[111] While differences in patterns of CLS according to partners' HIV-serostatus were found, this meta-analysis could not ascertain whether these behaviours were intentional strategies to reduce the risk of HIV transmission or merely sexual preferences.

Since then, some studies from HIV-diagnosed MSM in the USA and Australia have suggested an increase in the prevalence of receptive CLS-D[26,136,161] but no such evidence has been observed in the UK GMSS surveys.[134] There is evidence of HIV risk compensation during CLS-D from interim analyses of the PARTNER and *Opposites Attract* studies*,* as HIV-negative partners in both studies reported being the insertive partner more often than being the receptive partner.[9,161] In addition, when the HIV-negative partner was receptive, withdrawal before ejaculation by the HIV-positive partner was also more prevalent than ejaculation inside. It remains unclear how extensively these risk reduction approaches have been adopted in the UK among HIV-diagnosed MSM who may or may not have a stable serodifferent partner. Accrual of longer-term follow-up from these two cohorts will provide more precise estimates of HIV transmission risk and may in turn impact on trends of CLS-D.

Table 2.2: Summary of studies recruiting HIV-positive or HIV-diagnosed MSM from convenience samples in high-income countries (1996-2016)

Study / Data collection period	Recruitment, location, study type	Sample	On ART (%)	CLS recall window	Partner type	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
Active behavioural surveillance system [97,105,140,141] 1996-2004 UK	Self-completed, cross-sectional annual behavioural surveys of MSM recruited from gay venues (bar, club, sauna) and GUM clinics in the UK with HIV antibody testing (unlinked anonymous survey). Here showing data for HIV-positive only.	• N total= 14,193 • N tested HIV-positive=567 (4.0%)	*Not shown*	Previous 12 months	Casual	1996: 31.1% 2004: 43.9%	1996: 16.7% 2004: 30.6%	~19.0%	CLS-D: CLS with HIV-negative or HIV-unknown partners. CLS-C: CLS with partners of the same HIV-serostatus only.
Gay men in Sydney [160,162,163] 1996-2006 Australia	10 biannual cross-sectional surveys of MSM from gay community, social, sex-on-premises, and sexual health clinic. Data shown here are for self-reported HIV-positive MSM.	• N=14,165 • N HIV-positive: 2695 (19.6%)	*Not shown*	Previous 6 months	Main and casual	• 30.1% (of 462 with regular partner) • 41.6% (of 2146 with casual partners)	• 48.6% (of 146 with regular serodifferent partner) • 56.6% (of 881 had CLS with casual partner)	*Not shown*	CLS-D: with "serodiscordant" partner(s)
Seropositive Urban Men's Intervention Trial (SUMIT) [73,164] 2000-2001 USA	Baseline assessment of RCT on single or six-session intervention designed to reduce HIV transmission risk and promote serostatus disclosure. Self-identified HIV-positive MSM reporting sex with ≥1 HIV-serodifferent partner in past year recruited from community-based venues in NYC and San Francisco	• N HIV-positive=1168	75.1%	Previous 3 months	Casual or main	*Not shown*	CLS-D with casual partners • 17.8% with HIV-negative • 34.0% with HIV-unknown • Combined: 47.3% CLS-D with main partner: • 15.0% with HIV-negative • 6.3% with HIV-unknown • Combined: 21.3	24.5%	Combined CLS-D: CLS with HIV-negative and HIV-unknown status casual or main partners

Study / Data collection period		Recruitment, location, study type	Sample	On ART (%)	CLS recall window	Partner type	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
Gay Men's Sex Survey (GMSS) [134,144]	2001 and 2008 UK	Annual community-based sexual health needs assessment questionnaire survey of MSM recruited from gay venues and online in England. Data shown are for internet-recruited self-reported HIV-positive participants only.	• N total= 4953 • N HIV-positive=243 (4.9%)	*Not shown*	Previous 12 months	*Not shown*	2001: 73.7% 2008: 82.1% (p>0.05)‡	• CLS with HIV-negative: 2001: 19.7% 2008: 17.9% (p>0.05)‡ • CLS with HIV-unknown status partner: 2001: 44.9% 2008: 49.6% (p>0.05)‡	2001: 49.6% 2008: 52.0% (p>0.05)‡	-
London Gay Men's Sexual Health Survey (London GMSHS) [143]	2000-2013 UK	10 serial cross-sectional surveys of MSM (≥16 years) in London gay social venues (bars, clubs, saunas) using self-completed questionnaires and oral HIV antibody testing. Here showing results for HIV-diagnosed MSM only (excluding undiagnosed HIV-positive)	• N=11,876 • N HIV-diagnosed MSM= 981 (8.3%)	*Not shown*	Previous 12 months	New or casual	2000: 49% 2013: 64% (p=0.002)‡	• CLS with HIV-negative main partner: 15.0%	2000: 22% 2013: 30% (p=0.06)‡	CLS-D: CLS with new or casual partners and not exclusively serosorting CLS-C: 'exclusively serosorted'
Internet-recruited HIV-positive MSM[165]	2008 USA	Cross-sectional behavioural survey of adult MSM recruited through MSM-oriented sexual networking website. Survey was part of an RCT evaluating dramatic video-based interventions. This analysis on self-reported HIV-positive MSM.	• N total=8472 • N HIV-positive= 1010 (24.0%)	73.7%	3 most recent partners in the past 60 days	Any	50.3%	31.6%	29.0%	CLS-D: with HIV-negative and/or unknown status partners

Study / Data collection period		Recruitment, location, study type	Sample	On ART (%)	CLS recall window	Partner type	CLS overall (%)	CLS-D (%)	CLS-C (%)	Notes on definitions
National HIV Behavioural Surveillance (NHBS) [136]	2011-2014 USA	Serial cross sectional survey (collected every 3 years) of MSM recruited for interviews and HIV testing through venue-based, time-space sampling. This analysis restricted to self-reported HIV-positive MSM who had sex in past 12 months.	• N at every cycle 11,000* • N HIV-positive at every cycle 1340*	90% (2014)	At last sex	Any	2005: 34.2% 2014: 44.5% (p<0.001)◊	2005: 15.0% 2014: 19.0% (p<0.001)◊	2005: 19.0% 2014: 25.4% (p<0.001)◊	CLS-D: CLS with a partner of 'discordant' or unknown HIV status.
The Gay Community Periodic Surveys (GCPS) [166]	2013 Australia	Repeated (annual/biannual) cross-sectional questionnaire surveys of MSM recruited from gay social events, sex-on-premises venues, and clinics. Self-completed questionnaire. Data here on 2013 cycle from self-reported HIV positive MSM.	• N total=6161 • N HIV-positive= 573 (9.3%)	>70%	Previous 6 months	Casual	46.6%	21.0% "strategic positioning" (see notes)	55.4%	CLS-D not specified, "strategic positioning" as proxy: HIV-positive men in receptive role and HIV-negative or HIV-unknown men in insertive role during CLS. CLS-C: matching HIV status before CLS ("serosorting")

*ART: Antiretroviral Therapy; CLS: condomless sex; CLS-D: condomless sex with HIV-serodifferent partners; CLS-C: condomless sex with HIV-seroconcordant partners; GUM: GenitoUrinary Medicine (sexual health clinic); NS: not specified; ‡ p-value for difference in prevalence estimates between years shown; * Average number of participants at every three-year cycle (2005, 2008, 2011, 2014); ◊ p-value for test of linear trend; Not shown: study did not provide relevant information*

2.5.4 Higher HIV risk condomless sex with HIV-serodifferent partners

Up until publication of results from HPTN052 and PARTNER, showing extremely low risk of HIV transmission from HIV-positive partners on effective ART, [7,9,26,161] CLS-D was considered the main marker of HIV transmission risk sex for surveillance and epidemiological research. The vast majority of published literature still defines 'higher risk sex' as CLS-D only. Certain studies have adapted to include HIV risk reduction sexual behaviours adopted by some HIV-diagnosed MSM, such as insertive CLS-D.[143,167] However, in the current stage of the HIV epidemic these measures do not fully capture the complexity of sexual behaviours nor the actual estimated per-contact probability of HIV transmission.[87] Chapter 5 provides a literature review of studies that have defined sex with higher risk of HIV transmission, and examines various definitions of 'higher risk' CLS-D for HIV transmission in ASTRA MSM, incorporating VL, ART status, and other factors which could potentially affect VL suppression.

2.6 Overview of evidence on factors associated with condomless sex among HIV-diagnosed MSM

This section summarises literature incorporating individual-level factors (socio-demographic, HIV-related, psychological health, and sexual partner characteristics) which may be associated with higher prevalence of various types of CLS among HIV-diagnosed MSM. Lifestyle factors, such as recreational drug use and alcohol consumption, and their associations to CLS are reviewed and discussed separately in Chapter 6.

2.6.1 Socio-demographic characteristics

2.6.1.1 Participant's age

Evidence on the association between a participant's age and prevalence of CLS is mixed. Of the 15 studies that assessed this, eight have found no association between participant's age and CLS-D.[113,115,165,167–171] This includes the HIV-diagnosed MSM sample from the 'Internet and HIV' study, although the sample size was small.[151] Three studies showed that younger HIV-diagnosed MSM tend to report higher prevalence of CLS-D compared to their older counterparts.[143,156,172]Among over 2500 ART-naïve HIV-diagnosed MSM in the START trial, a significant negative trend with age was observed at baseline; older men (≥50 years) were 70% less likely to report CLS-D in the past two months compared to younger men (<30 years).[156] A similar significant finding was reported among 259 HIV-diagnosed MSM in the London GMSHS, (Table 2.2) where the odds of reporting CLS-D in the past year were more than twice as high among those aged 16-24 years compared to those over 45 years.[143]

The association between age and CLS-C is less well studied. For example, among 280 self-reported HIV-positive MSM from a US online HIV prevention study (2010-11), older men (≥40 years) were more likely to report CLS-C in the past six months compared to younger MSM.[173] Conversely, HIV-diagnosed MSM from the 'Internet and HIV' study who had CLS-C were significantly younger than those who did not have CLS-C.[151]

2.6.1.2 Ethnicity/race

There is, to date, little evidence on ethnic/racial differences in prevalence of CLS among HIV-diagnosed MSM in the UK.[151] A 2009 meta-analysis of 30 cross-sectional US studies found the prevalence of any CLS to be significantly lower in study samples that were majority HIV-diagnosed MSM of non-white ethnicities (versus majority white ethnicities).[111] Since then, no consistent association has been found between ethnicity/race and CLS or CLS-D among MSM living with HIV in a number of studies from the USA.[157,165,169–172] In the GMSHS, although the majority of HIV-diagnosed MSM were of white ethnic origin, non-white (black, Asian, mixed/other) HIV-diagnosed MSM were significantly more likely to report CLS-D compared to white MSM; the effect was most pronounced for black MSM (12% reported CLS-D in the past year compared to 4% of white MSM, $p<0.001$).[143]

2.6.1.3 Other socio-demographic characteristics

Markers of socio-economic status have not been found to exhibit a consistent association with CLS or CLS-D across the studies in which the association has been examined. Level of education has been shown to not have significant associations with CLS or CLS-D in a number of US and UK studies of HIV-diagnosed MSM.[103,156,165,171,174] In two other diverse studies, lower education was associated with higher prevalence of CLS-D with a stable partner; the US SAFE study (1997-2000) included 674 HIV-diagnosed MSM outpatients with a steady HIV-serodifferent partner (prevalence of CLS-D in the past year was 21%), among whom low educational levels (up to high school or less) were significantly associated with higher prevalence of CLS-D.[169] A similar association was also reported in the French ANRS PRIMO study (2000-2009, Table 2.1) of 670 HIV-diagnosed ART-naïve MSM with primary HIV infection (prevalence of CLS-D with stable partner since last visit was 10.3%).[115] Conversely, in the London GMSHS, HIV-diagnosed MSM who were more educated were significantly more likely to report CLS-D in the past year compared to those less educated (≥2 years education after age 16 versus none or up to age 16).[143]

Evidence from HIV-diagnosed MSM in the USA[110,113,175,176] and the UK[103,151] suggests that employment status is also not significantly associated with CLS. The literature review in this chapter yielded only one study in which unemployment was strongly associated with CLS-D; the USA ATN study(Table 2.1) of 688 young HIV-diagnosed MSM (65% were under 20 years) with detectable VL found that current unemployment was associated with 24% higher odds of CLS-D in the past three months.[177] However, ATN participants were of majority black race, had high levels of unemployment, history of incarceration, and low levels of ART coverage, and so are not representative of adult HIV-diagnosed MSM on effective ART with lower levels of overall deprivation.

2.6.2 HIV-related factors

2.6.2.1 Time living with diagnosed HIV

Various associations have been found between length of time since HIV diagnosis and CLS. Earlier results (prior to 2009) from cross-sectional studies suggested that the prevalence of CLS-D did not differ significantly by the length of time diagnosed, remaining stable at around 20-30% over 6 to 10 years since HIV diagnosis.[103,110,111,113,167,175] However, adjustment for participant's age was conducted in only three

of these studies,[103,113,167] while the remaining showed non-significant associations in unadjusted analyses only.[110,175,178] In START[156], as well as in four other USA studies,[135,165,179] a significant trend association was observed for HIV-diagnosed MSM, with prevalence of CLS-D in the past two months decreasing as the length of time since diagnosis increased. Among these studies, only START [156]and Fenway Health[180] adjusted for participants age.

A recent case-control study from Seattle, USA (2016) showed that HIV-diagnosed MSM modify their sexual behaviour soon after HIV diagnosis and sustain these changes for many years following[181]; 186 newly HIV-diagnosed MSM who had previously tested HIV-negative (retrospective seroconversion cohort) were frequency-matched to 1000 HIV-negative controls, and results showed that the prevalence of CLS with HIV-negative partners declined by 61% from pre- to post-HIV diagnosis ($p<0.001$) and did not significantly change for up to four years after diagnosis.[181] At the same time, the prevalence of CLS *only* with other HIV-positive partners increased by 56% after diagnosis and remained stable for the next four years. These findings show that the association between time since HIV diagnosis and CLS may be particularly dependent on whether participants who are recently diagnosed are excluded from analyses. This exclusion criterion ensures that participants are not reporting sexual behaviours occurring prior to HIV diagnosis. More research is needed to elucidate the role of length of time since HIV diagnosis on prevalence of various types of CLS, adjusting for the respondent's age.

2.6.2.2 Antiretroviral therapy status and viral load (VL)

As discussed in section 2.3.3, prevalence of CLS among HIV-diagnosed MSM has not been found to be significantly higher among those receiving ART (versus those not) or those with undetectable VL on ART (versus detectable VL on ART).[117]

It is hypothesized that individuals on treatment may modify their sexual behaviour according perceptions of personal virological status (perceived VL).[182] This measure is important, as inaccurately perceiving one's VL as suppressed (when it is detectable) may impact on HIV transmission. Findings from the Amsterdam Cohort study (n=57 HIV-diagnosed MSM outpatients, 2000-03) showed that perceived suppressed VL, rather than actual HIV RNA levels, was associated with almost six-fold higher prevalence of CLS-D with steady partners in the past six months.[183] These findings do not agree with those from Australia (n=536 HIV-positive MSM from the Positive Health and Sydney Gay Community Periodic Surveys, 2001-07), where men who perceived their VL as detectable were no more likely to have CLS-D with their stable partner than those who perceived their VL as undetectable.[184] Prior to the ASTRA study there were no studies that examined associations between perceived VL and CLS among HIV-diagnosed people in the UK.

2.6.2.3 Adherence to antiretroviral therapy

Studies on the relationship of ART adherence and measures of sexual risk behaviour have focused on heterosexual HIV-positive men and women and have not found a significant association.[154,185–188] Among HIV-positive MSM, a 2009 meta-analysis showed that reporting more than 90% adherence was not

associated with any CLS, although findings were based on a small subset of studies with available adherence information.[111] Few studies have since examined the relationship between ART adherence and CLS among MSM, and none from the UK. In a diverse sample of people living with HIV in the US recruited via community venues, no association was found between non-adherence (measured using an electronic medication monitor) and CLS among 156 HIV-positive MSM.[189]

2.6.3 Psychological well being

2.6.3.1 Symptoms of depression and anxiety

The directionality of the association between negative affects, such as symptoms of depression and anxiety, and CLS is unclear among people living with HIV. Psychological symptoms may promote sexual risk-taking, but CLS may also promote anxiety, depression, or other negative emotional states. A meta-analysis of 13 studies of people living with HIV (1990-1999) found limited evidence that depression or anxiety are associated with sexual risk behaviours (CLS, multiple sex partners, or other composite measures); the average weighted correlation for the overall association among men and women living with HIV was 0.7 (95%CI -0.30, 0.44), but no results were available from MSM. [190] Later studies from the UK and the USA have corroborated this finding among heterosexual HIV-diagnosed men and women.[113,151,175,191]

The association between depression, anxiety and CLS may not be linear, either. Early research hypothesized that negative affects, may disrupt a HIV-diagnosed person's ability to self-regulate emotions and perceive risk, thus leading to 'risky' sexual behaviours.[190] On the other hand, depression may also promote low libido and lack of interest in pleasurable activities, which may lead to lower levels of sexual activity.

At the individual level, there is some evidence that within-person associations do exist between depression and CLS. A USA study of 106 racially diverse HIV-positive MSM recruited via community venues (2007-09) conducted bi-weekly repeated online assessments and showed that when participants reported more symptoms of depression, episodes of CLS were more likely to occur.[192]

2.6.3.2 Perceived social support

Functional social support refers to the perception that supportive resources, such as emotional care and companionship as well as financial help, are available from one's social network if needed. There is very limited evidence that lack of perceived social support from partners, family members, and friends is associated with CLS among HIV-diagnosed MSM. Three small studies (<50 HIV-positive MSM) from the pre-ART era in the USA showed that lower social support (measured in various constructs) was associated with a lower prevalence of CLS.[193]

2.6.4 Partner-related factors

The literature review in the preceding section (2.5) has shown that CLS is interrelated to partners' HIV-serostatus and type of relationship (casual, main, or other type of partner).[194] A number of studies of

clinic and convenience samples have shown that among HIV-diagnosed MSM the prevalence of CLS with other HIV-positive partners is higher than with HIV-negative or HIV-unknown status partners.[113,134,136,143,152,166,195,196] However, evidence from the three UK HIV-clinic studies of HIV-diagnosed MSM ('London Gyms', 'East London', 'Internet and HIV') shows that the prevalence of CLS with HIV-seroconcordant partners in the past three months was lower than that for HIV-serodifferent partners.[128,131,139,150,151,197](Table 2.1) In addition, there is some evidence to suggest that HIV-diagnosed (or HIV-positive) MSM report higher prevalence of CLS with HIV-unknown than with HIV-negative partners,[73,134,151,164,191,197,198] but this is not the case in all studies that have examined CLS by partner's HIV-serostatus.[113,165] There are a multitude of reasons for which mixed results have been found on prevalence of CLS according to partners' HIV-serostatus. A number of studies reviewed in this chapter restricted eligibility for study participation to MSM who reported any CLS (or specifically with at least one HIV-serodifferent partner).[113,136,157,159,164,199] This may have led to overestimation of CLS prevalence estimates. In addition, most community studies of MSM used a 12 month recall period for CLS, which is not ideal for studies of HIV-diagnosed MSM; evidence suggests that sexual behaviour may change soon after diagnosis and in relation to factors such as starting ART and achieving VL suppression.[93] A shorter recall period (such as in the previous three months) is more appropriate for studies of HIV-diagnosed MSM and is particularly relevant when asking about CLS according to partners' HIV-serostatus.

Furthermore, evidence remains mixed on the association between type of relationship with a partner (casual or main/stable) and prevalence of CLS among HIV-diagnosed MSM. An earlier systematic review of 61 studies from high-income countries (1980-2001) found that CLS overall was no more likely to occur with stable than with casual partners.[193] However, this is not consistent with findings from HIV-diagnosed MSM in the 'London Gyms' study, in which any CLS with casual partners was more prevalent than with stable partners.(Figure 2.2) Among HIV-diagnosed MSM who have HIV-serodifferent sexual partners, results are not uniform across type of partner, either. Prevalence of CLS with casual partners has been shown to be lower than,[195,198,200] higher than,[98,103,131,150,196,201,202] and equal to[176,203] the prevalence of CLS with stable partners. The associations of partner type and partner HIV-serostatus with various types of CLS among HIV-diagnosed MSM thus remain unclear.

2.7 Conclusion

Studies of HIV-diagnosed MSM recruited from clinical settings in high-income countries since the introduction of effective ART in 1995 have reported broad ranges of estimates for CLS in the past three months overall (43-51%), CLS with HIV-serodifferent partners (15-27%), and CLS with HIV-seroconcordant partners (14-24%).[103,113,114,131,150–152,156,157,159] There is some indication of an increase in the prevalence of CLS over calendar time. Varying underlying trends are observed, with a suggestion of reduction in the prevalence of CLS with HIV-serodifferent partners concurrent with an increase in the prevalence of condomless sex with other HIV-positive partners.[94,99,115,126,140] Research also suggests that differences exist in sexual positioning according to a partner's HIV serostatus (insertive or receptive) among HIV-diagnosed MSM.[134,156,170,200,204]

A number of co-factors have been identified in the literature as related to CLS, but results vary according to study type, recruitment location, definition of co-factors, measurement of different types of 'risky sex', varying recall periods, adjustment for confounders, and sample sizes. There is now more consistent evidence that the use of ART is not associated with a higher prevalence of any CLS. As effective ART has led to a dramatic increase in life expectancy, the joint effects of ageing and living with HIV for longer on the prevalence of CLS are yet to be fully understood. Evidence on modification of sexual behaviours according to personal perceptions of virological status is scarce. There is also limited support for a positive association between symptoms of depression and anxiety and higher prevalence of CLS, although this has not been studied over calendar time. Condomless sex is linked to a partner's HIV serostatus (HIV-negative, positive, or unknown) and the type of relationship (casual or stable).

Hence, understanding the factors that contribute to different types of condomless sex among HIV-diagnosed MSM remains important for HIV and STI prevention.

3 Data and Methodology

3.1 Introduction

Analyses presented in chapters 4, 5, 6, 7, and 8 of this thesis have been undertaken using data from the 'Antiretrovirals, Sexual Transmission Risk and Attitudes' (ASTRA) study, an observational, cross-sectional self-administered questionnaire study of HIV outpatients attending one of eight UK NHS clinics from February 2011 to December 2012. The study also included an additional longitudinal component based on routine linked clinic data, with follow-up until July 2014. The current chapter describes the ASTRA study design, data collection and management, summarises the key questionnaire factors, and discusses the representativeness of the ASTRA sample in relation to the HIV-diagnosed population in the UK. An overview of the main statistical methods used for analyses in this thesis is also presented.

The ASTRA study was planned prior to this thesis being undertaken, and the recruitment period of ASTRA was ending at the start of my period of study for the PhD. I had no involvement in the study design and recruitment (presented in sections 3.3, 3.5) but did have responsibility for data management and cleaning procedures (section 3.8.1) and undertook all analyses presented in this thesis. The methodology of the ASTRA study has been published previously.[89]

3.2 ASTRA questionnaire study

The ASTRA study was designed to investigate sexual risk behaviours among HIV-diagnosed men and women in the UK. The primary aims of ASTRA were to: (i.) investigate the association of antiretroviral therapy (ART) use and self-reported viral suppression, with condomless sex with HIV-serodifferent status partners (CLS-D), (ii) assess beliefs about virological suppression and HIV transmission risk, and (iii) assess attitudes to early ART initiation among ART-naïve individuals. The secondary aims of ASTRA included investigating sexual behaviour and attitudes among key demographic subgroups and examining the association of a range of factors (socio-demographic, HIV, ART, and health-related, lifestyle) with specific sexual behaviour measures.[205] This thesis makes a contribution to these secondary aims (also covering the first primary aim stated above), and considers men who have sex with men (MSM) only.

3.3 Study design and population

Clinical centres were chosen to participate in ASTRA on the basis of previously successful research collaborations and on the expectation that they could provide a sufficient sample size of HIV-diagnosed patients, including key demographic subgroups (MSM and black African individuals). Eight NHS clinics participated in the study, five of which were located in London (Royal Free Hospital, Mortimer Market Clinic, Homerton University Hospital, Newham University Hospital, and Whipps Cross University Hospital) and three were located outside London (Brighton and Sussex University Hospital, Eastbourne Sexual Health Clinic, North Manchester General Hospital). Eligibility criteria for study participation were: lab-confirmed HIV-positive diagnosis, aged ≥18 years, attending for care. Participants were excluded if

they were unable to complete the questionnaire due to language or cognitive difficulties or if they were too ill or distressed.

3.4 Sample size estimation

Sample size estimation used the endpoint of CLS-D in the previous three months, based on the main objective of detecting a difference in the prevalence of CLS-D between participants on ART and those not on ART. Based on previous UK studies on HIV-outpatients, the overall prevalence of CLS-D in the previous three months was estimated to be 15%.[103,139,154] The calculation was based on 80% power, 5% two-sided significance level for this comparison, and assumed that 75% of participants would be on ART (based on national UK data on ART use in 2010[206]) and 15% would report CLS-D in the previous three months.[103–105,133] Thus it was estimated that a total of 3349 participants were required to detect a difference of 4% in the prevalence of CLS-D in the previous three months between those on ART and those not on ART (so that 16% of participants on ART would report CLS-D compared to 12% of those not on ART.) In line with previous UK HIV-clinic studies,[133] a 75% response rate was assumed and it was estimated that 3,825 individuals would participate in ASTRA, a sample size large enough to provide adequate power to answer the main objectives.

3.5 Recruitment procedures

Within each participating HIV outpatient clinic, during specific periods of recruitment to the study, patients attending the clinic were invited to participate by study nurses or HIV consultants while waiting for (or after) their outpatient appointments. Clinics were encouraged to select specific clinical sessions each week for study recruitment and to attempt to approach consecutive patients attending within these sessions. It was emphasised that sessions selected for recruitment should be those for which a diverse range of clinic patients would be expected to attend (for example recruitment should not restricted to specialist clinical sessions, or always occur on the same day of the week). A private area within each clinic was made available for completion of questionnaires, if desired.

3.5.1 Information sheet

A study information sheet was provided, which described the aims of the study, the requirement to fill out a questionnaire that included personal questions on health and sexual lifestyle (among others), and the option to withdraw consent to the study at any time. (Appendix I) The information sheet also stated that if agreeing to participate in the study, the participant's latest viral load (VL) and CD4 count would be recorded as part of the study data. A detailed explanation on anonymity was also on the information sheet. This explained that clinic staff would not open or read the completed questionnaires, or record any answers in the patient's clinic notes, and that anonymised responses would be presented in aggregate form in medical journals and conferences, with no individual participant identified in any way. The information sheet also explained that the participant would also be asked if they would provide additional consent to have their routine HIV clinical data (from the specific recruiting HIV clinic only) linked to their respective questionnaire answers. It was explained that this linkage would be performed on a number of occasions over the next few years; the required clinical information was detailed

(laboratory test results, HIV treatment, other routine HIV care information). The linkage was described as standard procedure for research studies, and it was explained that linkage would be performed in such a way that questionnaire responses would remain confidential and would never be linked to the participant's name or clinic number. Participants were further told that consent to this clinical linkage was optional and did not prevent them from study participation. The ASTRA study website and details of the study coordination department and funding were also made available on the same sheet.

3.5.2 **Consent form**

A separate consent form was provided to all those who, after reading the information sheet, agreed to participate in the study. (Appendix I) This included statements with accompanying fields for the participants' initials (to indicate agreement): confirming they have read and understood the information sheet, agree to take part in the study, and understand that participation is voluntary and can be withdrawn at any time without explanation. An additional statement asked whether participants consented or not with linkage of their questionnaire responses to their routine clinical data. The participant printed their name, dated, and signed the consent form, as did the person taking consent (study nurse or consultant). Once complete, two additional copies were made (one for the participant and one for the researcher site file) and the original consent form was kept in the patient notes.

3.5.3 **Study log**

The study log was a record (Excel spreadsheet) of each person approached for the study and asked to participate, regardless of whether they agreed to participate or not. The information collected is shown in Table 3.1. The study log supplied a unique anonymised study identifier (ID) for each successive individual approached and was the only document linking the patient's clinic number with their questionnaire study ID. The clinic number for each person approached was thus only recorded in the study log and never transferred to the research team at UCL. The study log was confidential to the study sites and securely stored on an encrypted hard drive. At each site, study nurses completed the required fields on the study log for each participant. All study log information except for the participant's clinic number was exported and emailed to the study data manager weekly, via secure NHSmail service. Clinics used a pre-designed programme that automatically removed clinic numbers from the log prior to export. The study log contained the latest VL and CD4 count for each participant; it was specified that these were the latest values that had been communicated to the participant.

Table 3.1: Study log fields

Field	Purpose / Description	Characteristics
Study ID	Anonymised identifier	Pre-assigned and non-editable. Consists of a letter identifying the study site and a 4 digit sequence number
Clinic ID	Clinic Number	Specific to each study site. Not to be transferred outside the clinic
Date patient attended		
CONSENT 1: Agreed to participate?	Consent to take part in the questionnaire study and supply latest CD4 counts and VL values	Yes/No If Yes, signed Consent Form must exist with 1st of 3 options initialled
The following fields were only completed if a signed Consent Form existed		
CONSENT 2: Agreed to use of past/future clinic data?	See information sheet and section 3.6 for details of clinic data to be collected based on this consent	Yes/No If Yes, signed Consent Form must exist with 4th "clinical linkage" Yes box initialled
Gender		Male/Female
Type of questionnaire	What questionnaire versions were completed	Laptop, Paper or Both
Paper questionnaire taken off-site?		Yes/No
Optional contact details	e.g. email address Only if questionnaire taken off-site	Used only to follow up on missing paper questionnaires
Comments	Any notes for the attention of the study researchers	
Latest viral load	Latest value known to patient	To be supplied for ALL patients who signed a Consent Form (does not matter if the 4th "clinical linkage" option is Yes or No). These should be the last results given to the patient (even if there is a more recent result the patient is not yet aware of).
Date for latest viral load		
Latest CD4 count	Latest value known to patient	
Date for latest CD4 count		

3.5.4 **Questionnaire administration**

The ASTRA questionnaire was self-administered, as a printed A5 booklet available in versions for males (blue) and females (pink). (Appendix I.) French translations of both questionnaire versions were also available. Study nurses completed the pre-assigned study ID (from the study log) and the date on the front of the questionnaire. Therefore, questionnaires only contained the study number and no other identifying information, such as name or person's clinic number. In order to ensure high response rates, participants were encouraged to complete the confidential questionnaire on the same day, in the clinic, placing it in a pre-supplied sealed envelope within a study-assigned box in the clinic. If this was not possible or desired, participants could complete the questionnaire at a later time, when most convenient, and post it to the research team in the pre-paid envelope. Study nurses ensured that sealed,

completed questionnaires were placed in the study-assigned box in the clinic; at the end of the day they collected all paper questionnaires from the box and stored them securely. Every month, study nurses ensured that completed questionnaires were collected and transferred to the core research team at UCL.

3.6 ASTRA linked clinical data

For consenting participants, linkage of ASTRA questionnaire responses with routine clinical data was completed within each study centre using the study log as a record of participants who completed the questionnaire. The clinical data was stored as encrypted, password protected excel spreadsheets and transferred by File Transfer Protocol (FTP) method to the study data manager at UCL, only including the study number, and no other identifying information; FTP is a standard network protocol for transferring files between clinics and main servers, which requires user authentication via username and password. Routine clinic data fields included, among others: date of first known positive HIV antibody test, date of first HIV attendance at the centre; results of laboratory test results: all HIV VL test results (in copies/mL) with dates; type of HIV RNA VL assay used for each test; all ART regimens prescribed with dates started and stopped; hepatitis laboratory test results with dates (including hepatitis C antibody and virus PCR/bDNA). The linked clinical data gives information on HIV history prior to the questionnaire and also allows for prospective analyses of specific virological or clinical outcomes, using the questionnaire as a baseline. Linked data were collated at the end of the data collection period (2012), and on several subsequent occasions up to 2016, from five of the eight NHS centres (Royal Free, Mortimer Market, Homerton, Brighton, Eastbourne, and Newham). All but one of these centres (Eastbourne) had existing established clinic databases (UKCHIC)[207] with which the ASTRA questionnaire was linked.

3.7 Ethical considerations

3.7.1 Ethical approval

Prior to study initiation, the study protocol, information sheet, consent form, and study questionnaires (men and women's versions) were submitted for ethical review. All amendments to the study protocol were also submitted and the study was approved by the North West London REC 2 research ethics committee (ref 10/H0720/70), receiving permission for clinical research at all participating NHS sites.

3.7.2 Confidentiality

The information sheet stated that the questionnaire included personal questions on sexual lifestyle, stating that if the questionnaire raised any issues or concerns to the participant, they could ask the nurse to arrange for them to discuss this with an appropriate healthcare professional (e.g. HIV clinic counsellor). Confidentiality was ensured at all stages: private areas were made available for questionnaire completion in clinic, the questionnaires contained no identifying information, sealed envelopes were provided, and participants were informed that their responses would not be seen by clinic staff or recorded in clinical notes. Linkage of clinical data, for those providing consent to linkage, was done within the clinical centre, ensuring that each participant's clinic number was removed before data were transferred to the UCL research department.

3.7.3 Data security

Data from paper questionnaires was double-entered into an electronic data entry package by a data company. Paper forms (including questionnaires and copies of the study log) were securely stored in locked cabinets at the UCL research department. The complete ASTRA questionnaires were scanned and along with the complete data set and clinical data, they were stored on a secure electronic encrypted PC or laptop drive (Truecrypt), protected by password and only accessible to the data manager, the primary investigator, and me. No patient names or clinic numbers were recorded in any of the study data sets held in the research department (including the clinical datasets transferred from each clinic to the research department). All information was treated as strictly confidential and no individual patient could be identified in any results presented or published.

3.8 The ASTRA questionnaire

3.8.1 Questionnaire data management and derivation of variables

The male questionnaire is shown in its entirety in Appendix I. It had approximately 60 questions and took between 15 and 30 minutes to complete. My involvement in the study started after ASTRA was designed and data was collated, in the form of extensive data management. I imported all raw questionnaire data from Excel into Stata software, cleaned, and prepared it for analysis. I coded responses to questions with optional free text responses (such as number of new sexual partners in the past year) into numerical categories; and also used free text responses to create variables that could be comparable to standardised measures (e.g. see education variable below). I performed range checks for each variable and assessed the extent of missing data. I also compared questionnaire variables with each other, where relevant, to ensure consistency between related questions and within subsections of questions, (an example of an inconsistent response would be reporting no anal sex in the previous three months but completing the section on CLS during the same period). I assessed the appropriate order of dates (e.g. date of HIV diagnosis must precede date of ART initiation). For each participant, I examined the scanned copy of the completed questionnaire (stored on encrypted hard drives) to resolve data queries and discrepancies. These were used to check for errors in the data entry process, and to check whether the participant had made additional indication or text comment that might clarify any missing or inconsistent response. In addition, where applicable, I completed missing information on the questionnaire using information from linked clinical records (e.g. age, time since HIV diagnosis, ART status). I also resolved any discrepancies between questionnaire and linked clinical data on a case-by-case basis.

3.8.2 Key socio-demographic, mental health, lifestyle variables defined

Throughout this thesis, a set of key socio-demographic, psychological, HIV-related, and lifestyle factors are used. I derived these from the questionnaire raw data as shown below. A discussion of the handling of missing data for each variable is also given as a proportion of the final dataset comprised of 2248 MSM (the ASTRA sample is described in section 3.10).

- **Men who have sex with men (MSM):** male participant who had either identified himself as 'gay' or 'bisexual', or had sex with another man in the previous three months. A total of 35 men had missing sexual orientation status and were assigned a category according to other available relevant information, such as transmission route indicated as sex with an HIV-positive man from the questionnaire or from available routine linked clinical data. There were no missing values for this variable.
- **Age** in years at the time of recruitment was derived from self-reported date of birth. Month of birth was missing for 972 MSM on the questionnaire and imputed to June; year of birth was missing for 78 MSM and was completed from dates of birth provided in the routine linked clinical data. An additional 7 inconsistencies between questionnaire and clinic date of birth were resolved. A total of 23 MSM (1.0% of all MSM in the final data set) remained with missing data for date of birth (and thus age), as these could not be reconciled (7 reported their clinic attendance date instead of their date of birth and the remaining 16 did not provide date of birth on the questionnaire and also did not consent to linkage with routine clinical data).
- **Ethnicity** was based on the UK Census ethnic groups as per below ("Which ethnic group best describes you?").
  A. White : white British, white Irish, or white other
  B. Black or black British: black African, black Caribbean, or black other
  C. Asian or Asian British: Indian, Pakistani, Bangladeshi, or other
  D. Mixed: white and black African, white and black Caribbean, white and Asian, mixed other
  E. Chinese or other ethnic group: Chinese, or any other ethnic group

  For those who indicated more than one ethnic category (n=15), ethnicity classification was made on individual basis and considering country of birth. Missing values for ethnicity (n=44) were re-coded either according to self-reported country of birth (for participants with non-UK country of birth) or according to clinic-recorded ethnicity (for those who consented to linkage with routine clinical data). A dichotomous variable was derived: 'white' (category A) and 'all other' (incorporating all in categories B through E). No missing values remained for this variable.
- **Employment**: of 10 possible response options to the question "What is your current work situation?", a three-category variable was derived:
  1. Employed (incorporating 'employed' or 'self-employed' full or part-time)
  2. Unemployed (incorporating 'unemployed and registered with benefits' or 'unemployed, not registered for benefits')
  3. Other (incorporating 'full time student/education/training', 'permanently sick/disabled (for 3 months or more)', 'temporarily sick/disabled (for less than 3 months)', 'looking after home/family/dependants full-time', 'retired', and 'other' free text option).

     A total of 37 MSM (1.7%) did not provide information on employment and were classified as missing.
- **Education** was ascertained by the question "At what level did you complete your education?" with five options. These were reclassified into a binary variable:

1. No qualifications, or up to A levels, or equivalent of 12 years of education (including 'finished education with no qualifications', 'O levels/GCSEs or equivalent qualifications at age 16', 'A levels or equivalent qualifications at age 18')
2. University degree or higher

In addition, I coded participants' free text responses ('other, please specify') according to attainment level and country where this was achieved. For example, the lowest level of 'National Vocational Qualifications' was equivalent to three GCSE exams and thus classified the participant as category 1 (no qualifications/or up to 12 years of education). A total of 39 MSM did not provide an answer to educational status and a further 4 ticked multiple (discordant) categories; this resulted in 43 (1.9%) missing values for this variable.

- **Financial hardship** was ascertained by the question "Do you have money to cover your basic needs (e.g. food, heating)?" with categorical answers, 1:'all the time', 2:'most of the time', 3:'some of the time', and 4:'no'. Where two or more consecutive answers were ticked, the lowest category (lower hardship) was selected; where two or more non-consecutive categories were selected, the middle category was used. There remained 33 participants with missing values (1.5% of all MSM), of whom 28 left the question blank and five ticked three or more categories.
- **Depression symptoms** were defined using the standardised Patient Health Questionnaire-9 (PHQ-9) questionnaire, which has high diagnostic validity.[208] This instrument is used for screening and diagnosing the severity of depression. Responders rate the frequency of specific symptoms over the past two weeks ("How often have you been bothered by any of the following problems?"), which included nine statements such as 'feeling down, depressed or hopeless' and 'thoughts that you would be better off dead, or of hurting yourself in some way'. Each of the nine symptoms was rated in frequency: 0 ('not at all'), 1 ('several days'), 2('more than half the days'), or 3 ('nearly every day'); the total was summed, producing a scale ranging from 0 to 27. Missing values for individual symptoms on PHQ-9 were coded as absence of symptoms (assigned score 0), as the most common response pattern was to tick only those symptoms that the participant experienced. As a result, there were no missing values for this variable. I derived a binary variable from this scale according to standard definitions[208]:
    1. No depression symptoms (a score of <10 on the PHQ-9, which indicates no, minimal, or mild depression, or a missing value.)
    2. Presence of depression symptoms (a score of ≥10 on the PHQ-9, indicating moderate, moderately severe, or severe depression.)

    A cut-off of ≥10 was used as this is the standard score-based definition and has been shown to have sensitivity of 76% and specificity of 88% for major depression among HIV-diagnosed individuals.[209]
- **Anxiety symptoms** were defined using the standardised Generalized Anxiety Disorder 7 item scale (GAD-7), a valid tool for screening and diagnosing the severity of anxiety.[210] GAD-7 uses the same normative scoring system as the PHQ-9. Responses for symptoms in the past two weeks (including 'feeling nervous, anxious, or on edge' and 'trouble relaxing') were coded in the same way as

depression, from 0 to 3, and summed to produce a scale ranging from 0 to 21. Missing values for individual symptoms were treated as absence of that symptom (score 0). I derived a binary variable from this scale:

1. No anxiety symptoms (a score of <10 on the GAD-7, which indicates no or mild anxiety, or a missing value.)
2. Presence of anxiety symptoms (a score of ≥10 on the GAD-7, indicating moderate or severe anxiety symptoms)

The cut-off of ≥10 was used as it is the standard definition and has been shown to have sensitivity of 89% and specificity of 82% for diagnosing generalised anxiety disorder.[210]

- **Low social support** was measured using a validated five-item version of the Duke-UNC Functional Social Support Questionnaire (FSSQ), designed to measure perceived social support.[211,212] Participants were asked to rate each of the following statements on a five-point Likert scale ranging from 1 ('much less than I would like') to 5 ('as much as 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'; and 'I get help when I am sick in bed'. The sum of scores from each question was used to create three categories of social support: 21-25 high, 13-20 medium, and 0-12 low. The mean individual score across all social support items ranged from 1 to 5 (rounded) and was used to reconcile discrepancies in scoring; where multiple consecutive responses were scored per question, the mean value was used (or the more extreme value if they were consecutive). A total of 20 MSM (0.9%) left all five FSSQ questions blank and the three-category variable of social support was coded as missing.
- **Higher alcohol consumption** was measured using an abbreviated version of the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), which was developed by the WHO as a screening method for excessive alcohol drinking, and for identifying people with drinking patterns described as hazardous (increasing the risk of harmful consequences to the user or others) and harmful (that result in consequences to physical and mental health).[213] Two of the original three AUDIT-C questions were used, which have been shown to have high internal consistency and validity.[214]

  1. "How often do you have a drink that contains alcohol?", scored from 0 to 4 (0:'never', 1:'monthly or less', 2:'two to four times a month', 3: 'two to three times a week', and 4:' 4 or more times a week')
  2. "How many units of alcohol do you drink a typical day when you are drinking? (one unit being half a pint of beer/cider or a small glass of wine or a single measure of spirits)", with five options scored from 0 to 4 (0: '1 or 2 units', 1: '3 or 4', 2: '5 or 6', 3: '7 to 9', and 4:'10 or more')

  There were 4 MSM (0.2%) who left both above questions blank; these missing values were recoded to the lowest categories ('never' and '1 or 2 units' respectively). To generate a binary variable classifying participants as having evidence of harmful or hazardous consumption, the frequency and units of alcohol consumed were summed on the two questions above and a score of ≥6 out of

8 was considered "higher alcohol consumption"; this cut-off has been shown to have sensitivity of 73% and specificity of 91% on the three-item AUDIT-C.[215]

- **Alcohol dependency** was assessed using the CAGE questionnaire[216], a screening instrument for alcoholism, comprised of four questions: "Have you ever…"
    1. Felt the need to cut down your drinking?
    2. Felt annoyed by criticism of your drinking?
    3. Had guilty feelings about drinking?
    4. Taken a morning eye opener?

  Each question was scored as 0 (no) or 1 (yes), and the sum of four questions ranged from 0 to 4. The recommended cut-off for CAGE is a total score of ≥2 as evidence of alcohol dependency.[217] This cut-off has been shown to have high sensitivity and specificity (both >75%) across a range of populations.

- **Recreational drug use** in the previous three months is discussed in detail in Chapter 6.
- **Stable partner status** was ascertained by the question "Are you currently in an ongoing relationship with a partner (wife/husband or civil partner or girlfriend/boyfriend)?" **Stable partner's HIV serostatus** was ascertained by the question "Does your partner have HIV?" with possible answers: 'Yes', 'No', or 'Don't know'. A categorical variable was derived:
    1. No stable partner
    2. HIV-positive stable partner
    3. HIV-negative or HIV-unknown status stable partner (includes those who answered 'don't know' and those who did not specify their stable partner's HIV-serostatus)

  As the latter category (3) includes those who did not specify their partner's serostatus, there were no missing answers for this variable. Participants were also asked whether they were co-habiting with their stable partner. The length of time in the specific long term relationship was estimated from months and/or years reported.

3.8.3 Key HIV-related variables defined

The main variables I derived relating to HIV diagnosis, treatment, and attitudes to HIV seropositivity are outlined in this section.

- **Time since HIV diagnosis** was calculated from self-reported month and year that the participant first found out they were HIV positive. When only year of diagnosis was reported (in 559 cases, 24.9% of all MSM), the month was imputed as June. Where dates of first diagnosis were unlikely (e.g. prior to licensing of the first ELISA test in 1985), inconsistent in comparison to the ART start date, or were missing, these were checked against the date of first known positive HIV antibody test from the linked routine clinical data, if available. Following this process, 12 MSM (0.5%) remained with missing values for time since HIV diagnosis. Years between HIV diagnosis and date of ASTRA questionnaire completion were calculated, and further grouped into categorical variables

according to analysis needs. This variable was used to flag and exclude MSM who were diagnosed with HIV for ≤3 months prior to ASTRA questionnaire completion (see section 3.9.1).

- **Disclosure of HIV serostatus** is discussed in detail in Chapter 7.
- **ART status** was ascertained by a positive answer to the question "Are you currently taking HIV treatment?" Missing answers on this question were reconciled with routine linked clinical data, where available; if there was a record of ART regimen prescribed at or near the date of the participant's questionnaire completion then this was taken to indicate that the participant was on ART. There remained 11 MSM (0.5% of all) with missing values for ART status.
- **Self-reported CD4 count** was ascertained by the question "At your last test what was your CD4 count?" with five categories in cells/mm^3: <200, 200-350, 351-500, >500, and 'don't know/can't remember'. Where a participant indicated last CD4 count in two consecutive categories, the lowest one was selected; for those who indicated two non-consecutive categories (e.g. <200 and >500) or who included 'don't know' in their response, these were re-coded into the 'don't known/can't remember' category. The question was left blank by 46 MSM (2.0%).
- **Self-reported viral load (VL)** was ascertained by the question "What was your viral load the last time you got your test results?" with three options: '50 copies/mL or less ('undetectable' or 'suppressed')'; 'more than 50 copies/mL ('detectable' or 'raised')'; and 'don't know'. A total of 343 MSM (15.3%) did not answer this question and so these were considered missing values. Using the ART status variable above, a new variable was derived also incorporating self-reported VL, with the following categories;
    1. On ART, reports undetectable VL
    2. On ART, does not report undetectable VL (includes responses to self-reported VL 'more than 50copies/mL' and 'don't know')
    3. Not on ART
- **Non-adherence to ART** (among participants on ART only) was measured using the following questions:
    1. Frequency of ART regimen (once a day, twice a day, or other)
    2. Number of ART doses missed in the last two weeks (none, 1, 2, 3, 4 to 6, 7 to 9, or 10 or more). Thus once a day ART equalled 14 doses in two weeks and twice a day ART equalled 28 doses in two weeks and so on.
    3. Whether reported missing ART for two or more consecutive days in the previous three months (yes, no, or 'don't know/can't remember'). The number of occasions this (3) occurred (once, two or three times, or more than three times) in the past three months was also specified.

    Using questions 1 and 3 above, the following dichotomous variable was derived (among MSM on ART only):

    (i.) Adherent to ART (either not missed any consecutive days of ART in the past three months, or missed ≥2 consecutive days of ART only once in the previous three months)

(ii.) Non-adherent to ART (missed ≥2 consecutive days of ART on ≥2 occasions in the past three months)

- Transmission risk beliefs were series of statements on HIV transmission risk and infectiousness in relation to undetectable VL, to which participants indicate agreement on a 5-level Likert scale ('strongly agree', 'tend to agree', 'undecided/no opinion', 'tend to disagree', and 'strongly disagree'). A transmission risk belief score was derived from the following statements: (A) "An undetectable HIV viral load makes someone less infectious to a sexual partner than if they had a high viral load" and (B) "When viral load is undetectable, a condom is not needed to prevent HIV transmission." The score thus classified people according to how 'conservative' (or risk-averse) their views on HIV transmission were:
    1. Least conservative ('strongly' or 'tend to' agree to statement A and 'strongly' or 'tend to' agree to statement B)
    2. Moderately conservative ('strongly' or 'tend to' *agree* to statement A and 'strongly' or 'tend to' *disagree* or 'undecided' on statement B; or 'strongly' or 'tend to' *disagree*, or 'undecided' to statement A and 'strongly' or 'tend to' agree to statement B)
    3. Most conservative ('strongly' or 'tend to' *disagree* or 'undecided' on statement A and `strongly' or 'tend to' *disagree* or 'undecided' on statement B)

Where participants indicated two consecutive levels of agreement for a single statement, the more extreme level was selected, (indicating least conservative transmission risk beliefs); if two non-consecutive agreement levels were selected (e.g. 'strongly agree' and 'undecided'), the average score was used. If participants selected inconsistent levels of agreement on the two statements (e.g. disagree to statement A and agree to statement B), they were classified as 2:'moderately conservative'. In the case of missing values in one of the two statements, the missing response was coded as 'undecided/no opinion'. A total of 44 (2.0%) of missing values could not be reconciled as the section was left blank.

3.8.4 **Sexual behaviour questionnaire section**

This section outlines the main derived sexual behaviour variables, throughout this thesis (detailed in Chapter 4). The questionnaire sexual behaviour section was prefaced with a statement reiterating that any information about recent sex life is completely confidential, that the participant's name or clinic is not written on the questionnaire, and that answers would never be seen by the clinic staff. (Appendix I) Two sub-sections were made available on the male questionnaire, one on sex with women and one on sex with other men. Specifically, vaginal sex was explained to be "a man's penis in a woman's vagina" and anal sex as "a man's penis in a partner's anus (rectum or back passage)". The questionnaire did not inquire about oral sex. Almost all questions in this section related to sex in the past three months. The main derived variables were:

- Sex in the past three months, ascertained as a positive answer to either of the following two questions: "In the past three months, have you had sex (vaginal or anal sex) with a woman?" and "In the past three months, have you had anal sex with a man?"

- Condomless sex (CLS) refers to sex with a man and/or a woman without a condom. This was defined by a positive answer to either of the following questions: "In the past three months, have you had sex (vaginal or anal) with a woman *without a condom*?" or "In the past three months, have you had anal sex with a man *without a* condom?"
- Condomless sex with HIV-serodifferent partners (CLS-D) was ascertained by a positive answer to either of: "In the past three months, have you had sex (vaginal or anal sex) without *a* condom with a woman *who did not have HIV or whose HIV-status you did not know*?" or "In the past three 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*?"
- Condomless sex with HIV-seroconcordant partners (CLS-C) was defined as a positive answer to either of: "In the past three months, have you had sex (vaginal or anal sex) without a condom with a woman *who you knew also had HIV*?" or "In the past three months, have you had anal sex without a condom with a man *who you knew also had HIV*?"

The variables on CLS with HIV-serodifferent (CLS-D) and with HIV-seroconcordant (CLS-C) partners are not mutually exclusive, meaning that those who had CLS-C may have also reported CLS-D in the same time period. Section 4.3.2 details derivation of variables examining exclusive CLS-C.

For all CLS variables, all participants were assigned to a category (variables were derived with no missing values); absence of information on a specific CLS measure was taken to indicate negative response, with the exception of response patterns detailed below. Consistency was ensured between responses for CLS, CLS-C, and CLS-D. If participants left the question on sex in the past three months blank (or selected 'no'), but had a positive answer in one or more of the questions on CLS, CLS-D, or CLS-C, I then re-classified them as having had sex in the past three months. Similarly, if no or a negative answer was given to the question on CLS, but positive answers were selected for one or more of the questions on CLS-D or CLS-C, then I re-classified participants as having had CLS in the past three months. Additional sexual behaviour variables were considered on an individual basis if it was unclear whether the participant reported having CLS-D or CLS-C. For example, in certain cases a positive answer was given for CLS in the past three months, but both questions on CLS-D *and* CLS-C were either left blank or were negative, and the participant indicated either CLS-C or CLS-D "with only one sexual partner, my long term partner". In this case, I used the stable partner's reported HIV-serostatus to assign whether CLS-C or CLS-D had occurred, on a case by case basis. For a minority of individuals who indicated having CLS but did not indicate either CLS-C or CLS-D, it was not possible to impute their partners' HIV-serostatus, as either they did not have a stable partner, or they indicated sex with more than one partner. These individuals were classified as 'CLS-unspecified' (discussed in detail in section 4.4.7). Participants with missing information and those with insufficient information to classify as CLS were categorised as not having CLS.

- Total **number of sexual partners in the past three months** was derived from combining the number of women and men the participant reported having had sex with; whether any of

these was the participant's stable partner was also ascertained (only among those who reported being in a stable relationship). Participants were also asked how many HIV-serodifferent men and/or women they had sex with without a condom (number of CLS-D partners) as well as how many HIV-positive men and/or women they had sex with without a condom (number of CLS-C partners) in the previous three months; and whether any of these CLS-D or CLS-C partners was the participant's stable partner. If the total number of male or female sex partners in the past three months was lower than the sum of the number of CLS-D and CLS-C partners reported, then the total number of partners was replaced with the sum of CLS-D *and* CLS-C partners. A small number of participants indicated having more than one sexual partner in the past three months, but did not specify an exact number; where free text options were used to indicate a high number of partners, the number of partners was reconciled on an individual basis to either be closest to the number reported (e.g. "Hundreds" would be classified as '≥100 partners') or the 75th percentile of each variable (e.g. "Too many, lost count" would be the 75th percentile for the mean of total number of new partners for MSM).

- Types of condomless sex with HIV-serodifferent partners (CLS-D) were examined. **Ejaculation inside a partner** (male or female) was considered (only among those who reported CLS-D in the previous three months) either 'some or all of the times' or 'no-none of the times'. **Positioning** during sex refers to the act of choosing a different sexual position (the receptive/"bottom" or the insertive/"top" position) during anal CLS with other men depending on the partner's HIV-serostatus. Participants were asked which partner they were when they had CLS with HIV-serodifferent male partners in the past three months, choosing from three options: (i) 'always the insertive partner (your penis was inside your partner)', (ii) always the receptive partner ('your partner's penis was inside you'), and (iii) sometimes the insertive partner and sometimes the receptive partner. A hierarchical variable was created, reflecting decreasing HIV transmission risk reduction measures taken during anal CLS-D:
    1. Always the receptive partner
    2. Sometimes or always insertive but no ejaculation
    3. Sometimes or always insertive with ejaculation

Only participants who reported having CLS-D were included in this variable; I recoded the remaining to missing.

- **Group sex** was referred to as "sex with more than one other person on the same occasion in the past three months". A total of 51 (2.3%) MSM did not answer this question and were recoded to missing values.
- Participants were also asked whether they had "been diagnosed with a **sexually transmitted infection** (not including HIV) in the past three months", further selecting one or more of the following if applicable: syphilis, gonorrhoea, chlamydia, LGV, new hepatitis B or C, new or recurrent genital herpes or warts, trichomonas, NSU (Non Specific Urethritis)/NGU (Non

Gonococcal Urethritis), or other. Those who specified other STIs were re-classified in the above categories if possible (details in section 8.3.1). There were 31 missing values (1.8%) for MSM who left this question blank. The questionnaire also included inquiry on "ever being told by a doctor that you have hepatitis C", which was considered separately from other STIs as **lifetime hepatitis C diagnosis**. A total of 44 MSM (2.0%) did not answer this question.

- Total **number of new sexual partners in the past 12 months** was ascertained by the question "In the past 12 months, how many *new* sexual partners have you had? (this means people you have not had sex with before)". Two choices were given: 'none' or 'one or more' with a free text option for the approximate number. A binary variable was created based on whether or not ≥10 new partners in the past year were reported:
    1. Yes (reported ≥10 new partners)
    2. No or missing answer (reported either: (i) <10 new partners in the past year, (ii) no new partners, (iii) >1 new partner but not the exact number, or (iv) did not complete this question and also did not provide the number of partners in the past three months from which to extrapolate number of new partners-see below.)

There were 87 (4.0% of all) MSM who did not answer both questions on number of partners (in the past 3 months and new partners in the past year); I incorporated them in the 'no or missing answer' category of this variable (category 2 above). For participants reporting one or more new partners but not the exact number, I extrapolated this from the total number of partners (or of the number of CLS-D or CLS-C partners) in the past three months: if participants reported having more than one (male or female) partner in the past three months (but did not say how many were *new* in the past year), then I calculated the number of new partners in the past year to be twice the number of partners in the past three months, subtracting one if sex with the participant's stable partner was indicated. For example, if a participant reported four partners in the past three months, one of whom was their stable partner, and also reported more than one *new* partner in the past year but not the exact number, I imputed this to be six new sexual partners in the past year.

3.9 Statistical analysis

This section provides an overview of the main statistical methods I used to analyse data throughout this thesis. Details of specific eligibility criteria for analyses and additional statistical methods used are presented in detail in the methods section of each respective chapter, and summarised in Table 3.2. Stata 13 was used for statistical analysis.[218]

3.9.1 Exclusion of recently diagnosed participants

MSM who were diagnosed with HIV up to three months prior to questionnaire completion may have reported condomless sex (CLS) and other sexual behaviours that took place prior to their positive HIV diagnosis. As this thesis explores the sexual behaviours associated with HIV-seropositivity, those participants who reported being diagnosed with HIV for three or fewer months were excluded from the sample for all analyses (see Table 3.2). A detailed discussion of the characteristics of this group is provided in section 4.4.1.

3.9.2 **Summary statistics**

Summary statistics were used to describe the population under study, and to assist in data error checking prior to statistical analysis. The total number of patients (denoted by N) and the row or column percentage (%) in each category was reported. For continuous variables the mean and standard deviation (SD) were presented if the data was normally distributed; the median and interquartile range (IQR) was presented for skewed data.

3.9.3 **Univariable analyses**

This section describes the methods used to examine whether associations between the distribution of individuals among categories of one variable is independent of their distribution among the categories of another. The Pearson chi-squared test was used for binary independent variables with a binary dependent variable. When the expected numbers were too small, chi-squared tests were not considered a good approximation; in this case Fisher's exact test was used, particularly when the overall total of a contingency table was <20 or was between 20 and 40 and the smallest expected value was <5.[219] For ordered categorical independent variables with a binary dependent variable, the chi-squared test for trend was used. In this case, approximation of chi-squared tests is valid if less than 20% of the expected numbers in a contingency table are <5 and none are <1; if this occurred, categorical variables were further collapsed or treated as continuous (if numerical). To evaluate the difference between means for a continuous dependent variable, t-tests were used if comparing two groups (binary independent variable) and analysis of variance (ANOVA) when comparing more than two groups.

All statistical tests performed were two-sided and a p-value of less than 0.05 was considered statistically significant. The 5% threshold was interpreted as being small enough to justify rejection of the null hypothesis of no difference between groups. In interpreting results, patterns of association, the magnitude of association and width and limits of confidence intervals, and the sample size were also considered.

Table 3.2: Summary of datasets, eligibility criteria, and statistical methods used in this thesis

					Regression methods used		
Chapter/Title		**Dataset**	**Eligibility criteria**	**N MSM included**	**Modified Poisson**	**Multinomial Logistic**	**Cox proportional hazards**
4	Condomless sex among HIV-diagnosed MSM	ASTRA	MSM diagnosed with HIV for ≥3 months prior to ASTRA questionnaire completion	2189	✓	✓	
5	Characterising higher HIV risk CLS-D			2189	*descriptive statistics only*		
6	Recreational drug use and condomless sex			2189	✓	✓	
7	Non-disclosure of HIV-serostatus and condomless sex			2189	✓	✓	

8	Hepatitis C, other STI co-infections, and condomless sex	ASTRA with linked clinical data	MSM diagnosed with HIV for ≥3 months prior to ASTRA questionnaire completion and consenting to linkage of routine clinical data, with available hepatitis C test results	1810	✓		✓

3.9.4 Multivariable analyses

Statistical models were used to quantify the associations between variables of interest, while controlling for other factors. This section provides an overview of the main multivariable models used in this thesis.

3.9.4.1 Logistic regression

Logistic regression models the association of a binary dependent variable and one or more independent variables in terms of odds ratios (ORs). In this context, data can be represented as in Table 3.3

Table 3.3: Notation for contingency table of binary outcome (dependent) variable with two exposure groups (independent variable)

	Outcome (dependent variable)		
Exposure (independent variable)	Experienced outcome	Did not experience outcome	Total
Exposed	d_1	h_1	n_1
Unexposed	d_0	h_0	n_0
Total	$\boldsymbol{d}$	$\boldsymbol{h}$	$\boldsymbol{n}$

The odds are estimated by the number of individuals who experience the outcome (d) divided by the number who do not experience the outcome (h):

$$Odds = \frac{p}{1-p} = \frac{\frac{d}{n}}{1-(\frac{d}{n})} = \frac{\frac{d}{n}}{\frac{h}{n}} = \frac{d}{h}$$

Where p refers to the probability or risk that the outcome is experienced. Consequently, the odds ratio (OR) is estimated by:

$$OR = \frac{odds\ in\ exposed\ group}{odds\ in\ unexposed\ group} = \frac{\frac{d_1}{h_1}}{\frac{d_0}{h_0}} = \frac{d_1 \times\ h_0}{d_0\ \times h_1}$$

Logistic regression derives its name from the *logit* function, which describes the transformation of p, the probability or risk of the outcome occurring, into log odds of p.(Equation 3.1) Thus logistic regression fits models on a log scale; log odds are not constrained and can take any value between -∞ and ∞, as opposed to probabilities, which must lie between 0 and 1.[219]

Equation 3.1: The logit function

$$Logit(p) = \frac{\log(p)}{\log(1-p)}$$

The two parameters in the logistic regression model are the baseline odds (in the unexposed group, with the independent variable) and the exposure odds ratio (odds in the exposed/odds in the unexposed group), which are multiplied together on the log scale as: log (odds) = log (baseline odds) + log (exposure odds ratio). This takes the form shown in Equation 3.2, where β_p refers to the estimated linear regression coefficients and x_p refers to the exposure variables.

Equation 3.2: The logistic regression model

$$\log odds\ of\ outcome = \beta_0 + \beta_1 x_1 + \beta_2\ x_2 + \beta_3 x_3 + \cdots + \beta_p x_p$$

The regression coefficients thus describe the effect of each independent variable on the dependent variable, adjusted for other independent variables. For example if the dependent variable is whether or not the participant reported having condomless sex and one of the independent variables is ART status (on ART or not on ART), then the odds of reporting condomless sex could be said to be higher or lower for those on ART compared to those not on ART.

A likelihood-ratio test is used to derive p-values for each variable in the model. This is done by estimating two nested models; one model is considered nested within the other if the first model can be generated by imposing restrictions on the parameters of the second. In this case, the restriction is that the parameter is equal to zero (meaning that the parameter, or independent variable, is removed from the model). The log likelihood of the two models is compared (the fit of the nested model is compared to the fit of the first model) and if the difference is statistically significant then the first model is said to fit the data significantly better than the nested model; this implies that including the independent variable that was removed creates a statistically significant improvement in the fit of the model.

3.9.4.2 Multinomial logistic regression (MNL)

Logistic regression can be extended to model a dependent variable that has more than two categories (categorical variable). In this case, the model estimates the effect of one or more independent variables on the probability that the dependent variable is in a particular category. MNL assumes that the dependent variable categories are independent of each other, meaning that being in one category is not related to being in another category. It also assumes non-perfect separation of the dependent variable categories (if they are perfectly separated by the independent variable then unrealistic coefficients will be estimated and effect sizes can be exaggerated).[220] For example, Chapter 4 will examine, among MSM who report sex in the past three months, risk factors for three categories of sexual behaviour (condom-protected sex only, condomless sex with HIV-seroconcordant partners, and condomless sex with HIV-serodifferent partners). The outcome level 'condom-protected sex' is chosen as the reference group (comparison level) and $(n-1)$ regression coefficients (or odds ratios if exponentiated) corresponding to the other two categories of condomless sex are estimated for each exposure variable in the regression model (e.g. age, drug use etc.).

3.9.4.3 Comparison of odds and risk ratios

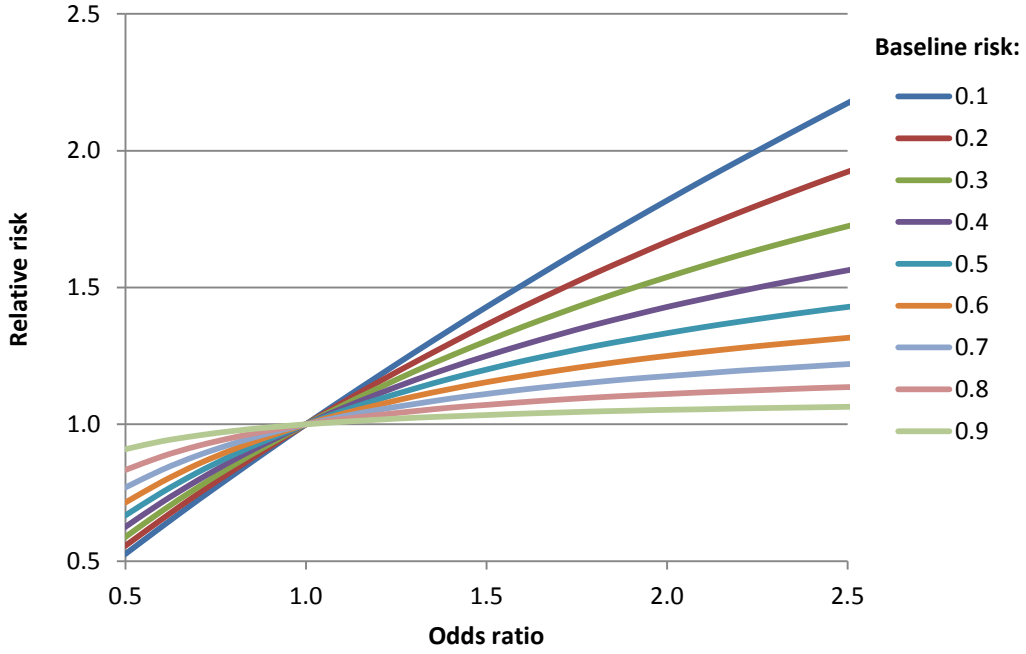
The logistic regression model was initially adapted for case-control studies, for which the appropriate measure of association is the odds ratio (OR).[221] The OR is a common measure in epidemiological literature, but can be commonly misinterpreted as if it were a risk ratio. Risk ratios are measures of effect that describe the ratio of the proportion with the dependent variable in the exposed group (p_1, with the independent variable) to the proportion with the dependent variable in the unexposed group (p_0). Using notation from Table 3.3, the risk ratio (RR) is estimated by:

$$RR = \frac{risk\ in\ exposed\ group}{risk\ in\ unexposed\ group} = \frac{p_1}{p_0} = \frac{\frac{d_1}{n_1}}{\frac{d_0}{n_0}}$$

In cross sectional studies, such as ASTRA, the risk ratio is referred to as a prevalence ratio (PR), as it describes the ratio of the prevalence of the dependent variable in those exposed (with the independent variable) divided by the prevalence in the unexposed. When the outcome of interest is rare in the population (baseline risk <0.1, i.e. prevalence of <10%), the odds ratio approximates the prevalence ratio. (Figure 3.1) When the outcome is not rare, the odds ratio is numerically discrepant to the prevalence ratio by orders of magnitude. As shown in Figure 3.1, when the PR>1, the OR will always be greater than the PR, and when the PR<1, the OR will always be smaller. When the rare event assumption is not considered, ORs are often misinterpreted as PRs, which may lead to inaccurate conclusions.[222] For example, if the baseline risk is 0.5 (50% prevalence) then an OR of 2.0 is equivalent to a PR of 1.3, meaning that the OR of 2 mustn't be interpreted as 'double the risk' of the outcome. As discussed in section 3.9.4.1, while odds can take any value between 0 and ∞, the risk (or prevalence in the unexposed group, p_0) remains constrained between 0 and 1.[219] For this reason, this thesis estimates prevalence ratios using modified Poisson regression as an alternative to logistic regression (discussed in section 3.9.4.6). In addition, as unadjusted associations are usually presented in terms of percentages, presenting adjusted associations as prevalence ratios is the natural extension to this.

Odds ratios have one advantage over prevalence ratios, particularly when comparing the magnitude of an association between a single independent variable with many dependent binary variables of varying prevalence (for example, recreational drug use and various types of condomless sex, CLS, as in Chapter 6). Comparing the prevalence ratios between different models (e.g. drug use and CLS-D versus drugs use and CLS-C) would not be appropriate due to different prevalence in the reference group; comparison of odds ratios would be preferable in this case. (This has been done as sensitivity analyses in sections 6.3.3.5 and 7.3.6).

Figure 3.1: Relationship between odds ratio and relative risk according to baseline risk. *Adapted from* [223]



3.9.4.4 Rate ratios

The rate of occurrence of an outcome event measures the number of new events that occur per person per unit time (denoted byλ):

$$Rate, \lambda = \frac{number\ of\ events}{total\ person - time\ of\ observation} = \frac{d}{T}$$

To compare rates of an outcome in two exposure groups (exposed denoted by 0 and unexposed by 1), the rate ratio (RR) is used:

$$RR = \frac{rate\ in\ exposed}{rate\ in\ unexposed} = \frac{\lambda_1}{\lambda_0} = \frac{\frac{d_1}{T_1}}{\frac{d_0}{T_0}} = \frac{d_1 \times T_0}{d_0 \times T_1}$$

3.9.4.5 Poisson regression

Poisson regression estimates rate ratios in the same way that logistic regression estimates odds ratios between different exposure groups. The Poisson distribution describes the number of times an event d occurs (counts) over a period of time, provided that the events occur independently of each other and at random.[219] The distribution depends on a single parameter, the mean number of occurrences (μ) per interval (during periods of time with the same duration). This is specified by:

Equation 3.3: The Poisson distribution function

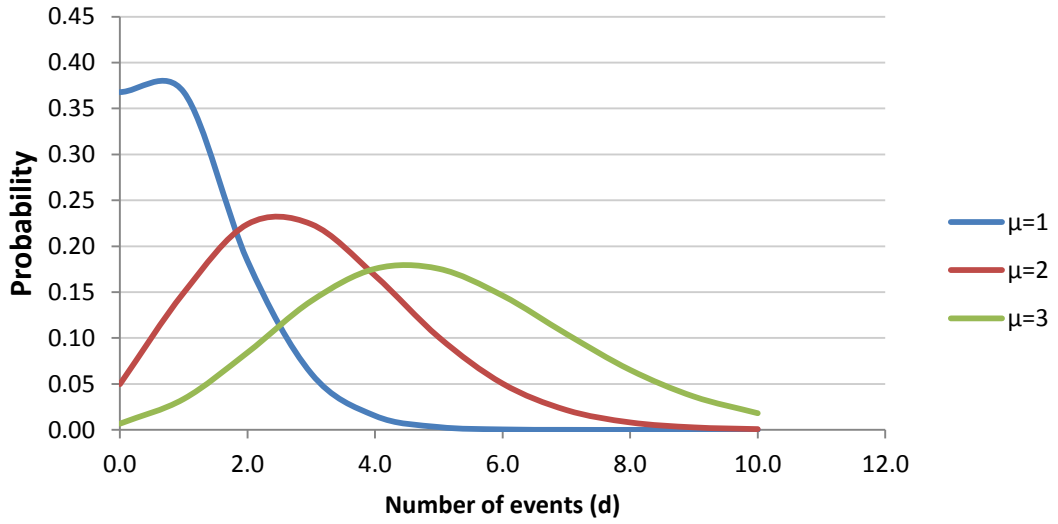
$$\boldsymbol{Probability(d) = \frac{e^{-\mu} \times \mu^{d}}{d!}}$$

Where $d! = 1, 2, 3$ … and so on, indicating the number of times the outcome occurred.

Figure 3.2 shows the predicted probabilities for different values of the Poisson distribution mean, μ. When the mean is small, the distribution is skewed towards a probability of zero events occurring.

Conversely, the distribution is symmetrical for larger means and approximates the normal distribution when $\mu \geq 10$. One of the main assumptions of the Poisson distribution is that the mean (μ) is equal to the variance (the square of the standard deviation,σ^2), referred to as equidispersion. Poisson is thus appropriate for analysis of rare outcomes when individuals are followed up for a variable length of time.[224]

Figure 3.2: Shape of the Poisson distribution at various values of the mean (μ).*Adapted from* [219,225]



Poisson regression models are fitted on a log scale and results are exponentiated to derive rate ratios and confidence intervals. The two model parameters are the baseline rate (in the unexposed group) and the exposure rate ratio (rate in the exposed group/rate in the unexposed group), which, as with logistic regression, are summarised in the form:

Equation 3.4: The Poisson regression model

$$\log rate = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \cdots + \beta_p x_p$$

Where β_p refers to the regression coefficient associated with the *p* exposure variables x_1 tox_p.

The equivalent model on the ratio scale is then:

$$Rate\ of\ outcome = e^{\beta_0} \times e^{(\beta_1 x_1)}$$

This is also referred to as an incidence rate (IR).

3.9.4.6 Modified Poisson regression

So far Poisson regression has been discussed in the context of estimating rate ratios applied using count data. To examine the effect of an independent variable to the log of the risk of a binary dependent variable (rather than the log of the odds), generalised linear models can be used for a range of dependent variable distributions and link functions. Equation 3.1 shows that logistic regression assumes a binomial distribution for the dependent variable and thus uses a logit link function. To model the effect of independent variables as relative risks (instead of odds ratios), a log link function can be used (as in Equation 3.4), which specifies the log risk of the outcome occurring, $\log(p)$.[226] Hence, the log link allows the log risk to not be constrained and Poisson regression can be applied to a binomial distribution (rather than a Poisson distribution) to model the effect of an exposure variable as a prevalence ratio.[219]

In this case, the outcome distribution is still binomial, the mean is still equal to the variance, and the model has the same form as Equation 3.4.

An issue that arises from the application of Poisson to binomial data, is that the error for the prevalence ratios are overestimated and the confidence intervals become too wide.[224] To counteract this, a robust error variance procedure is used, called 'sandwich estimation'; when Poisson regression is used on binomial data with a log link function and sandwich estimation, it is henceforth referred to as 'modified' Poisson regression. Modified Poisson has been extensively used and validated, and is regarded as reliable even with small sample sizes.[221,225] In this thesis, when the outcome of interest (dependent variable) is not rare (≥10% prevalence) modified Poisson is used to derive prevalence ratios.

3.9.5 Multivariable model strategy

Throughout analyses in Chapters 4, 6, 7, and 8, multivariable models were developed in order to assess the independent associations of a number of exposures with a particular dependent variable. Two adjustment strategies were used for each analysis. Firstly, each factor (exposure or independent variable) was adjusted *in separate models* for a set of 'core' factors; age (<30, 30-39, 40-49, 50-59, ≥60 years, or <40, ≥40 in underpowered analyses), ethnicity (white, all other), time since HIV diagnosis (≤2, 2-5, 5-10, 10-15, ≥15 years or <5, 5-10, >10 years in underpowered analyses), ART status (on ART, off ART), and stable partner status (HIV-positive, HIV-negative or unknown status, no stable partner). This strategy (referred to as 'Models 1' in relevant tables) included variables of known importance or relevance to CLS among HIV-diagnosed MSM, regardless of their statistical significance. Secondly, a stepwise adjustment strategy was used, so that any factor with p<0.10 at unadjusted analysis was a candidate for inclusion in a *single* multivariable model in addition to clinic (referred to as 'Model 2'); variables that were correlated or which incorporated the same factors were examined critically in terms of their importance and relevance and excluded accordingly (detailed for each analysis in relevant sections).

3.10 ASTRA sample description

3.10.1 Methods

3.10.1.1 Recruitment and patient populations

For each participating clinic, the following proportions of patients (men and women) were calculated; invited to participate (approached), consented to participate, completed the questionnaire (respondents), consented to participate but did not return/complete the questionnaire (non-respondents), and consented to linkage of the questionnaire with routine clinical data.

3.10.1.2 Comparison of ASTRA participants by response status

Study log-recorded gender, VL, and CD4 count were compared between ASTRA respondents and non-respondents using chi-squared tests.

3.10.1.3 Characteristics of ASTRA MSM participants

The distribution of main socio-demographic, psychological, and HIV-related derived variables (defined in sections 3.8.2 and 3.8.3) was examined by gender/sexuality of ASTRA respondents (MSM versus heterosexual men and women) and compared by chi-squared tests or Fisher's exact test. Results are shown for heterosexual men and women in this chapter only to provide context, and are not discussed in detail; instead, the focus of this thesis is MSM who participated in ASTRA only. In addition, the distributions of the main sexual behaviour variables defined in section 3.8.4 are presented in Chapter 4.

3.10.1.4 Comparison of ASTRA MSM by consent to clinical linkage

MSM who did not consent to linkage of their questionnaire data with routine HIV clinical data were compared to those who consented to linkage, on key socio-demographic and HIV-related factors, using chi-squared tests.

3.10.1.5 Comparison of ASTRA sample to UK HIV-diagnosed population

To assess the generalisability of the ASTRA sample with the population of HIV-diagnosed men and women living in the UK as of the end of recruitment (2012), ASTRA respondents were compared to the individuals included in the Survey of Prevalent HIV Infections Diagnosed (SOPHID) in 2011 and 2012. SOPHID is a cross-sectional survey of all HIV-diagnosed individuals attending for HIV care at NHS sites in England, Wales, Northern Ireland, and incorporates Scottish data from Health Protection Scotland to produce UK totals.[227] Public Health England collects information bi-annually in London and annually outside London via aggregated data in SOPHID, including: the number of individuals living with diagnosed HIV at UK and regional level, by age, sex, probable route of HIV transmission (exposure group), ART status, CD4 count, and last measured VL. SOPHID therefore constitutes a reliable measure of the annual prevalence of diagnosed HIV.

3.10.2 Results

3.10.2.1 Recruitment and patient populations

Table 3.4 describes the response rates of men and women approached to participate to the ASTRA study in eight clinics during 2011-2012. A total of 5112 HIV-diagnosed individuals met eligibility criteria and were approached and asked to participate in the study. Of those approached, 4200 (82.2%) consented to participate in the study, and 912 (17.8%) did not consent. (Table 3.4) A total of 3258 HIV-diagnosed individuals completed the ASTRA questionnaire, resulting in a total response rate of 63.7% across all clinics. Consent to clinical linkage of ASTRA questionnaire with routine clinical data was very high (>90%). Among 3258 ASTRA participants, 2248 (69.0%) were MSM.

3.10.2.2 Comparison of consenting participants by response status

Among 4200 men and women who provided written consent, 942 did not complete/return the questionnaire.(Table 3.5) There were no significant differences between those who completed the questionnaire (respondents) and those who did not (non-respondents) in terms of gender, VL, or CD4 count.

3.10.2.3 Characteristics of ASTRA MSM participants: Socio-demographic, psychological, and lifestyle factors

Table 3.6 shows the distribution of main socio-demographic, psychological, and lifestyle factors (described in section 3.8.2) among 3258 ASTRA participants, by gender/sexual orientation. There were significant differences between MSM and heterosexual men and women on almost all variables. Results are discussed in the context of the 2248 MSM, who are the focus of this thesis. The mean age of MSM was 45.5 years (SD 9.5), the majority identified as white (British, Irish, or other), and as not belonging to any particular religion. Over 70% were either born in the UK or had been living in the UK for five or more years if not UK-born. A minority were unemployed (14.6%) and over 55% had had been educated up to the equivalent of A levels. Prevalence of financial hardship was relatively low, with 52.0% of MSM reporting always having money for basic needs. Symptoms of depression and anxiety were evidenced in 27.1% and 20.9% of MSM respectively. Over 59% reported having a high level of social support. Higher alcohol consumption was evident in 16.7% of MSM, and over half of MSM reported using recreational drugs in the previous three months (both discussed further in Chapter 6).

Table 3.4: Recruitment and consent to the ASTRA study clinical centres during 2011-2012

		Eligible patients approached	Did not consent to study participation (% of approached)	Consented to study participation (% of approached = consent rate)	Completed questionnaire-respondents (% of approached = response rate)	Consented to clinical linkage (% of respondents)	Gender/sexual orientation of those completed questionnaire (% of respondents)	
							MSM	Heterosexual men and women
All sites	**N (%)**	5,112 -	912 (17.8)	4200 (82.2)	3258 (63.7)	2983 (91.6)	2248 (69.0)	1010 (31.0)
Royal Sussex County Hospital Brighton	**n (%)**	787 -	69 (8.8)	718 (91.2)	523 (66.5)	484 (92.5)	451 (86.2)	72 (13.8)
Eastbourne Sexual Health Clinic	**n (%)**	104 -	22 (21.2)	82 (78.8)	61 (58.7)	60 (98.4)	35 (57.4)	26 (42.6)
Homerton University Hospital	**n (%)**	465 -	91 (19.6)	374 (80.4)	269 (57.8)	233 (86.6)	73 (27.1)	196 (72.9)
Mortimer Market Clinic	**n (%)**	1,317 -	185 (14.0)	1,132 (86.0)	907 (68.9)	842 (92.8)	743 (81.9)	164 (18.1)
Newham University Hospital	**n (%)**	276 -	80 (29.0)	196 (71.0)	179 (64.9)	147 (82.1)	37 (20.7)	142 (79.3)
North Manchester General Hospital	**n (%)**	732 -	209 (28.6)	523 (71.4)	355 (48.5)	345 (97.2)	235 (66.2)	120 (33.8)
Royal Free Hospital	**n (%)**	1,336 -	249 (18.6)	1,087 (81.4)	899 (67.3)	809 (90.0)	651 (72.4)	248 (27.6)
Whipps Cross University Hospital	**n (%)**	95 -	7 (7.4)	88 (92.6)	65 (68.4)	63 (96.9)	23 (35.4)	42 (64.6)

Table 3.5: Comparison of 4200 HIV-diagnosed men and women consenting to ASTRA participation according to questionnaire completion status

	Respondents (n=3258)		Non-respondents (n=942)		
	n	(row %)	n	(row %)	p-value
Gender (N=4200)					
Male	2621	(78.0)	739	(22.0)	
Female	637	(75.8)	203	(24.2)	0.177
Viral load (c/mL) (N=4124)					
≤50	1788	(76.9)	536	(23.1)	
>50	1424	(79.1)	376	(20.9)	0.095
CD4 count (cells/mm^3) (N=4130)					
≤350	598	(75.4)	195	(24.6)	
>350	2619	(78.5)	718	(21.5)	0.061

p-value by chi-squared test; study-log recorded latest VL and CD4 count communicated to the participant

3.10.2.4 Characteristics of ASTRA MSM participants: HIV-related factors

Over 73% of MSM had been diagnosed with HIV for more than five years (Table 3.7); 59 MSM (2.6%) were recently diagnosed (within ≤3 months of ASTRA completion) and were excluded from analyses which included inquiry on sexual behaviour in the past three months, as they may have been describing behaviour that occurred prior to their positive HIV diagnosis (section 3.9.1). A small minority (5.0%) of MSM had not disclosed their HIV-serostatus to anyone in their social circle, which is further discussed in Chapter 7. Prevalence of ART use at the time of the questionnaire was high (85.1% on ART), with 53.0% of MSM being on ART for five years or longer. Over 6% of MSM did not know their personal CD4 count and 7.7% did not know their VL. A total of 83.8% of MSM had a study log-recorded CD4 count of >350 cells/mm^3, and 76.0% had suppressed VL (≤50c/mL). For MSM on ART, VL was suppressed for 88.1% (n/N=1654/1878). Adherence to ART was overall high (76.9%). Only 4.7% reported least conservative transmission risk beliefs (see sections 3.8.2 and 3.8.3 for detailed definitions of all variables).

3.10.2.5 Comparison of respondents by consent to clinical linkage

Comparison of all ASTRA participants who provided consent to clinical linkage (n=2983) with those who did not (n=275) showed no significant differences in terms of age, education, employment, time since HIV diagnosis, ART status, and study log-recorded VL distributions (p>0.05, results not shown). When examining MSM separately, there were no significant differences between those who did and did not provide consent to linkage, in terms of age, education, employment, time since HIV diagnosis, ART status, and study log-recorded VL or CD4 count. (Table 3.8) Over 20% of MSM who did not consent were of non-white ethnicities as compared to 10.1% of MSM who gave consent to linkage (p<0.001). Similarly, MSM who were not born in the UK were more likely to not provide consent to linkage with clinical data as compared to UK-born MSM (p<0.001). By December 2016, four of the eight participating clinics had provided linked clinical data for 1811 MSM.

Table 3.6: Socio-demographic, mental health, and lifestyle characteristics among 3258 ASTRA participants according to gender/sexual orientation

	MSM (N=2248)		Heterosexual men and women (N=1010)		
	n	(%)	n	(%)	p-value
Age at recruitment (N=3114), years					
<30	107	(4.9)	59	(6.4)	
30-39	496	(22.6)	230	(24.9)	
40-49	935	(42.7)	403	(43.7)	
50-59	504	(23.0)	173	(18.8)	
≥60	150	(6.8)	57	(6.2)	0.037
Mean [SD] age years	45.5	[9.5]	44.5	[9.7]	0.004 (T)
Ethnic group (N=3174)					
White	1974	(89.3)	242	(25.1)	
Black African	23	(1.0)	583	(60.5)	
Black Caribbean or other	53	(2.4)	69	(7.2)	
Asian or Asian British	32	(1.4)	19	(2.0)	
Mixed or other	129	(5.8)	50	(5.2)	<0.001
Religious (N=3204)					
Yes	947	(42.8)	848	(85.4)	
No	1264	(57.2)	145	(14.6)	<0.001
Born in UK/time lived in UK (N=3258)					
Born in the UK	1540	(68.5)	209	(20.7)	
Non-UK born lived in UK<5yrs	88	(3.9)	72	(7.1)	
Non-UK born lived in UK>5yrs	537	(23.9)	651	(64.5)	
Non-UK born (time not specified)	83	(3.7)	78	(7.7)	<0.001
Education (N=3144)					
University degree or above	983	(44.6)	333	(35.5)	
No qualifications or up to A levels	1222	(55.4)	606	(64.5)	<0.001
Employment status (N=3139)					
Employed	1357	(61.8)	449	(47.7)	
Unemployed	320	(14.6)	261	(27.7)	
Other	520	(23.7)	232	(24.6)	<0.001
Financial hardship (money for basic needs) (N=3186)					
Always	1151	(52.0)	238	(24.5)	
Mostly/sometimes	886	(40.0)	511	(52.6)	
No	178	(8.0)	222	(22.9)	<0.001 (T)
Depression symptoms (N=3258)					
No/missing	1639	(72.9)	735	(72.8)	
Yes	609	(27.1)	275	(27.2)	0.935
Anxiety symptoms (N=3258)					
No/missing	1778	(79.1)	771	(76.3)	
Yes	470	(20.9)	239	(23.7)	0.078
Social support (N=3196)					
High	1330	(59.7)	549	(56.7)	
Medium	678	(30.4)	310	(32.0)	
Low	220	(9.9)	109	(11.3)	0.093 (T)
Harmful/hazardous alcohol consumption (N=3258)					
No/missing	1872	(83.3)	954	(94.5)	
Possible	376	(16.7)	56	(5.5)	<0.001
Recreational drug use in past 3 months (N=3258)					
No/missing	1110	(49.4)	906	(89.7)	
Yes	1138	(50.6)	104	(10.3)	<0.001

p-values by chi-squared test or chi-squared test for trend (T); All factors defined in sections 3.8.2 and 3.8.3

Table 3.7: HIV-related characteristics among 3258 ASTRA participants by gender/sexual orientation

	MSM (N=2248)		Heterosexual men and women (N=1010)		
	n	(%)	n	(%)	p-value
Time since HIV diagnosis (N=3,226)					
≤3 months	59	(2.6)	20	(2.0)	
3 months-2 years	189	(8.5)	112	(11.3)	
2-5 years	340	(15.2)	165	(16.6)	
5-15 years	1,004	(44.9)	520	(52.4)	
>15 years	642	(28.7)	175	(17.6)	<0.001 (T)
Disclosure of HIV-serostatus (N=3,233)					
Disclosed to at least one person	2,128	(95.0)	834	(84.0)	
Not disclosed to anyone	112	(5.0)	159	(16.0)	<0.001
ART status (N=3,232)					
On ART	1,904	(85.1)	886	(89.0)	
Not on ART	333	(14.9)	109	(11.0)	0.003
Self-reported CD4 count, cells/mm^3 (N=3,158)					
<200	177	(8.0)	116	(12.1)	
200-350	308	(14.0)	139	(14.5)	
351-500	571	(25.9)	203	(21.2)	
>500	996	(45.2)	311	(32.5)	
"Don't know"	150	(6.8)	187	(19.6)	<0.001
Study log CD4 count, cells/mm^3 (N=3,217)					
≤350	359	(16.2)	254	(25.4)	
>350	1,859	(83.8)	745	(74.6)	<0.001
Self-reported viral load, c/mL (N=2,766)					
≤50	1,571	(82.5)	587	(68.2)	
>50	188	(9.9)	86	(10.0)	
"Don't know"	146	(7.7)	188	(21.8)	<0.001
Study log viral load, c/mL (N=3,212)					
≤50	1,682	(76.0)	768	(77.0)	
>50	532	(24.0)	230	(23.0)	0.545
Adherence to ART (N=2,790 on ART)					
Adherent	1,721	(76.9)	761	(76.5)	
Non-adherent	183	(8.2)	125	(12.6)	<0.001
HIV transmission risk beliefs (N=3,145)					
Most conservative	1,052	(47.7)	512	(54.4)	
Moderately conservative	1,049	(47.6)	347	(36.9)	
Least conservative	103	(4.7)	82	(8.7)	0.261 (T)
p-values by chi-squared test or chi-squared test for trend (T);All factors defined in section 3.8.3					

Table 3.8: Comparison of 2,248 MSM respondents according to status of consent to linkage with clinical data

	MSM consenting to linkage with clinical data (N=2,117)		MSM not consenting to linkage with clinical data (N=131)		
	n	(%)	n	(%)	p-value
Age group, years (N=2,224)					
<30	107	(5.1)	3	(2.5)	
30-39	465	(22.1)	38	(31.4)	
40-49	895	(42.6)	53	(43.8)	
50-59	488	(23.2)	21	(17.4)	
≥60	148	(7.0)	6	(5.0)	0.118 (T)
Ethnicity (N=2,211)					
White	1872	(89.9)	102	(79.7)	
Black of black British	67	(3.2)	9	(7.0)	
Asian or Asian British	39	(1.9)	6	(4.7)	
Mixed	81	(3.9)	6	(4.7)	
Other ethnic group	24	(1.2)	5	(3.9)	0.002 (F)
Born in the UK (N=2,248)					
No	646	(30.5)	62	(47.3)	
Yes	1471	(69.5)	69	(52.7)	<0.001
Education (N=2,205)					
University degree or above	922	(44.4)	61	(47.7)	
No qualifications or up to A levels	1155	(55.6)	67	(52.3)	0.471
Employment status (N=2,197)					
Employed	1276	(61.6)	81	(64.3)	
Unemployed	298	(14.4)	22	(17.5)	
Other	497	(24.0)	23	(18.3)	0.278
Time since HIV diagnosis (N=2,234)					
≤3 months	57	(2.7)	2	(1.6)	
3 months-2 years	175	(8.3)	14	(11.1)	
2-5 years	319	(15.1)	21	(16.7)	
5-15 years	948	(45.0)	56	(44.4)	
>15 years	609	(28.9)	33	(26.2)	0.479 (T)
ART status (N=2,237)					
On ART	1797	(85.3)	107	(82.3)	
Not on ART	310	(14.7)	23	(17.7)	0.354
Study log VL, c/mL (N=2,214)					
≤50	1069	(51.2)	66	(52.4)	
>50	1019	(48.8)	60	(47.6)	0.796
Study log CD4 count, cells/mm^3 (N=2,218)					
≤350	322	(15.4)	26	(20.6)	
>350	1770	(84.6)	100	(79.4)	0.116

p-values by chi-squared test, chi-squared test for trend (T), or Fisher's exact test (F); All factors defined in sections 3.8.2 and 3.8.3

3.10.2.6 Comparison to the UK HIV-diagnosed MSM population

Comparison of key characteristics of SOPHID (section 3.10.1.5) to ASTRA data during the same period (2011-2012) allows assessment of how similar the ASTRA MSM study population is to the UK HIV-diagnosed MSM population accessing NHS care for HIV.(Table 3.9.) Overall, the distribution of HIV exposure categories varied, with ASTRA having higher prevalence of HIV acquisition through sex

between men compared to the general HIV-diagnosed population, where the prevalence through heterosexual contact is higher than in ASTRA.

Focussing further on MSM, ASTRA had a higher estimate of men recruited from London compared to the rest of the UK (five of the eight participating clinics were located in London.(Table 3.9) As ASTRA was conducted in England, there were no MSM recruited in Wales, Northern Ireland, or Scotland, which account for 8.1% of all HIV-diagnosed MSM accessing care in the UK in 2011-2012. As a result, ASTRA MSM represented the following proportions of HIV-diagnosed MSM accessing care by region: up to 7.6% in all of England (specifically up to 10.2% in London, up to 12.9% in South East England, up to 6.8% in North West England) but 0% in the remaining regions of England.

The age distribution differed between ASTRA and SOPHID MSM, with a lower proportion of men being in the younger age groups (15-34 years) in the former. Specifically, HIV-diagnosed MSM aged 15-24 years made up less than 1% of the ASTRA MSM sample, as compared to almost 3% of SOPHID MSM. The distribution of age followed a similar pattern for MSM aged between 35 to 64 in ASTRA and SOPHID. MSM who were over 65 years tended to be represented more in SOPHID than in ASTRA (2.6% vs 3.6% respectively). Overall, ASTRA MSM represented up to 1.8% of SOPHID MSM under 24 years accessing HIV care in 2011-2012, up to 7% of SOPHID MSM between 25 and 64 years, and up to 5.5% of MSM over 65 years.

The distribution of ethnicity among MSM in ASTRA closely followed that of SOPHID, with the majority of HIV-diagnosed MSM in ASTRA being of white ethnicity (<87% for both populations). There was higher prevalence of black ethnicities (black Caribbean, black African, and black other/unspecified) in SOPHID MSM compared to ASTRA MSM, but higher prevalence of mixed ethnicities in ASTRA compared to SOPHID MSM. In addition, the ASTRA sample was comprised of less than 0.8% Indian, Pakistani, Bangladeshi, or other Asian ethnicities/nationalities, as compared to up to 1.8% in SOPHID MSM. The highest proportions of MSM in ASTRA represented in SOPHID according to ethnicity were other/mixed (up to 7.7%) and white (up to 7%), and the lowest was black other/unspecified (3.0-3.2%).

The vast majority of HIV-diagnosed MSM in both SOPHID and ASTRA were on ART (>83% in both) and had a high CD4 counts. The ASTRA study is representative of up to 7.1% of HIV-diagnosed SOPHID MSM on ART and 6.6% of MSM with a CD4 count >350cells/mm^3.

Hence, the 2248 MSM who participated in ASTRA represented between up to 7.0% of the HIV-diagnosed MSM SOPHID accessing NHS care in 2011 and 2012.

Table 3.9: Comparison of HIV-diagnosed MSM receiving HIV care in the UK (SOPHID) in 2011 and 2012 to MSM participating in the ASTRA study (2011-12)

	SOPHID MSM 2011 (N=32,204)		SOPHID MSM 2012 (N=34,453)		ASTRA MSM 2011-2012 (N=2,248)		% MSM in ASTRA represented in SOPHID	
							2011	2012
	n	(%)	n	(%)	n	(%)	(%)	(%)
Area of residence								
London	14962	(46.5)	15790	(45.8)	1527	(67.9)	(10.2)	(9.7)
East of England	1338	(4.2)	1484	(4.3)	-	-	-	-
East Midlands	951	(3.0)	1065	(3.1)	-	-	-	-
West Midlands	1679	(5.2)	1789	(5.2)	-	-	-	-
North East	592	(1.8)	659	(1.9)	-	-	-	-
North West	3464	(10.8)	3691	(10.7)	235	(10.5)	(6.8)	(6.4)
Yorkshire and Humber	1173	(3.6)	1309	(3.8)	-	-	-	-
South East	3757	(11.7)	4026	(11.7)	486	(21.6)	(12.9)	(12.1)
South West	1502	(4.7)	1641	(4.8)	-	-	-	-
England (Total)	29418	(91.3)	31454	(91.3)	2248	(100)	(7.6)	(7.1)
Wales	788	(2.4)	833	(2.4)	-	-	-	-
Northern Ireland	271	(0.8)	339	(1.0)	-	-	-	-
Scotland	1561	(4.8)	1609	(4.7)	-	-	-	-
Other†	166	(0.5)	218	(0.6)	-	-	-	-
Age group (years)								
15-24	903	(2.8)	980	(2.8)	16	(0.7)	(1.8)	(1.6)
25-34	5894	(18.3)	6361	(18.5)	300	(13.3)	(5.1)	(4.7)
35-44	10896	(33.8)	10898	(31.6)	728	(32.4)	(6.7)	(6.7)
45-54	10030	(31.1)	11081	(32.2)	817	(36.3)	(8.1)	(7.4)
55-64	3425	(10.6)	3879	(11.3)	273	(12.1)	(8.0)	(7.0)
>65	1056	(3.3)	1254	(3.6)	58	(2.6)	(5.5)	(4.6)
Ethnicity								
White	28159	(87.4)	29987	(87.0)	1974	(87.8)	(7.0)	(6.6)
Black-Caribbean	683	(2.1)	729	(2.1)	42	(1.9)	(6.1)	(5.8)
Black-African	468	(1.5)	527	(1.5)	23	(1.0)	(4.9)	(4.4)
Black-other/Black-unspecified	343	(1.1)	372	(1.1)	11	(0.5)	(3.2)	(3.0)
Indian/Pakistani/Bangladeshi	410	(1.3)	444	(1.3)	17	(0.8)	(4.1)	(3.8)
Other Asian/Oriental	534	(1.7)	629	(1.8)	28	(1.2)	(5.2)	(4.5)
Other/mixed	1508	(4.7)	1635	(4.7)	116	(5.2)	(7.7)	(7.1)
On ART	26921	(83.6)	29573	(85.8)	1904	(84.7)	(7.1)	(6.4)
CD4 count (cells/mm3)*								
<350	4993	(15.5)	4520	(13.1)	348	(15.5)	(7.0)	(7.7)
350-499	8067	(25.0)	7816	(22.7)	539	(24.0)	(6.7)	(6.9)
>499	18497	(57.4)	20332	(59.0)	1331	(59.2)	(7.2)	(6.5)
Not reported	647	(2.0)	1785	(5.2)	30	(1.3)	(4.6)	(1.7)

*† Other area of residence: British isles, no fixed abode, not reported, or abroad; * CD4 count recorded from study log for ASTRA MSM.*

3.11 Conclusion

Overall, comparison to SOPHID data showed that MSM are over-represented in ASTRA while black African individuals and women are under-represented. While this may present limitations in terms of how informative the study is to the HIV-diagnosed women and black African people receiving HIV care in the UK, the focus of this thesis is MSM only. The socio-demographic characteristics of ASTRA participants differed between participating clinics, reflecting the variability of local populations in terms of ethnicity, gender/sexuality, and socio-economic status.

The comparisons presented in this chapter suggest that the ASTRA study sample represents up to 7% of HIV-diagnosed MSM accessing NHS care in the UK during 2011-2012. While ASTRA does have some limitations in terms of addressing the aims of the thesis, these are discussed in detail in relation to specific analyses in relevant results chapters, and in the final chapter. Due to the substantive sample size, comprehensive data collection and linkage to clinical data, the ASTRA study can offer enhanced understanding of sexual behaviours of HIV-diagnosed MSM in the UK, and of the co-factors (socio-demographic, psychological, health, lifestyle, HIV-related) that these may be associated with. The study's results will thus have important implications for improved care of HIV-diagnosed people and for targeting national HIV prevention efforts.

4 Condomless sex among HIV-diagnosed MSM: prevalence and co-factors

4.1 Chapter aims

This chapter examines the prevalence of and factors associated with recent condomless sex and other sexual behaviours among HIV-diagnosed MSM participating in the ASTRA study. The aims of these analyses are to investigate: (i) the prevalence of measures of recent condomless sex (CLS), other sexual behaviours, sexually transmitted infections (STIs), and attitudes to condom use, (ii) the association of socio-demographic, HIV-related, and psychological factors with CLS and CLS with HIV-serodifferent partners (CLS-D), (iii) the factors associated with reporting CLS-D and CLS with HIV-seroconcordant partners only (CLS-C without CLS-D) versus condom-protected sex, and (iv) the prevalence of other measures of sexual behaviour among those reporting CLS-D, and CLS-C without CLS-D, compared to condom-protected sex. Results from these analyses are then discussed in the context of studies reviewed in Chapter 2. Associations of lifestyle factors (recreational drug use and alcohol) with sexual behaviour are presented in chapter 6.

4.2 Introduction

The concept of CLS as 'high risk' has evolved substantially over the past two decades, firstly with the introduction of combination antiretroviral therapy (ART) for treatment of HIV (1995/1996), secondly, with the first change in advice about high risk sex in the 'Swiss Statement' (2008), and subsequently with increasing evidence from observational studies and randomised controlled trials on the crucial role of HIV viral load (VL) suppression on reducing HIV transmission (2008 onwards). Results from recent trials (since 2012) have also shown the substantial protective effect conferred by oral pre-exposure prophylaxis (PrEP) in reducing the risk of HIV acquisition among HIV-negative individuals (section 1.3.5). As a result, the concept of high risk CLS continues to evolve with additional evidence and use of PrEP. There have been few studies of sexual behaviour among HIV-diagnosed MSM in the UK since the 'Swiss Statement'. It is important to understand the factors that contribute to having different types of CLS (with HIV-serodifferent, HIV-seroconcordant partners or both) as opposed to having condom-protected sex or not having sex among HIV-diagnosed MSM.

4.3 Methods

4.3.1 Study population

MSM who were diagnosed for three or fewer months prior to ASTRA questionnaire completion may potentially be reporting sexual behaviours that occurred prior to their HIV positive diagnosis. (Section 3.10.2.1) To examine whether there were any significant differences between MSM diagnosed for ≤3

months ('recently diagnosed') and MSM diagnosed for >3 months prior to ASTRA, these two groups were compared in univariable analysis on key socio-demographic, lifestyle, psychological, and HIV-related factors, using chi-squared tests. As the majority of sexual behaviour questions had a three month recall period, and to improve validity of sexual behaviour questions, recently diagnosed MSM were then excluded from remaining analyses in this chapter; the sample was thus comprised of MSM diagnosed with HIV for longer than three months prior to ASTRA questionnaire completion.

4.3.2 Condomless sex (CLS) definitions

Detailed definitions of derived variables for sexual behaviours have been given in section 3.8.4. In brief, sex refers to reporting any anal sex with a man and/or vaginal or anal sex with a woman in the previous three months. Condomless sex (CLS) refers to sex without a condom; CLS with an HIV-serodifferent partner (CLS-D) refers to CLS with a partner who did not have HIV or whose HIV-status the participant did not know; CLS with an HIV-seroconcordant partner (CLS-C) refers to CLS with a partner who was known to also have HIV. Condom-protected sex was defined as reporting having sex in the previous three months but not having CLS (including not having CLS-D and/or CLS-C). All questions on CLS had a three-month recall period.

4.3.3 Sexual behaviour classification

A single variable was derived, classifying all MSM into one of the following four mutually exclusive hierarchical categories according to sexual behaviour in the past three months, in the following order:

1. Condomless sex with HIV-serodifferent partners (CLS-D)
2. Condomless sex with HIV-seroconcordant partners only ('CLS-C without CLS-D')
3. Condom-protected sex only
4. No anal or vaginal sex

Therefore, a man who reported CLS-D and CLS-C would be classified as having CLS-D (category 1), while a man who reported anal or vaginal sex but did not report CLS-D or CLS-C would be classified as having condom-protected sex only (category 3).

A small number of participants reported having CLS but did not specify their partner' HIV-serostatus ('CLS-unspecified'). In order to incorporate all MSM into the single variable of sexual behaviour, this group was examined separately. The socio-demographic, lifestyle, and sexual behaviours and attitudes of MSM who reported CLS-unspecified were compared to those of MSM who reported 'CLS-C without CLS-D' (category 2) and those who reported CLS-D (category 1), in two separate univariable analyses. The CLS-unspecified group were similar to the CLS-D group in terms of socio-demographic and behavioural characteristics, (Appendix IV) and so throughout this thesis, the CLS-unspecified group were incorporated into the group reporting any CLS-D (including category 1 CLS-D, above).

4.3.4 CLS-D-specific behaviours

Among MSM who had CLS-D in the previous three months, additional questions were asked; number of times had CLS-D (once, 2-10, 11-30, more than 30 times); sexual positioning (seropositioning) and ejaculation inside a partner. (Section 3.8.4)

4.3.5 Other sexual behaviours, STIs, and attitudes towards condom use

Definitions for sexual behaviour variables described in this section can be found in section 3.8.4. To recap, among all MSM the following were reported; stable partner's HIV-serostatus (if in a relationship), number of new sexual partners in the past year, self-reported lifetime diagnosis of hepatitis C (HCV); in the past three months: number of total, CLS, CLS-D, CLS-C partners, self-reported diagnosis with another STI, group sex, used the internet to find a sexual partner, transactional sex (received money or drugs in exchange for having sex). Current symptoms of STIs (at questionnaire completion) were any of: abnormal discharge from penis, anal discharge, pain on passing urine, pain in the genital area or anus, red sores or rash on the genital area or anus. Transmission risk beliefs are series of statements on HIV transmission risk and virus undetectability, which categorised participants into 'most', 'moderately', and 'least' conservative.

Level of agreement to a series of statements on condom use and HIV transmission was determined using a 5-level Likert scale (from 'strongly agree' to 'strongly disagree'), including: 'low condom self-efficacy' (defined as tend to or strongly disagree to the statement "I feel confident I can ensure a condom is used with any partner in any situation"); 'difficulty negotiating condom use' (defined as strongly or tend to agree to "It is difficult for me to discuss condom use with a new sexual partner"); 'lower condom use with casual partners' (defined as strongly or tend to agree to "I am less likely to use a condom with a casual partner"), and 'worry about HIV transmission' (defined as strongly or tend to agree to "I'm worried I could have infected someone else with HIV in the past few months")

Participants were asked whether any of their HIV-negative sexual partners "have taken HIV drugs to reduce the risk of getting HIV", with options: PrEP ("antiretroviral drugs taken before sex), PEPSE ("antiretroviral drugs taken after sex"), and No/"Don't know".

4.3.6 Statistical analysis

4.3.6.1 Prevalence of sexual behaviours

The prevalence and 95%CIs of various sexual behaviours was established among all MSM diagnosed with HIV for longer than three months prior to ASTRA completion (described in section 4.3.5).

4.3.6.2 Factors associated with any condomless sex

Detailed definitions of all independent variables used in the below analyses are presented in sections 3.8.2 and 3.8.3. Associations were examined of socio-demographic factors (age, ethnicity, employment,

place of birth, religion, education, financial hardship, social support), psychological symptoms (depression, anxiety), stable partner status, HIV-related variables (time living with HIV, ART status, non-adherence to ART, study log-recorded and self-reported VL) and reporting:

(i.) Any condomless sex (CLS) in the previous three months versus not reporting CLS (includes MSM who did not have anal or vaginal sex)

(ii.) Condomless sex with HIV-serodifferent partners (CLS-D) in the previous three months versus not reporting CLS-D (incudes MSM who did not have anal or vaginal sex)

Unadjusted and adjusted modified Poisson regression models were used with robust error variances. In multivariable analyses, the two adjustment strategies described in section 3.9.5 were used. Firstly, each factor was adjusted separately for a set of 'core' factors; age (<30, 30-39, 40-49, 50-59, ≥60 years), ethnicity (white, all other), time since HIV diagnosis (≤2, 2-5, 5-10, 10-15, ≥15 years), ART status (on ART, off ART), and stable partner status (HIV-positive, HIV-negative or unknown status, no stable partner). In the second adjustment strategy, any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in the multivariable model in addition to clinic; variables that were correlated were examined critically in terms of their importance and relevance and excluded accordingly (specifics for each model are discussed in sections 4.4.5 and 4.4.6) Lifestyle factors (recreational drug use, alcohol consumption) and non-disclosure of HIV-serostatus were not included in this analysis as they are presented in Chapters 6 and 7 respectively.

4.3.6.3 Sexual behaviours according to single variable

The prevalence (95%CI) of sexual behaviours in the past three months was established according to the mutually exclusive four category variable (CLS-D, 'CLS-C without CLS-D', condom-protected sex, and no sex, as described in section 4.3.3). Associations of socio-demographic characteristics, psychological symptoms, HIV-related factors (as in 4.3.6.2) and this measure of sexual behaviour were examined. Chi-squared tests (or Fisher's exact according to cell size), chi-squared tests for trend, or ANOVA were used to compare all four groups as well as the three sexually active groups separately. P-values for linear trend were derived by Wald test using unadjusted multinomial logistic regression for numerical independent variables (age and time since HIV diagnosis) and categorical independent variables with natural ordering (e.g. decreasing levels of social support). The distribution of the number of partners in the past year according to the single variable of sexual behaviour in the past three months was assessed by chi-squared test for linear trend.

4.3.6.4 Factors associated with reporting condomless or condom-protected sex

Multinomial logistic regression (MNL) was used to examine socio-demographic, psychological, and HIV-related factors associated with having CLS compared to condom-protected sex. Only MSM who reported anal or vaginal sex in the past three months were included in this analysis, which compared MSM who had CLS-D and those who had 'CLS-C without CLS-D' to those who had condom-protected sex only

(baseline). Any variables with p<0.10 in unadjusted analysis were included in separate MNL models only adjusted for clinic; any remaining variables with p<0.05 in clinic-adjusted MNL were then mutually adjusted in a single MNL model, in addition to clinic.

The association of other sexual behaviours, STIs, and attitudes and the three categories of sexual activity in the past three months (CLS-D, 'CLS-C without CLS-D', and condom-protected sex) was examined using chi-squared tests, or Fisher's exact where appropriate.

4.4 Results

4.4.1 Recently diagnosed MSM

A total of 59 (of 2248, 2.6%) MSM had been diagnosed with HIV for three or fewer months prior to ASTRA completion. There were significant differences on various factors between recently diagnosed MSM and those diagnosed for longer than three months.(Table 4.1) Compared to MSM diagnosed with HIV for longer, recently diagnosed MSM were significantly younger, more likely to be of non-white ethnicities, and to have higher educational attainment (all p<0.05). MSM who were recently diagnosed also reported higher levels of social support, with only 3.4% reporting low social support as compared to 10.0% of MSM not recently diagnosed (p-trend=0.009). There was some evidence to suggest that MSM who were diagnosed for longer had higher prevalence of depression and anxiety symptoms as compared to those recently diagnosed. Prevalence of ART use and VL suppression was lower among the recently diagnosed MSM compared to MSM diagnosed for longer (p<0.001 for both). There was weak evidence to suggest that prevalence of CLS-D in the past three months was higher among recently diagnosed MSM (p=0.06).

All remaining analyses in this chapter (and any other chapters identified in Table 3.2) excluded 59 recently diagnosed MSM, deriving a sample of 2189 ASTRA MSM participants who had been diagnosed with HIV for longer than three months.

Table 4.1: Differences in socio-demographic, psychological, and HIV-related factors between MSM diagnosed with HIV for >3 months or ≤3 months (N=2248)

	Diagnosed with HIV >3 months ago (N=2,189)		Recently diagnosed with HIV (≤3 months ago) (N=59)		
	n	(%)	n	(%)	p-value
Age group, years (N=2224)					
<30	96	(4.4)	13	(22.4)	
30-49	1416	(65.3)	37	(63.8)	
≥50	655	(30.2)	8	(13.8)	<0.001 (T)
Mean age [SD], years (N=2224)	45.5	[9.4]	39.9	[10.0]	<0.001 (T)
Ethnicity (N=2211)					
White	1928	(89.5)	46	(80.7)	
All other (black, Asian, Mixed, other)	226	(10.5)	11	(19.3)	0.034
Born in the UK (N=2248)					
No	687	(31.4)	21	(35.6)	
Yes	1502	(68.6)	38	(64.4)	0.492
Education (N=2205)					
University degree or above	950	(44.2)	33	(58.9)	
No qualifications or up to A levels	1199	(55.8)	23	(41.1)	0.029
Employment (N=2211)					
Employed	1318	(61.2)	39	(68.4)	
Unemployed or other (student, carer, retired)	836	(38.8)	18	(31.6)	0.268
Money for basic needs (financial hardship) (N=2215)					
Always	1114	(51.6)	37	(64.9)	
Mostly/sometimes	871	(40.4)	15	(26.3)	
No	173	(8.0)	5	(8.8)	0.143 (T)
Depressive symptoms (N=2248)					
No	1590	(72.6)	49	(83.1)	
Yes	599	(27.4)	10	(16.9)	0.076
Anxiety symptoms (N=2248)					
No	1726	(78.8)	52	(88.1)	
Yes	463	(21.2)	7	(11.9)	0.083
Social support score (N=2228)					
High	1286	(59.3)	44	(75.9)	
Medium	666	(30.7)	12	(20.7)	
Low	218	(10.0)	2	(3.4)	0.009 (T)
ART status (N=2237)					
On ART	1888	(86.7)	16	(27.1)	
Not on ART	290	(13.3)	43	(72.9)	<0.001
Study log CD4 count, cells/mm^3 (N=2218)					
≤350	329	(15.2)	30	(51.7)	
>350	1831	(84.8)	28	(48.3)	<0.001
Self-reported viral load, c/mL (N=1905)					
≤50	1570	(83.1)	1	(6.7)	
>50	180	(9.5)	8	(53.3)	
"Don't know"	140	(7.4)	6	(40.0)	<0.001 (F)
Study log viral load, c/mL (N=2214)					
≤50	1680	(77.8)	2	(3.6)	
>50	479	(22.2)	53	(96.4)	<0.001 (F)
HIV transmission risk beliefs (N=2204)					
Most conservative	1029	(47.9)	23	(41.1)	
Moderately conservative	1020	(47.5)	29	(51.8)	

	Diagnosed with HIV >3 months ago (N=2,189)		Recently diagnosed with HIV (≤3 months ago) (N=59)		
	n	(%)	n	(%)	p-value
Least conservative	99	(4.6)	4	(7.1)	0.234 (T)
Any anal or vaginal sex (N=2248) *					
No	797	(36.4)	16	(27.1)	
Yes	1392	(63.6)	43	(72.9)	0.143
Any condomless sex (N=2248) *					
No	1353	(61.8)	34	(57.6)	
Yes	836	(38.2)	25	(42.4)	0.514
Condomless sex with HIV-serodifferent partners (N=2248)*					
No	1832	(83.7)	44	(74.6)	
Yes	357	(16.3)	15	(25.4)	0.063
Condomless sex with HIV-seroconcordant partners(N=2248)*					
No	1561	(71.3)	48	(81.4)	
Yes	628	(28.7)	11	(18.6)	0.091
*p-values by chi-squared test, chi-squared test-for-trend (T), or Fisher's exact test (F)*Three month recall period; All factors defined in section 3.8.*					

4.4.2 **Prevalence of sexual behaviours**

The prevalence of sexual behaviours, other STIs, and attitudes was assessed among 2189 MSM. (Table 4.2) A total of 1182 (54.5%) MSM reported having a stable partner, of whom 23.3% had an HIV-positive stable partner and 31.7% (29.9-33.7%) had an HIV-serodifferent status stable partner. The prevalence of any anal/vaginal sex in the past three months was 63.6%. A total of 836 (38.2%) MSM reported having any CLS; 326 (16.3%) had CLS-D and 628 (28.7%) had CLS-C. Self-reported diagnosis with another STI in the past three months was 10.9% of 2159 MSM with available data (further discussed in Chapter 8). Lifetime diagnosis of hepatitis C virus (HCV) was reported by 15.8% (14.3-17.4%) of 2145 MSM. Over a fifth of 2141 MSM reported having group sex in the past three months. Only 0.6% of MSM (13/2162) reported having transactional sex. The median number of new sexual partners in the past year was 7 [IQR 3-10]. Over 26% (n=586) of MSM reported having 10 or more *new* sexual partners in the past year (including 53 MSM who had more than one new partner but did not specify the exact number, see section 3.8.4).

Table 4.2: Prevalence (95%CI) of sexual behaviours among 2189 HIV-diagnosed MSM

	n	%	(95%CI)
Stable partner's HIV-serostatus (N=2189)			
HIV-positive	510	23.3	(21.6, 25.1)
HIV-negative or HIV-unknown status (incl. missing)	694	31.7	(29.8, 33.7)
No stable partner	985	45.0	(42.8, 47.0)
Any anal and/or vaginal sex (N=2189)	1,392	63.6	(61.6, 65.6)
Any condomless sex (CLS) (N=2189)	836	38.2	(36.2, 40.2)
CLS with HIV-serodifferent partners (CLS-D) (N=2189)	357	16.3	(14.8, 17.9)
CLS with HIV-seroconcordant partners (CLS-C) (N=2189)	628	28.7	(26.8, 30.6)
Sexually transmitted infections (STI) (N=2160)	236	10.9	(9.7, 12.3)
Lifetime hepatitis C (N=2145)	338	15.8	(14.3, 17.4)
Current STI symptoms (N=2186)	273	12.5	(11.2, 13.9)
Group sex (N=2141)	453	21.2	(19.5, 22.9)
Used the internet to find sex (N=2144)	796	37.1	(35.1, 39.2)
Transactional sex (N=2189) ‡	82	3.7	(3.0,4.6)
Low condom self-efficacy (N=2142) ‡	139	6.5	(5.5,7.6)
Difficulty negotiating condom use (N=2125) ‡	319	14.9	(13.4,16.5)
Lower condom use with casual partners (N=2126) ‡	355	16.7	(15.2,18.4)
Worry about HIV transmission (N=2186) ‡	141	6.6	(5.6,7.8)
≥10 new sexual partners in past year (N=2189)	586	26.8	(25.0,28.7)

Three month recall unless otherwise specified; ‡ Factors defined in section 4.3.5

4.4.3 Number of sexual partners in the past three months

Among 1391 MSM who reported any anal/vaginal sex in the past three months, information on number of sexual partners was available for 1356.(Table 4.3) MSM who reported more than one partner in the past three months but did not specify the exact number were excluded from calculations of summary statistics. The median number of total partners was 2 [IQR: 1-5], with 73.2% reporting up to four partners in the past three months. Over 51% of MSM who had CLS-C reported one CLS-C partner only, and 57.5% of MSM who had CLS-D also reported only having one CLS-D partner in the past three months; 6.0% reported having 20 or more total partners.

Table 4.3: Distribution and type of sexual partners in the past three months (N=1356*)

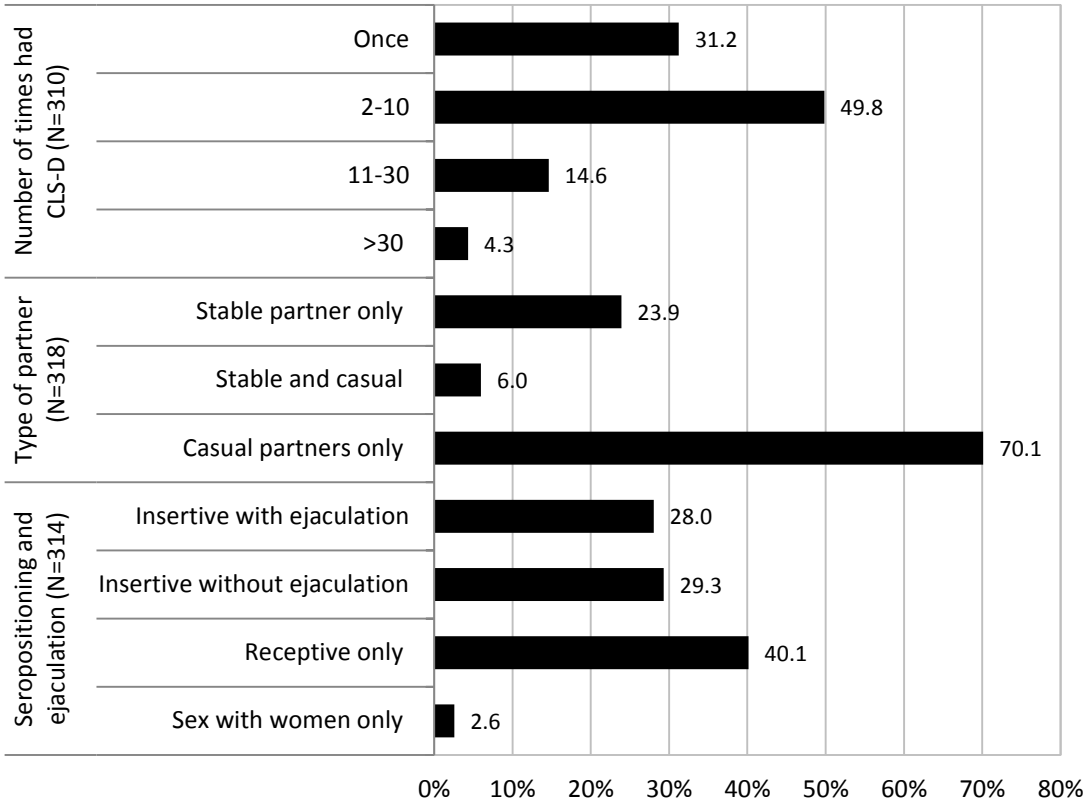
	Total anal or vaginal sex partners	CLS-C partners	CLS-D partners
Median [IQR]	2 [1-5]	1 [1-4]	1 [1-3]
Range	1-150	1-100	1-100
Mean [SD]	4.9 [10.0]	3.9 [7.2]	3.3 [7.8]
% reporting number of partners			
1	44.7	51.5	57.5
2-4	28.5	27.4	28.8
5-9	12.9	11.1	7.0
10-19	8.0	6.7	3.8
≥20	6.0	3.4	2.9

**Of 1391 MSM reporting any anal or vaginal sex in past 3 months, information on number of partners available for 1356, of whom excluded MSM who reported >1 partner but did not specify exact number; n=28 anal or vaginal sex partners, n=13 CLS-C, n=13 CLS-D*

4.4.4 **CLS-D specific behaviours**

Among 357 MSM who had CLS-D in the previous three months, 310 provided information on the number of times they had CLS-D; the majority had CLS-D between two and ten times, and 4.3% reported having CLS-D more than 30 times in the past three months. (Figure 4.1) Over 70% reported having CLS-D with casual partners only in the past three months, while 6.0% reported having CLS-D with a stable partner and casual partners. Information on sexual positioning was available for 314 MSM who had CLS-D, of whom 88 (28.0%) were the insertive partner and reported ejaculating inside their partner, 92 (29.3%) were insertive but did not ejaculate inside their partner, and 126 (40.1%) were the receptive partner only.

Figure 4.1: Sexual behaviours among MSM reporting CLS-D in the past three months



4.4.5 **Associations of socio-demographic characteristics, psychological symptoms, HIV-related factors, and reporting condomless sex (CLS)**

Table 4.4 shows, among all 2189 MSM, unadjusted and adjusted associations of various factors and reporting condomless sex (CLS) in the previous three months (n=836, versus to not reporting CLS, which includes condom-protected sex and no anal or vaginal sex). In unadjusted analysis, younger age and more recent HIV diagnosis were significantly associated with CLS (ptrend<0.001). The prevalence of CLS was lower soon after HIV diagnosis (3 months-2 years), increased to a peak five years post-diagnosis (46%), and decreased steadily thereafter to the lowest levels at 15 or more years post-diagnosis (30%).

Educational qualifications and being employed were associated with higher prevalence of CLS ($p<0.05$ for both). Over 60% of MSM who had a stable HIV-positive partner reported having CLS ($p<0.001$). Not being on ART was associated with 30% higher prevalence of CLS in relative terms compared to being on ART. Almost 45% of MSM with detectable study log-recorded VL (>50 c/mL) had CLS ($p<0.001$). No significant association was found of ethnicity, place of birth, religion, financial hardship (money for basic needs), social support, depression or anxiety symptoms, and reporting any CLS.

In the first multivariable adjustment strategy (Models 1: Table 4.4), each factor was included in a separate model adjusted for core factors. While the trend association of younger age and CLS remained robust after adjustment for core factors (p-trend<0.001), the trend association of time since HIV diagnosis and CLS was no longer significant (p-trend>0.05). Having a stable partner who was HIV-positive remained associated with higher prevalence of CLS. The association of ART status, study log VL, and CLS was no longer significant, due to adjustment for time since HIV diagnosis. However, MSM who were on ART with self-reported undetectable VL remained more likely to report having CLS, after adjustment for core factors.

In the second multivariable strategy (Model 2: Table 4.4), any factor with $p<0.10$ in unadjusted analysis was a candidate for inclusion in the multivariable model, in addition to clinic. These were: age, time since HIV diagnosis, education, employment, stable partner status, ART status, ART adherence, ART status/self-reported VL, and study log-recorded VL. As ART status was collinear with the latter three ART variables, only one ART-related variable was selected for inclusion in the model. The role of ART was explored in Models 1, so it was decided to only include ART status/self-reported VL in this model. Hence, after adjustment for age, time since HIV diagnosis, education, employment, stable partner status, ART status/self-reported VL, and clinic, strong associations remained of younger age and CLS, as well as having a HIV-positive stable partner and CLS ($p<0.05$ for both). There remained an association of being on ART with self-reported undetectable VL and reporting CLS ($p=0.046$).

Table 4.4: Association of socio-demographic, psychological, HIV-related factors, and reporting any condomless sex (CLS) in the previous 3 months (N=2189)

	Had condomless sex (CLS) (N=836/2,189)							
	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=2167)								
<30	56/96	58.3	2.7 [1.9,3.8]		2.1 [1.5,3.0]		2.2 [1.5,3.1]	
30-39	233/487	47.8	2.2 [1.6,3.0]		1.8 [1.3,2.4]		1.8 [1.3,2.5]	
40-49	354/929	38.1	1.7 [1.2,2.4]		1.6 [1.2,2.1]		1.5 [1.1,2.1]	
50-59	154/503	30.6	1.4 [1.0,1.9]		1.3 [1.0,1.8]		1.3 [0.9,1.8]	
≥60	33/152	21.7	1.0	<0.001(T)	1.0	<0.001(T)	1.0	<0.001(T)
Ethnicity (N=2154)								
White	738/1928	38.3	1.0		1.0			
All other (black, Asian, Mixed, other)	86/226	38.1	1.0 [0.8,1.2]	0.948	1.0 [0.8,1.1]	0.751	-	
Time since HIV diagnosis (N=2177)								
3 months-2 years	72/184	39.1	1.0		1.0		1.0	
2-5 years	157/338	46.4	1.2 [1.0,1.5]		1.2 [0.9,1.4]		1.1 [0.9,1.4]	
5-10 years	240/550	43.6	1.1 [0.9,1.4]		1.2 [1.0,1.4]		1.1 [0.9,1.4]	
10-15 years	168/461	36.4	0.9 [0.7,1.2]		1.0 [0.8,1.3]		1.0 [0.8,1.2]	
>15 years	195/644	30.3	0.8 [0.6,1.0]	<0.001 (T)	0.9 [0.7,1.2]	0.061(T)	0.9 [0.7,1.1]	0.063(T)
Place of birth (N=2189)								
UK	569/1502	37.9	1.0		1.0			
Outside the UK	267/687	38.9	1.0 [0.9,1.2]	0.660	1.0 [0.9,1.1]	0.791	-	
Religious (N=2152)								
Yes	337/919	36.7	1.0		1.0		-	
No	487/1233	39.5	1.1 [1.0,1.2]	0.184	1.0 [0.9,1.1]	0.819		
Education (N=2149)								
University degree or above	387/950	40.7	1.0		1.0		1.0	
No educational qualifications/up to A levels	437/1199	36.4	0.9 [0.8,1.0]	0.042	0.9 [0.8,1.0]	0.075	1.0 [0.9,1.1]	0.557
Employment (N=2142)								
Employed full- or part-time	557/1318	42.3	1.0		1.0		1.0	
Unemployed	109/310	35.2	0.8 [0.7,1.0]		0.9 [0.8,1.1]		0.9 [0.8,1.1]	
Other (carer retired student)	156/514	30.4	0.7 [0.6,0.8]	<0.001	0.9 [0.8,1.0]	0.182	0.9 [0.8,1.1]	0.467

	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Money for basic needs (N=2158) ‡								
Always	430/1114	38.6	1.0		1.0			
Mostly	223/596	37.4	1.0 [0.9,1.1]		1.0 [0.9,1.1]		-	
Sometimes	107/275	38.9	1.0 [0.9,1.2]		1.0 [0.9,1.2]			
No	65/173	37.6	1.0 [0.8,1.2]	0.834 (T)	1.0 [0.8,1.2]	0.871(T)		
Social support (N=2170) ‡								
Highest	493/1286	38.3	1.0		1.0		-	
Medium	262/666	39.3	1.0 [0.9,1.2]		1.1 [1.0,1.2]			
Low	76/218	34.9	0.9 [0.7,1.1]	0.446 (T)	1.1 [0.9,1.3]	0.239(T)		
Depressive symptoms (N=2189) ‡								
No	606/1590	38.1	1.0		1.0			
Yes	230/599	38.4	1.0 [0.9,1.1]	0.903	1.1 [0.9,1.2]	0.334	-	
Anxiety symptoms (N=2189) ‡								
No	661/1726	38.3	1.0		1.0			
Yes	175/463	37.8	1.0 [0.9,1.1]	0.845	1.0 [0.9,1.2]	0.607	-	
Stable partner status (N=2189)								
HIV-positive stable partner	309/510	60.6	1.0		1.0		1.0	
HIV-negative or HIV-unknown status stable partner	202/694	29.1	0.5 [0.4,0.6]		0.5 [0.4,0.6]		0.8 [0.7,1.0]	
None	325/985	33.0	0.5 [0.5,0.6]	<0.001	0.6 [0.5,0.6]	<0.001	1.1 [0.9,1.3]	<0.001
ART status (N=2178)								
On ART	693/1888	36.7	1.0		1.0		-	
Not on ART	140/290	48.3	1.3 [1.2,1.5]	<0.001	1.1 [1.0,1.3]	0.147		

	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
ART adherence (N=2178) ‡								
On ART adherent	617/1705	36.2	1.0		1.0			
On ART non-adherent	76/183	41.5	1.1 [1.0,1.4]		1.1 [1.0,1.4]		-	
Not on ART	140/290	48.3	1.3 [1.2,1.5]	<0.001	1.2 [1.0,1.3]	0.056		
ART status/self-reported VL (N=2143) ‡								
On ART reports undetectable VL	594/1568	37.9	1.0		1.0		1.0	
On ART does not report undetectable VL	90/285	31.6	0.8 [0.7,1.0]		0.8 [0.7,1.0]		0.8 [0.7,1.0]	
Not on ART	140/290	48.3	1.3 [1.1,1.5]	0.001	1.1 [0.9,1.3]	0.012	1.1 [0.9,1.3]	0.046
Study log-recorded VL (N=2159)								
≤50c/mL	612/1680	36.4	1.0		1.0		-	
>50 c/mL	215/479	44.9	1.2 [1.1,1.4]	<0.001	1.1 [1.0,1.2]	0.195		

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; ‡ Factors defined in chapter 3 VL: viral load; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, ART status. Denominators vary due to missing data in each model. Models for ART adherence, ART status/self-reported VL, and study log VL omit variable on ART due to collinearity.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic.*

4.4.6 Associations of socio-demographic, psychological, HIV-related factors, and reporting condomless sex with HIV-serodifferent partners (CLS-D)

Table 4.5 shows, among 2189 MSM, associations of various factors with having CLS-D in the previous three months (n=357), versus not reporting CLS-D (which includes having 'CLS-C without CLS-D', condom-protected sex, and no anal or vaginal sex). In unadjusted analysis, a significant negative trend was observed with increasing age; 25% of MSM under 30 years had CLS-D compared to 12% of those over 60 years (p-trend=0.004). The prevalence of CLS-D was also lower among those diagnosed for longer compared to those recently diagnosed (up to two years ago). Having an HIV-serodifferent stable partner was associated with almost two-fold higher prevalence of CLS-D compared to having an HIV-positive partner (p<0.001). There was a weak indication that the prevalence of CLS-D was 20% higher among those not on ART compared to those on ART (p=0.092). There was no significant association between CLS-D and ethnicity, place of birth, religion, education, employment, financial hardship, social support, depression or anxiety symptoms, ART adherence, and study log-recorded viral load.

In core-adjusted models (Models 1: Table 4.5), only stable partner status remained significantly associated with reporting CLS-D; the prevalence of CLS-D was two-fold higher for those with an HIV-serodifferent stable partner compared to an HIV-positive partner (p<0.001). There was a weak indication that the prevalence of CLS-D was higher among younger MSM (p-trend=0.10).

In the second multivariable strategy (Model 2: Table 4.5), the following factors with p<0.10 in unadjusted analysis were candidates for inclusion in a single model in addition to clinic: age, time since HIV diagnosis, ART status, and ART status/self-reported VL. As the last two variables were collinear, only ART status/self-reported VL was retained in the final model. Younger age and having and HIV-serodifferent stable partner remained significantly associated with reporting CLS-D (p<0.05 for both). There remained no association of time since HIV diagnosis, ART status/self-reported VL, with CLS-D.

Table 4.5: Association of socio-demographic, psychological, HIV-related factors and reporting any condomless sex with HIV-serodifferent partners (CLS-D) in the previous 3 months (N=2189)

	Had condomless sex with HIV-serodifferent partner(s) (CLS-D) (N=357/2189)							
	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]		Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=2167)								
<30	24/96	25.0	2.1 [1.2,3.6]		1.8 [1.0,3.2]		2.0 [1.1,3.7]	
30-39	83/487	17.0	1.5 [0.9,2.3]		1.2 [0.7,2.0]		1.4 [0.8,2.3]	
40-49	159/929	17.1	1.4 [0.9,2.3]		1.3 [0.8,2.1]		1.4 [0.9,2.3]	
50-59	69/503	13.7	1.1 [0.7,1.8]		1.1 [0.7,1.8]		1.2 [0.7,2.0]	
≥60	18/152	11.8	1.0	0.004(T)	1.0	0.099(T)	1.0	0.029(T)
Ethnicity (N=2154)								
White	310/1928	16.1	1.0		1.0			
All other (black Asian Mixed other)	40/226	17.7	1.1 [0.8,1.5]	0.529	1.1 [0.8,1.4]	0.613	-	
Time since HIV diagnosis (N=2177)								
3 months-2 years	32/184	17.4	1.0		1.0		1.0	
2-5 years	63/338	18.6	1.1 [0.7,1.6]		1.2 [0.8,1.8]		1.1 [0.7,1.6]	
5-10 years	100/550	18.2	1.0 [0.7,1.5]		1.2 [0.8,1.8]		1.0 [0.7,1.5]	
10-15 years	74/461	16.1	0.9 [0.6,1.3]		1.1 [0.7,1.6]		0.9 [0.6,1.4]	
>15 years	86/644	13.4	0.8 [0.5,1.1]	0.018(T)	0.9 [0.6,1.3]	0.180(T)	0.8 [0.5,1.2]	0.105(T)
Place of birth (N=2189)								
UK	241/1502	16.0	1.0		1.0			
Outside the UK	116/687	16.9	1.0 [0.8,1.2]	0.621	1.0 [0.8,1.2]	0.928	-	
Religious (N=2152)								
Yes	156/919	17.0	1.0		1.0			
No	192/1233	15.6	0.9 [0.8,1.1]	0.382	0.9 [0.7,1.1]	0.239	-	
Education (N=2149)								
University degree or above	158/950	16.6	1.0		1.0			
No educational qualifications/up to A levels	192/1199	16.0	1.0 [0.8,1.2]	0.700	1.0 [0.8,1.2]	0.985	-	

	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]		Model 2: aPR [95%CI]	p-value
Employment (N=2142)								
Employed full- or part-time	226/1318	17.1	1.0		1.0			
Unemployed	51/310	16.5	1.0 [0.7,1.3]		1.1 [0.8,1.5]		-	
Other (carer retired student)	71/514	13.8	0.8 [0.6,1.0]	0.228	0.9 [0.7,1.2]	0.538		
Money for basic needs (N=2158) ‡								
Always	176/1114	15.8	1.0		1.0			
Mostly	92/596	15.4	1.0 [0.8,1.2]		1.0 [0.8,1.3]		-	
Sometimes	45/275	16.4	1.0 [0.8,1.4]		1.0 [0.8,1.4]			
No	37/173	21.4	1.4 [1.0,1.9]	0.166(T)	1.4 [1.0,1.9]	0.125(T)		
Social support (N=2170) ‡								
Highest	206/1286	16.0	1.0		1.0			
Medium	119/666	17.9	1.1 [0.9,1.4]		1.2 [0.9,1.4]		-	
Low	31/218	14.2	0.9 [0.6,1.3]	0.985(T)	0.9 [0.6,1.4]	0.624(T)		
Depressive symptoms (N=2189) ‡								
No	255/1590	16.0	1.0		1.0			
Yes	102/599	17.0	1.1 [0.9,1.3]	0.575	1.1 [0.9,1.3]	0.549	-	
Anxiety symptoms (N=2189) ‡								
No	276/1726	16.0	1.0		1.0			
Yes	81/463	17.5	1.1 [0.9,1.4]	0.435	1.1 [0.8,1.4]	0.566	-	
Stable partner status (N=2189)								
HIV-positive stable partner	56/510	11.0	1.0		1.0		1.0	
HIV-negative or HIV-unknown status stable partne	148/694	21.3	1.9 [1.5,2.6]		2.0 [1.5,2.7]		2.0 [1.5,2.6]	
None	153/985	15.5	1.4 [1.1,1.9]	<0.001	1.4 [1.1,1.9]	<0.001	1.4 [1.1,1.9]	<0.001
ART status (N=2178)								
On ART	298/1888	15.8	1.0		1.0		-	
Not on ART	57/290	19.7	1.2 [1.0,1.6]	0.092	1.1 [0.9,1.5]	0.386		

	n had CLS/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]		Model 2: aPR [95%CI]	p-value
ART adherence (N=2178) ‡								
On ART adherent	274/1705	16.1	1.0		1.0			
On ART non-adherent	24/183	13.1	0.8 [0.6,1.2]		0.8 [0.5,1.2]		-	
Not on ART	57/290	19.7	1.2 [0.9,1.6]	0.147	1.1 [0.8,1.5]	0.394		
ART status/self-reported VL (N=2143) ‡								
On ART reports undetectable VL	259/1568	16.5	1.0		1.0		1.0	
On ART does not report undetectable VL	35/285	12.3	0.7 [0.5,1.0]		0.7 [0.5,1.0]		0.7 [0.5,1.0]	
Not on ART	57/290	19.7	1.2 [0.9,1.5]	0.059	1.1 [0.8,1.4]	0.131	1.0 [0.8,1.4]	0.189
Study log-recorded viral load (N=2159)								
≤50 c/mL	264/1680	15.7	1.0		1.0			
>50 c/mL	89/479	18.6	1.2 [1.0,1.5]	0.132	1.1 [0.8,1.4]	0.608	-	

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; ‡ Factors defined in chapter 3; VL: viral load; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, ART status. Denominators vary due to missing data in each model. Models for ART adherence, ART status/self-reported VL, and study log VL omit variable ART status due to collinearity.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic.*

4.4.7 Prevalence of sexual activity according to single variable

Using the single variable classifying all 2189 MSM into four mutually exclusive categories of sexual behaviour in the past three months, the prevalence was:

1. CLS-D: N=357, 16.3% (95%CI 14.8-17.9%)
2. 'CLS-C without CLS-D': N=479, 21.9% (20.2-23.7%)
3. Condom-protected sex only: N=556, 25.4% (23.6-27.3%)
4. No anal or vaginal sex: N=797, 36.4% (34.4-38.4%)

A total of 31 MSM reported having CLS but did not report their partners' HIV-serostatus (CLS-unspecified). The CLS-unspecified group was compared to 479 MSM who had 'CLS-C without CLS-D', and 326 MSM who had CLS-D. (Appendix IV) Overall, men who had CLS-unspecified tended to be more similar to the CLS-D group than the 'CLS-C without CLS-D' group on a number of factors including: time living with diagnosed HIV, stable partner status, other STIs, hepatitis C, number of sexual partners, and attitudes to condom use and HIV transmission. (Appendix IV) On the basis of these results, the CLS-unspecified group was incorporated into the CLS-D group (1) in the single variable classifying sexual behaviour in the past three months.

4.4.7.1 Associations of socio-demographic, psychological, and HIV-related factors with single variable of sexual behaviour

The four categories of sexual behaviour in the past three months were compared on key factors. (Table 4.6) Compared to the three sexually active groups (CLS-D, 'CLS-C without CLS-D', and condom-protected sex), MSM who did not have sex in the previous three months were significantly different on almost all factors ($p<0.05$); they tended to be older, diagnosed with HIV for longer, were less likely to be born in the UK, have educational qualifications, and to be employed. Prevalence of low social support, symptoms of depression and anxiety were highest among MSM who did not have sex compared to the other three groups ($p<0.05$ for all). MSM who did not have sex were also more likely to not have a stable partner compared to the three sexually active groups ($p<0.001$). This group were also more likely to be on ART and virally suppressed. Over 40% of those who did not have sex reported being on ART with self-reported detectable VL, the highest prevalence of all groups ($p<0.001$).

There were few significant differences in socio-demographic factors between the three sexually active groups, except for age; MSM who had 'CLS-C without CLS-D' were slightly younger than MSM who had CLS-D or condom-protected sex (Table 4.6). In addition, MSM who had CLS-D were more likely to report financial hardship compared to those who had CLS-C and those who had condom-protected sex (p-trend=0.021). The prevalence of depression and anxiety symptoms followed a similar pattern, being higher in the CLS-D group, followed by CLS-C, and lowest for the condom-protected group ($p<0.10$ for both). No significant differences were found between the three sexually active groups on HIV-related

factors; the prevalence of ART use, ART adherence and viral load non-suppression was similarly distributed.

Multinomial logistic regression (MNL) was used to examine associations between factors and reporting CLS-C or CLS-D as compared to condom-protected sex (baseline).(Table 4.7) In unadjusted MNL, younger age, having a stable partner, and reporting symptoms of depression were significantly associated with having CLS-C relative to condom-protected sex ($p<0.05$ for all). The odds of having CLS-D relative to condom-protected sex were 1.55 times greater for MSM reporting financial hardship compared to those who did not $p=0.01$). Not knowing one's personal VL was associated with lower prevalence of CLS-C and CLS-D relative to condom-protected sex compared to knowing personal VL ($p<0.05$ for both). In multivariable MNL adjusting for clinic plus all factors with $p<0.10$ in unadjusted MNL (age, financial hardship, stable partner, depression symptoms, and self-reported VL), these associations remained significant. The prevalence of CLS-D relative to condom-protected sex was 39% lower among those who knew their personal VL compared to those who did not ($p=0.007$).

Table 4.6: Socio-demographic, psychological, HIV-related factors according to mutually exclusive categories of sexual behaviour in past 3 months (N=2189)

	(1) CLS-D (n=357)*		(2) 'CLS-C without CLS-D' (n=479)		(3) Condom-protected sex only (n=556)		(4) No anal/vaginal sex (n=797)		p-value across groups 1-4	p-value across groups 1-3
	n	%	n	%	n	%	n	%		
Mean age [SD] (N=2167)	44.6	(9.3)	42.9	(8.8)	44.7	(9.6)	48.6	(9.0)	<0.001(T)	0.003(T)
Median years since HIV diagnosis [IQR] (N=2177)	9	[4-15]	8	[4-14]	9	[4-15]	12	[7-18]	<0.001(T)	0.711(T)
Ethnicity (N=2154)										
White	310	(88.6)	428	(90.3)	477	(87.5)	713	(90.8)		
All other	40	(11.4)	46	(9.7)	68	(12.5)	72	(9.2)	0.223	0.374
Place of birth (N=2189)										
UK	241	(67.5)	328	(68.5)	357	(64.2)	576	(72.3)		
Outside the UK	116	(32.5)	151	(31.5)	199	(35.8)	221	(27.7)	0.017	0.315
Religious (N=2152)										
No	192	(44.8)	181	(38.0)	232	(42.6)	350	(44.6)		
Yes	156	(44.8)	181	(38.0)	232	(42.6)	350	(44.6)	0.107	0.120
Education (N=2149)										
University degree or above	158	(45.1)	229	(48.3)	255	(46.6)	308	(39.6)		
No educational qualifications/up to A levels only	192	(54.9)	245	(51.7)	292	(53.4)	470	(60.4)	0.010	0.661
Employment (N=2142)										
Employed full- or part-time	226	(64.9)	331	(69.8)	370	(68.1)	391	(50.3)		
Unemployed	51	(14.7)	58	(12.2)	84	(15.5)	117	(15.1)		
Other (carer retired student)	71	(20.4)	85	(17.9)	89	(16.4)	269	(34.6)	<0.001	0.334
Money for basic needs (N=2158)										
Always	176	(50.3)	254	(53.5)	313	(57.3)	371	(47.1)		
Mostly	92	(26.3)	131	(27.6)	143	(26.2)	230	(29.2)		
Sometimes	45	(12.9)	62	(13.1)	53	(9.7)	115	(14.6)		
Never	37	(10.6)	28	(5.9)	37	(6.8)	71	(9.0)	0.001(T)	0.021(T)
Social support (N=2170) ǂ										
Highest	111	(31.2)	158	(33.3)	198	(35.7)	217	(27.6)		
Medium	202	(56.7)	265	(55.8)	303	(54.7)	458	(58.3)		
Lowest	43	(12.1)	52	(10.9)	53	(9.6)	110	(14.0)	0.003(T)	0.239(T)

	(1) CLS-D (n=357)*		(2) 'CLS-C without CLS-D' (n=479)		(3) Condom-protected sex only (n=556)		(4) No anal/vaginal sex (n=797)		p-value across groups 1-4	p-value across groups 1-3
	n	%	n	%	n	%	n	%		
Depression symptoms (N=2189) ‡										
No	255	(71.4)	351	(73.3)	443	(79.7)	541	(67.9)		
Yes	102	(28.6)	128	(26.7)	113	(20.3)	256	(32.1)	<0.001	0.008
Anxiety symptoms (N=2189) ‡										
No	276	(77.3)	385	(80.4)	464	(83.5)	601	(75.4)		
Yes	81	(22.7)	94	(19.6)	92	(16.5)	196	(24.6)	0.003	0.068
Stable partner status (N=2189)										
None	153	(42.9)	172	(35.9)	241	(43.3)	419	(52.6)		
HIV-positive stable partner	56	(15.7)	253	(52.8)	80	(14.4)	121	(15.2)		
HIV-negative or HIV-unknown	148	(41.5)	54	(11.3)	235	(42.3)	257	(32.2)	<0.001	<0.001
ART status (N=2178)										
On ART	264	(74.8)	348	(73.4)	421	(76.4)	647	(82.8)		
Not on ART	57	(16.1)	83	(17.4)	82	(14.8)	68	(8.6)	<0.001	0.534
ART adherence (N=2178) ‡										
On ART adherent	274	(77.2)	343	(71.8)	431	(77.8)	657	(83.1)		
On ART non-adherent	24	(6.8)	52	(10.9)	41	(7.4)	66	(8.3)		
Not on ART	57	(16.1)	83	(17.4)	82	(14.8)	68	(8.6)	<0.001	0.102
ART status/self-reported VL (N=2143) ‡										
On ART reports undetectable VL	259	(73.8)	335	(70.8)	381	(70.0)	593	(76.5)		
On ART does not report undetectable VL	35	(10.0)	55	(11.6)	81	(14.8)	114	(14.7)		
Not on ART	57	(16.2)	83	(17.6)	82	(17.1)	68	(8.8)	<0.001	0.202
Study log-recorded viral load (N=2159)										
≤50 c/mL	264	(74.8)	348	(73.4)	421	(76.4)	647	(82.8)		
>50 c/mL	89	(25.2)	126	(26.6)	130	(23.6)	134	(17.2)	<0.001	0.543

*P-values by chi-squared test or (T): chi-squared test for linear trend (Wald test by multinomial logistic regression); * CLS-D includes 31 MSM who reported CLS but did not specify the HIV serostatus of their sexual partners ('CLS-unspecified'; ‡ Factors are defined in chapter 3*

Table 4.7: Odds ratios (ORs) and confidence intervals (95%CIs) for the association of factors with CLS-C or CLS-D as compared to condom-protected sex in the past 3 months (multinomial logistic regression among 1392 HIV-diagnosed MSM who reported sex in past 3 months)

			Condom-protected sex (N=556)	CLS-C but not CLS-D (N=479)			CLS-D (N=357)		
		N*		RRR	[95%CI]	p-value	RRR	[95%CI]	p-value
Unadjusted models	Age at recruitment (per year increase)	1362	ref	0.98	[0.97,0.99]	0.002	1.00	[0.98,1.01]	0.890
	White ethnicity (vs all other)	1369	ref	1.33	[0.89,1.97]	0.162	1.10	[0.73,1.67]	0.639
	Time since HIV diagnosis (per year increase)	1375	ref	1.00	[1.00,1.01]	0.475	1.00	[0.99,1.01]	0.866
	Financial hardship (vs none‡)	1371	ref	1.18	[0.86,1.63]	0.303	1.55	[1.11,2.17]	0.010
	Has stable partner (vs does not)	1380	ref	1.39	[1.08,1.79]	0.010	1.04	[0.79,1.36]	0.795
	Depression symptoms (vs none)	1392	ref	1.43	[1.07,1.91]	0.015	1.57	[1.15,2.14]	0.004
	Anxiety symptoms (vs none)	1392	ref	1.23	[0.90,1.69]	0.199	1.48	[1.06,2.07]	0.021
	Not on ART (vs on ART)	1387	ref	1.21	[0.87,1.69]	0.263	1.10	[0.76,1.59]	0.608
	Unknown self-reported viral load (vs known)	1171	ref	0.63	[0.37,1.05]	0.076	0.40	[0.21,0.76]	0.005
	Self-reported viral load >50c/mL (vs unknown)	194	ref	0.65	[0.33,1.27]	0.207	0.34	[0.15,0.73]	0.006
Adjusted model	Age at recruitment (per year increase)	1130	ref	0.97	[0.96,0.99]	0.001	0.99	[0.98,1.01]	0.370
	White ethnicity (vs all other)		-		-			-	
	Time since HIV diagnosis (per year increase)		-		-			-	
	Financial hardship (vs none‡)		ref	1.25	[0.85,1.83]	0.265	1.54	[1.03,2.28]	0.035
	Has stable partner (vs does not)		ref	1.67	[1.25,2.24]	0.001	1.19	[0.88,1.62]	0.263
	Depression symptoms (vs none)			1.42	[1.01,2.01]	0.046	1.53	[1.07,2.20]	0.020
	Anxiety symptoms (vs none)		-		-			-	
	Not on ART (vs on ART)		-		-			-	
	Unknown self-reported viral load (vs known)		ref	0.60	[0.35,1.04]	0.069	0.39	[0.20,0.77]	0.007
	Self-reported viral load >50c/mL (vs unknown)		-		-			-	

**Number with available information in each model; adjusted model includes all variables with p<0.15 in unadjusted models plus clinic; ref: reference category; ‡Financial hardship defined as money for basic needs: "sometimes or never" versus "always or most of the time"*

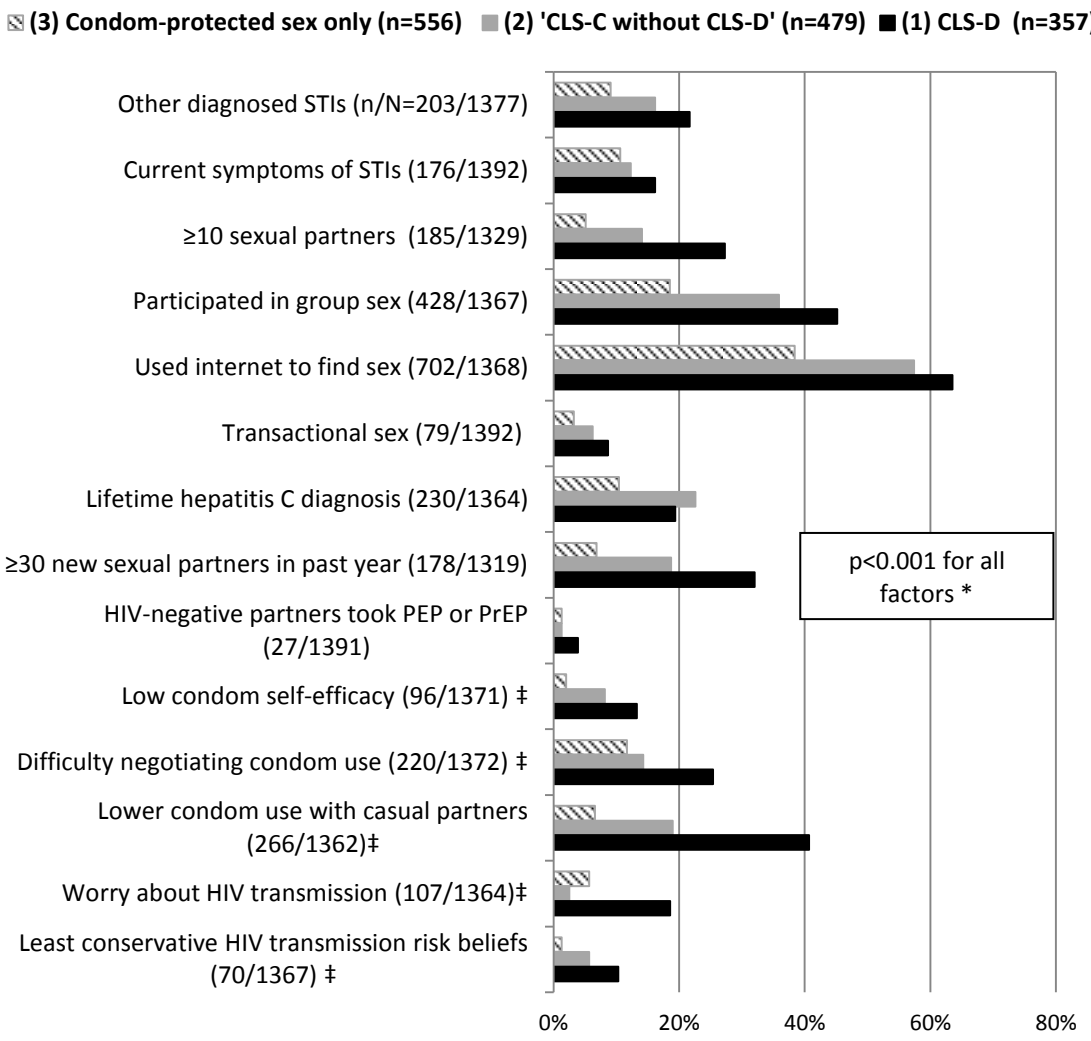
4.4.7.2 Prevalence of other sexual behaviours according to single variable of sexual activity

Among 1392 MSM who reported having sex in the previous three months, the prevalence of various sexual behaviours, STIs, and attitudes was assessed according to sexual activity in the past three months (CLS-D, 'CLS-C without CLS-D', or condom-protected sex). (Figure 4.2) There were significant differences in prevalence of all other sexual factors in the past three months between the three sexually active groups ($p<0.05$). Overall, prevalence of all other sexual behaviour measures was lower among the condom-protected sex group than the two CLS groups. The prevalence of other diagnosed STIs, current STI symptoms, higher partner numbers, group sex, and use of the internet to find sex were highest among men having CLS-D, followed by CLS-C, and then condom-protected sex. Prevalence of lifetime HCV diagnosis was higher in the CLS-C group compared to the CLS-D (22.6% vs 19.4%, $p<0.001$). Men reporting CLS-D were more likely than the other two sexually active groups to report 30 or more new sexual partners in the past year and low condom self-efficacy ($p<0.001$ for both). Worry about HIV transmission was highest in the CLS-D group (40.7%), followed by the condom-protected group (5.7%), and was lowest for the CLS-C group (2.5%, $p<0.001$ across 3 groups). The pattern of agreement to statements on difficulty in discussing and using condoms was similar, being highest for MSM in the CLS-D group, followed by the CLS-C, and condom-protected groups. Only 1.3% of MSM who had condom-protected sex were categorised as 'least conservative' with regards to their views on HIV transmission risk, as compared to 5.7% and 10.3% of MSM who had CLS-C and CLS-D respectively ($p<0.001$).

4.4.8 New sexual partners in the past year

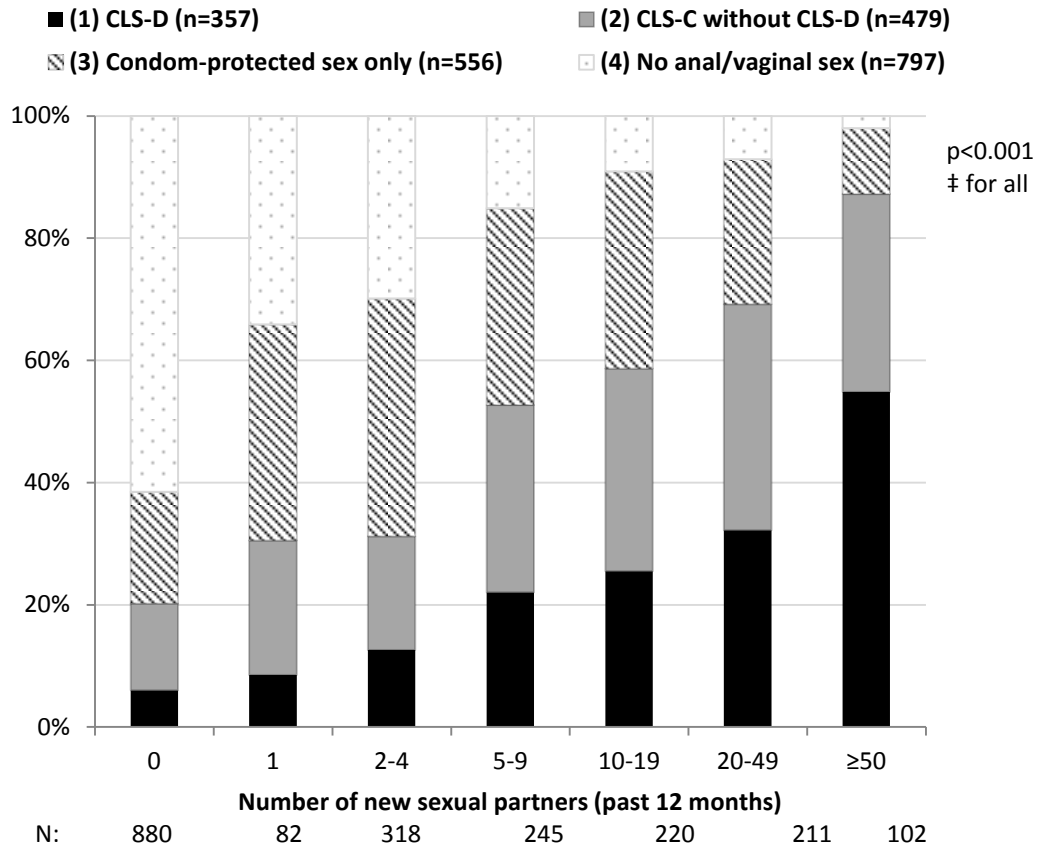
The number of new sex partners in the past 12 months was tabulated against the single variable of sexual behaviour in the past three months for all 2189 MSM. (Figure 4.3) Prevalence of all CLS in the previous three months, particularly of CLS-D, increased with increasing number of new sexual partners in the past year (p-trend<0.001). Of the 102 MSM who reported 50 or more new partners in the past year, 87.2% reported having CLS (54.9% had CLS-D) in the previous three months, compared to 880 MSM who did not have any new sex partners, of whom 20.2% reported having CLS (6.0% had CLS-D).

Figure 4.2: Prevalence of other sexual behaviours according to three mutually exclusive categories of sexual activity in the past three months (N=1392 reporting any anal or vaginal sex in past three months)



*Three month recall unless otherwise specified; *p-values by chi-squared test or Fisher's exact (F) across groups 1-3; ‡Factors defined in chapter 3, section 4.3.5; CLS-D: condomless sex with HIV-serodifferent partners; CLS-C: condomless sex with HIV-seroconcordant partners; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infection*

Figure 4.3: Number of *new* sexual partners in the past 12 months according to prevalence of each mutually exclusive category of sexual behaviour in the past 3 months (N=2189)



‡ test for linear trend for each category (1-4)

4.5 Discussion

4.5.1 Summary of findings

In this study of 2189 HIV-diagnosed MSM in the UK, over 63% reported having any anal or vaginal sex in the previous three months. Condomless sex (CLS) in the previous three months was prevalent (38%): 29% had CLS-C and 16% had CLS-D. When categorising sexual behaviour in mutually exclusive groups, 16% of MSM had CLS-D, 22% had CLS-C only (without any CLS-D partners), 25% had condom-protected sex, and 36% did not have any anal or vaginal sex in the past three months. Younger age and having an HIV-positive stable partner were associated with higher prevalence of any CLS in the past three months, after adjustment for socio-demographic and HIV-related factors. Compared to MSM who had any anal or vaginal sex, MSM who did not have sex were older, diagnosed with HIV for longer, had low educational qualifications, low social support, symptoms of depression and anxiety, but were more likely to be on ART with suppressed VL. There were few significant differences between the three sexually active groups (CLS-D, 'CLS-C without CLS-D', and condom-protected sex); compared to those who had condom-protected sex only, those who had CLS-D reported greater financial hardship and

symptoms of depression, were more likely to know their personal VL, and had higher prevalence of other STIs, group sex, and high partner numbers. Those who had 'CLS-C without CLS-D' tended to be younger than those who had condom-protected sex only, and were more likely to have an HIV-positive stable partner, symptoms of depression, and lifetime HCV infection.

4.5.2 Prevalence of condomless sex (CLS)

There have been few representative studies of sexual behaviour among HIV-diagnosed MSM in the UK in the past decade (summarised in Table 2.1 and Table 2.2).

4.5.2.1 Any CLS

Similar prevalence estimates of CLS were observed in earlier self-completed questionnaire studies of HIV-diagnosed MSM recruited from HIV-outpatient clinics in the UK; over 38% reported any condomless CLS in the past three months in ASTRA, compared to 38% in the East London study (2004-2005) and 51% in the HIV clinic sample of the London Gyms study (2008).[103,131] The prevalence in ASTRA is also comparable to pooled estimates from a US meta-analysis of 30 cross-sectional studies (1996-2009), in which prevalence of any CLS in the past three months ranged from 25% to 68%.[111] Two recent studies of HIV-outpatient MSM have found differing prevalence estimates; 46% in the past three months in the USA ATN study of 991 young HIV-diagnosed MSM[177] and 46% in the past six months among 300 outpatient HIV-diagnosed MSM in the Netherlands.[201]

Studies of HIV-positive MSM from convenience samples (gay and other community venues, bars, saunas) report variable estimates of greater magnitude compared to clinic-based studies.(Table 2.2) The prevalence of any CLS among HIV-positive MSM in the past year was: 44% (n=187 HIV-positive MSM) in the UK behavioural surveillance system (2004)[97,140], 82.1% (n=243) in the GMSS (2008)[134,144], 25% (n=59) in the Scotland GMSHS (2011)[142], and 52.6% (n=1494) in the London GMSHS (2013).[143] Samples of self-reported HIV-positive MSM recruited from venue-based studies are not representative of all HIV-diagnosed MSM in the UK in terms of patterns of sexual behaviour. Studies that systematically recruit HIV-positive MSM from hospital clinics are likely to be the most representative, as in the UK the vast majority of adults newly diagnosed with HIV (98%) attend for care at specialist National Health Service (NHS) clinics, and rates of retention in care are high.[228]

4.5.2.2 Condomless sex with HIV-serodifferent partners (CLS-D)

The prevalence of CLS with HIV-serodifferent partners (HIV-negative or HIV-unknown) in the past three months was 16% (n/N=357/2189) in ASTRA. Earlier UK studies of HIV-diagnosed MSM recruited from clinics have found variable estimates (using the same definition of CLS-D and recall period as in ASTRA), but are based on much smaller sample sizes. In addition, these studies have not excluded participants with a date of diagnosis occurring within the recall period of sexual behaviour. If such individuals are not excluded from the ASTRA sample, the prevalence of CLS-D in the past three months was 15.6% (n/N=357/2248), as compared to: 27% (n/N=40/148) in 'London Gyms', 5% (25/481) in the clinic sample

of the 'Internet and HIV' study, 20% (144/715) in the 'East London' study, and 15% (69/415) in the 'Switching' study.[103,114,131,151] The prevalence of CLS-D in the past three months in ASTRA is lower than the pooled CLS-D estimate reported in the earlier US meta-analysis (26%)[111]; this difference may be due to population characteristics, as studies included in the meta-analysis recruited self-reported HIV-positive MSM from gay venues in addition to HIV-diagnosed MSM from HIV clinics. In the US Medical Monitoring Project (see Table 2.1), the prevalence of CLS-D among 1010 HIV-diagnosed MSM was 20.0% (95%CI 17.0-23.0%) in the past year.[157] Findings from ASTRA are also in line with those from the START trial of early versus deferred ART initiation.[156] Among 1173 HIV-diagnosed ART-naïve MSM in the European START sub-sample, 15.1% reported CLS-D (with HIV-negative or unknown status partners) in the past two months.[156] When excluding MSM diagnosed in the past three months (as in this ASTRA analysis) the prevalence of CLS-D was 12.1%.

While a number of studies have examined the prevalence of CLS-D among HIV-outpatient MSM in the USA[113,152,157,169,180,181] and Western Europe[124,229], comparison between estimates is not straightforward. Estimates from convenience samples (gay clubs, saunas, and websites) of HIV-positive MSM vary widely, but again, tend to be of higher magnitude compared to clinic studies.[73,105,134,142,143,171,230] This is likely due to overestimation of the prevalence of sexual risk behaviour inherent in populations sampled from commercial gay venues or the internet, which may select more 'high risk' MSM.[231] Interpreting estimates of CLS-D from different studies can thus be challenging, as the sampled population may not be representative of the underlying population of HIV-diagnosed MSM. Studies also define CLS-D in different ways (with HIV-unknown status or HIV-negative partners, or both), and have different recall windows (in the past 3, 6, 12 months or at last sex). Nevertheless, the consistency in estimates of CLS-D prevalence between the aforementioned UK clinic-based studies and ASTRA is encouraging in supporting our ability to reliably and repeatedly measure such behaviour and capture trends. These results suggest that prevalence of CLS-D among HIV-diagnosed MSM in the UK attending for care has remained fairly stable during the past decade.

A minority of MSM who reported CLS but did not specify their partner's serostatus ('CLS-unspecified') in ASTRA had similar sexual behaviours as MSM who had CLS-D, including high partner numbers and prevalence of other STIs. (Appendix IV) When including this group, prevalence of CLS-D rose slightly, to 16.3% in the previous three months.

Consistent with other studies,[9,73,111] results from ASTRA suggest that perceived risk reduction strategies, such as being the receptive partner and withdrawal before ejaculation, are (to a certain extent) being used during CLS-D. It remains unclear whether these were consciously chosen strategies to avoid HIV transmission or circumstantial preferences.[111,232]

4.5.2.3 Condomless sex with HIV-seroconcordant partners (CLS-C)

In this study, CLS with other HIV-positive partners was prevalent, suggesting actual or perceived serosorting (selecting sexual partners based on HIV status). When including all MSM reporting CLS-C in ASTRA (including those who also reported CLS-D), prevalence was 28.6% in the past three months. This is comparable to the earlier meta-analysis of US cross-sectional studies among HIV-diagnosed MSM, which reported pooled prevalence estimates of CLS-C at any point in time of 30% (95%CI 25-35%).[111] It was not possible to ascertain whether the HIV-positive status of reported CLS-C partners was assumed or known with confidence. However, the prevalence of CLS-C excluding those who also reported CLS-D in the previous three months in ASTRA (21.9%) is similar to that observed in the earlier UK clinic studies, which had smaller sample sizes; prevalence of CLS-C in the previous three months among HIV-diagnosed MSM was 24.3% (36/148) in the clinic sample of 'London Gyms' (in 2008), 14% (98/715) in the 'East London' study, and 7.1% (34/481) in the clinic sample of 'Internet and HIV'.[103,128] Some studies from the USA have reported variable estimates of CLS-C compared to ASTRA; 36% (178/496) in the previous three months among HIV-diagnosed clinic attendees in the Positive STEPS study[113] and 39% in the previous 12 months among HIV-diagnosed STI clinic outpatients in Seattle.[181]

4.5.3 Factors associated with CLS

4.5.3.1 Socio-demographic characteristics

A number of co-factors have been identified as correlates of CLS among HIV-diagnosed MSM, but these vary according to the population sampled, the range of factors considered and the study design.(Section 2.6) In ASTRA, CLS was significantly more common among younger men (under 30 years), a finding corroborated in the European START sub-sample, the Swiss HIV Cohort study, and the Australian 'Positive Health' surveys,[9,124,233] but not in the earlier 'East London' and 'Internet and HIV' studies.[103,151] The association with younger age could be explained by the variation in sexual function by life stage observed in the general population as well; stratified probability surveys in the UK, such as the National Survey of Sexual Attitudes and Lifestyles (Natsal), show that low sexual activity overall is associated with increasing age.[234] The discrepant findings observed may also be due to diverse recruitment methods. Online surveys of MSM (of mixed HIV-serostatus), such as EMIS, tend to be biased towards a lower median age of participants, but this is not the case for HIV-diagnosed MSM, who have been overrepresented in older age groups.[235]

No consistent association has been found between ethnicity/race and CLS or CLS-D among MSM living with HIV in a number of studies from the USA.[157,165,169–172] In ASTRA the majority of MSM were of white ethnicity and no differences were observed in the prevalence of any CLS by ethnicity.

While there was some indication that HIV-diagnosed MSM who had lower educational levels and were not employed reported lower prevalence of CLS, the associations were not significant after adjustment

for age. The lack of association between these two factors and CLS has been previously reported in studies from the UK[103] and USA.[110,113,175,176] However, in the London GMSHS (2000-2013), HIV-positive MSM educated up to two years after age 16 were 30% more likely to report CLS in the past year compared to those educated up to age 16.[143] However, this group included MSM with undiagnosed HIV as well as HIV-diagnosed MSM who had CLS, and so the true effect of education on CLS in HIV-diagnosed MSM could not be untangled. In ASTRA, HIV-diagnosed MSM who reported not having anal or vaginal sex in the previous three months were significantly more likely to not have any educational qualifications or employment, compared to those who had sex (condomless or condom-protected). The majority of studies in the past decade have examined educational and employment status within the context of reporting any sex (i.e. comparing condomless sex versus condom-protected sex). Our study shows that HIV-diagnosed MSM who are disadvantaged in terms of education and employment are more likely to report not having any sex, compared to those who report having sex.

4.5.3.2 HIV-related factors

Uncertainty remains around the association of time elapsed since an HIV diagnosis and CLS. Longitudinal studies among MSM have observed a sharp reduction in the prevalence of CLS after a HIV-positive diagnosis, followed by an increase and then plateauing long-term.[93,111,181] In ASTRA, prevalence of CLS and CLS-D was lower soon after diagnosis (up to 2 years), then increased (at 2-5 years), and steadily decreased thereafter to the lowest levels (at >15 years post-diagnosis). The association remained significant even after adjustment for participant's age. These findings are in line with START and other recent USA studies,[110,179,181,230] but not with earlier studies of clinic outpatients from the UK or the USA, which did not find the prevalence of CLS to vary by the length of time diagnosed.[103,111,113,167,175] The association of time since HIV diagnosis and CLS may be dependent on whether participants who are recently HIV-diagnosed are excluded; this ensures that participants reporting CLS prior to HIV diagnosis are not accounted for.

In line with the 2009 meta-analysis of 30 cross-sectional US studies and the earlier 'East London' study,[103,111] ASTRA shows that MSM who were on ART were less likely to report any CLS. This association, however, was not independent of time since HIV diagnosis. The prevalence of CLS-D was lower among MSM on ART compared to those not on ART. There was some evidence to suggest that MSM with detectable study log-recorded VL (>50c/mL) were slightly more likely to report CLS, but not with HIV-serodifferent partners. It is thus possible that this association is driven by MSM with detectable VL who have CLS with other HIV-positive partners only.

Perceived virological status may also affect decisions on condom use. In ASTRA, a small proportion of MSM reported not knowing their personal VL (6.4% of 2189); this group were less likely to have any CLS (including CLS-D) compared to those who reported having suppressed VL (<50c/mL). In addition, MSM who did not know their VL were more likely to report having condom-protected sex compared to any

CLS, even after adjustment for socio-demographic and other factors. Among MSM on ART, prevalence of CLS and CLS-D tended to be higher among those with self-reported *undetectable* VL compared to those on ART without undetectable VL (including those who did not know their VL and those who had detectable VL). These findings may indicate that decisions on condom use may be influenced by perceived viral load status. Coupled with the high prevalence of detectable viremia among those who reported 'CLS-C without CLS-D', these results may also suggest HIV-serosorting for transmission risk reduction, especially in the absence of effective ART.

There have been no studies examining the association of non-adherence to ART and CLS in the UK to date. MSM who reported non-adherence in ASTRA tended to be less likely to report having CLS-D compared to those who reported good adherence. Comparison across different sexual behaviours in the past three months showed that almost a third of MSM who were non-adherent reported not having anal or vaginal sex (versus condomless or condom protected sex). The earlier US meta-analysis (2009) showed that HIV-positive MSM reporting more than 90% adherence were not more likely to have CLS, but these findings were based on a small subset of studies with available adherence information.[111]

4.5.3.3 Psychological wellbeing

Symptoms of depression or anxiety were not found to be significantly associated with the binary classification of CLS in ASTRA, in line with previous research of HIV-diagnosed heterosexual men and women.[154,186–188,236] Disentangling the causality of the association between psychological factors (such as depression and anxiety) and CLS is challenging, especially in cross-sectional studies. The association may be bidirectional, as negative affects could promote CLS or CLS may in turn promote anxiety and depression. Use of the mutually exclusive categories of sexual behaviour, however, highlighted more complex underlying associations of depression with different types of sex; MSM with symptoms of depression or anxiety were significantly more likely to report not having anal or vaginal sex compared to having sex. The prevalence of psychological symptoms was also high among those who had CLS (and was higher for those who had CLS-D rather than CLS-C) compared to those who had condom-protected sex. Hence, depression may have a curvilinear relationship with sexual behaviour, being associated with both low levels of sexual activity and more sexual risk behaviours.[190] HIV-positive people with symptoms of depression may have low libido overall or experience higher sensitivity to potential risks, thus adopting more risk-averse behaviours; on the other hand, those with depression may also have maladaptive thought processes which reduce motivations for effective self-care and lead to 'riskier' behaviours (such as recreational drug use or CLS).[190]

Our study did not have completely overlapping periods for the measures of psychological symptoms and sexual behaviours (depression and anxiety measured in the past two weeks and sexual behaviours in the past three months), which may have underestimated the strength of any association. However, the PHQ-9 and GAD-7 have been found to have high accuracy and validity among HIV-positive people.[209,237]

Few studies have examined the relationship between perceived social support and CLS among HIV-diagnosed MSM, all having small sample sizes. (Section 2.6.3) An association similar to that of depression and sexual behaviour was observed for low functional social support and sexual behaviours. While low social support was not associated with reporting CLS overall (using the binary classification), when using the mutually exclusive categories, a curvilinear association emerged; prevalence of low social support was highest among MSM who did not have anal or vaginal sex, followed by those who had CLS-D (14% vs 12% respectively).

4.5.3.4 Partner-related factors

Having a stable partner was significantly associated with having CLS in ASTRA. Specifically, MSM were more likely to report CLS with an HIV-positive stable partner, than with an HIV-negative or HIV-unknown status stable partner. This finding, corroborated in other studies,[113,134,136,143,152,166,195,196] may indicate that HIV-diagnosed MSM are more likely to use condoms when there is perceived risk of HIV transmission. Preference for seroconcordant stable relationships may also be a lifestyle choice in reducing the risk of HIV transmission to HIV-serodifferent partners. For those with an HIV-serodifferent stable partner, however, the likelihood of reporting CLS-D was much higher than for those who did not have a partner or who had an HIV-positive stable partner. The concordance between stable partner's serostatus and reporting CLS/CLS-D is encouraging as it shows that the measure of CLS-D used in the ASTRA questionnaire has a degree of internal validity.

4.5.3.5 Other sexual behaviours and STIs

Compared to MSM who had 'CLS-C without CLS-D' and those who had condom-protected sex only, MSM who had CLS-D were more likely to also report high partner numbers, recent STI diagnoses and symptoms, group sex, and to have least conservative beliefs about HIV transmission risk. There was a strong association between the number of new sex partners in the past year and any CLS in the past three months, particularly for CLS-D. Maintaining consistent condom use is likely to be challenging in the context of high partner numbers for HIV-diagnosed MSM. Accurate ascertainment of partners' HIV status may be harder and uncertain with high partner numbers. Specifically, a number of men reporting 'CLS-C without CLS-D' indicated high numbers of CLS-C partners (>50 in the past year), which suggests a higher possibility of assumed rather than confirmed HIV-positive status of partners. The association also suggests that reporting high turnover of *new* partners among MSM with HIV could be considered a marker of CLS in research or clinical settings.

MSM who reported 'CLS-C without CLS-D' in the previous three months were significantly more likely to have a stable HIV-positive partner compared to those who had CLS-D or condom-protected sex. Few studies have distinguished between CLS with HIV-seroconcordant partners exclusively (no HIV-serodifferent partners) and CLS with HIV-seroconcordant *and* HIV-serodifferent partners. In the latter

case, if an HIV-positive partner's status is not known with confidence, the risk of HIV transmission remains. While it is encouraging that a sizeable proportion of HIV-diagnosed MSM in ASTRA appear to restrict CLS to partners with HIV, this behaviour does not eliminate the risk of transmission of other STIs. In fact, MSM who had CLS-C only had the highest prevalence of lifetime HCV, high prevalence of group sex, and high partner numbers. Dense sexual networks of serosorting HIV-diagnosed MSM may contribute to transmission of other STIs, as evidenced in recent UK studies linking CLS-C with ongoing outbreaks of other STIs (discussed in Chapter 8).[147,238]

4.5.4 **Conclusions and Implications**

Overall, evidence from this chapter shows that there were not marked associations between socio-demographic factors and measures of CLS. This indicates that HIV/STI prevention efforts remain important across all socio-demographic groups. However, the consistent associations of CLS measures with younger age may suggest the need for particular focus on younger men with HIV.

Measures of condomless sex tended to be more prevalent among those not on ART and those recently diagnosed. These findings further support a policy of earlier ART initiation for HIV and STI prevention. Although levels of CLS (and, possibly, of CLS-D) were higher among those on ART with self-reported *undetectable* VL, compared to those on ART without self-reported undetectable VL, levels still tended to be lower than those among MSM not on ART.

The vast majority of epidemiological studies examining factors associated with sexual behaviours of HIV-diagnosed MSM use binary classifications of CLS (versus no CLS) and CLS-D (versus no CLS-D). Analyses from this chapter showed that in addition to use of this binary classification, use of the mutually exclusive categories of sexual behaviour (CLS-D, 'CLS-C without CLS-D', condom-protected sex, no sex) is particularly helpful in disentangling complex underlying associations of various co-factors with different sexual behaviours. This was particularly the case for examining the effect of psychological symptoms, self-reported VL, and social support on sexual behaviours, which were lost using the binary classification.

In conclusion, among HIV-diagnosed MSM in the UK, condomless sex in the previous three months was prevalent, but in line with results from similar UK studies in the past decade. The high prevalence of condomless sex with other HIV-positive partners may indicate active serosorting and warrants further attention as transmission of other STIs remains high. Being on ART was not associated with higher prevalence of CLS, or CLS-D. As ART use expands it will remain crucial to promote sustained high ART adherence, regular viral load monitoring, and ongoing awareness of personal viral load level.[182]

5 Characterising higher HIV transmission risk condomless sex with HIV-serodifferent partners

5.1 Chapter aims

This chapter aims to characterise and assess the prevalence of higher HIV risk condomless sex with HIV-serodifferent partners (CLS-D) using definitions that incorporate various criteria that could impact on HIV infectiousness. A literature review is provided of studies that have examined CLS-D with an appreciable risk of HIV transmission among HIV-diagnosed MSM in high-income countries. The prevalence of higher HIV transmission risk CLS-D is assessed among all ASTRA MSM who were diagnosed with HIV for at least three months, according to differing criteria, including clinic-recorded viral load (VL) level, ART non-adherence, time since started ART, and self-reported diagnoses of other sexually transmitted infections (STIs). Characteristics of MSM who had higher HIV risk CLS-D are compared to those of MSM who had other CLS-D.

5.2 Introduction

In the era of effective ART, pre-exposure prophylaxis, and treatment as prevention, further refining what constitutes sex with a higher risk of HIV transmission is important to consider in the context of HIV prevention. Historically, CLS-D denoted 'risky' sex in the context of HIV transmission. HIV infectiousness now needs to be conceptualised within a broader context of ART treatment.[239] The following sections discuss findings of studies published after conclusive evidence emerged on the extremely low risk of HIV transmission during CLS-D while the HIV-positive partner is virally suppressed on ART. [7,9]

5.2.1 Evidence on CLS-D with higher risk of HIV transmission

Few studies have examined prevalence of CLS-D with higher risk of HIV transmission among HIV-diagnosed MSM. There is, currently, no consensus definition on this concept in epidemiological research. Studies that incorporate clinic-recorded VL level into the concept of higher HIV transmission risk CLS-D emerged two years after ASTRA concluded recruitment (2014). These studies (summarised in Table 5.1) were carried out among HIV-outpatient populations in the USA, France, Thailand, and Brazil, and use a variety of definitions for 'high risk' sexual behaviour, incorporating a number of other factors in addition to VL, such as: counts of sexual partners, proportion of CLS acts, other STI co-infections, or ART status. Two of the eight studies shown in Table 5.1 provide estimates of higher HIV risk CLS-D from HIV-diagnosed men and women (denoted by *) while the remaining show estimates from HIV-diagnosed MSM only (denoted by ◊).

One of the first constructs of HIV transmission risk sex was examined in a sub-study of the international SMART trial (2002-2006) of continuous versus CD4-guided episodic ART; this smaller study included sites from the USA and measured CLS-D (with HIV-negative or unknown status partners) in the previous two months while having VL>1500c/mL.[112] A total of 6.2% of 875 trial participants (men and women) were

classified as having “transmission risk to HIV negative persons or those with unknown serostatus”. While a higher prevalence of this measure was observed over the 2 year follow-up in the ART interruption arm, this was because participants spent a longer time with detectable VL.[112] Results were not stratified by gender/sexual orientation and so no estimates are available for MSM.

Direct comparison between prevalence estimates across studies is not possible due to different definitions of higher HIV risk CLS-D. Other factors that differ between studies include study design (such as eligibility criteria and sampling frame) and implementation (such as method of data collection), which may also play an important role in determining the prevalence higher transmission risk CLS-D. In the UK Gay Men’s Sexual Health Surveys (GMSHS), between 2000 and 2013, HIV-diagnosed MSM were classified as “at risk of transmitting HIV” if they reported CLS but not exclusive serosorting in the previous 12 months; this represented 26.4% of all HIV-diagnosed MSM (or 17.1% of all HIV-positive MSM) over the study period.[143] However, the GMSHS did not collect information on ART status or VL level, thus misclassifying all HIV-positive men who had CLS-D as potential transmitters of HIV, despite the evidence of extremely low transmission risk on effective ART. Consequently the group of MSM who actually had CLS-D with a risk of transmitting HIV in the GMSHS is likely to be much smaller.[240] Similarly, a cross-sectional survey from internet sex-seeking MSM living in Latin America (2012) defined high transmission sex as CLS-D while not on ART in the previous three months, but did not collect information on VL status.[168] These two studies are not included in Table 5.8 as they did not use a VL criterion in their definition of higher HIV risk CLS-D.

Table 5.1: Summary of studies measuring CLS-D with higher risk of HIV transmission (CLS-D-HIV-risk) among HIV-diagnosed clinic populations, accounting for viral load (VL)

Study / Data collection period / Country		Recruitment, population, study type	Eligibility criteria	N total N HIV-diagnosed MSM (%)	CLS-D recall period	Prevalence of CLS or CLS-D (all men and women* or MSM only◊)	Definition of CLS-D-HIV-risk	Prevalence of CLS-D-HIV-risk (all men and women* or MSM only◊)	Comments
SMART[112]	2002-2006 USA	Longitudinal sub-study of RCT on continuous versus CD4-guided episodic ART among people living with HIV from USA sites. Questionnaire on sexual behaviours and testing for other STIs at baseline, months 4, 12, and annually thereafter. Results shown here are at baseline for <u>all</u> participants.	CD4>350 cells/mm^3 and willing to start or discontinue ART according to randomizatio n assignment	N=875 N MSM=416 (47.1%)	Past 2 months	CLS at baseline (all participants): 15.4% *	Any of the following when VL>1500c/mL: CLS-D, needle-sharing, or a new diagnosis of gonorrhoea, chlamydia, or syphilis.	At baseline (among all participants): 6.2% (n/N=54/875) *	Data not available for MSM
Fenway Health[180]	2004-2007 USA	HIV-diagnosed MSM clinic attendees participating in RCT aimed at increasing condom use with serodifferent partners. Self-completed questionnaire, testing for STIs at baseline, and medical record extraction for CD4/VL/ART use subsequently.	Consent to participate to HIV prevention RCT	N MSM=201 (100%)	Past 6 months	CLS-D: 69.3% ◊	Insertive or receptive CLS-D and either: VL>75c/mL or STI diagnosis (gonorrhoea, syphilis, chlamydia) in past year.	CLS-D-HIV-risk: 45.0% (90/201) ◊ 2 criteria met: • CLS-D and VL>75: 33.8% (68/201) • CLS-D and STI: 4.0% (8/201) 3 criteria met: • CLS-D and VL>75 and STI: 7.0% (14/201)	High prevalence of detectable VL (50.3% had VL>75c/m) and low ART use (43.3% not on ART)
HOPS[241]	2007-2010 USA	Open prospective cohort of HIV-diagnosed people receiving care in 6 clinics, with annual automated telephone survey on socio-demographic, sexual factors. Results here for MSM.	HIV-diagnosed MSM completing survey	N=1291 N MSM=902 (70.4%)	Past 6 months	CLS: 71.9% ◊ CLS-D insertive:16.7% ◊	Insertive CLS-D and VL≥400c/mL	3.4% (24/902) ◊	Respondents more likely to be white, university-educated MSM

Study / Data collection period / Country		Recruitment, population, study type	Eligibility criteria	N total N HIV-diagnosed MSM (%)	CLS-D recall period	Prevalence of CLS or CLS-D (all men and women* or MSM only◊)	Definition of CLS-D-HIV-risk	Prevalence of CLS-D-HIV-risk (all men and women* or MSM only◊)	Comments
MMP[157,158]	2009-2010 USA	Nationally representative annual cross-sectional sample of HIV-diagnosed clinic attendees. Face-to-face interviews on sexual behaviours and ART, VL from medical records. Results here for MSM only.	HIV-diagnosed for ≥12 months	N=4094 N MSM=1897 (46.3%)	Past 12 months	CLS-D: 13.0% ◊	CLS-D and VL ≥400c/mL on ≥1 occasion in past 12 months	6.0% (114/1897)◊	Social desirability bias from face-to-face interviewing may have led to underreporting of CLS-D
HPTN063[174]	2010-2012	Cohort study of HIV-diagnosed people in care in Zambia, Thailand, Brazil, with self-completed questionnaire and STI testing at baseline. VL data only available in Thailand and Brazil. Results here for MSM only.	Had to have 'HIV transmission risk' in past 12 months (any CLS, or self-reported STI) and ≥2 clinic visits in past 9 months	N=749 N MSM=200 (26.7%)	Past 3 months	CLS-D: 69.5% ◊	CLS-D and 'detectable' VL or an STI	34% (68/200) ◊	Exact VL cut-off not specified ('detectable' within 6 months of assessment)
ANRS-VESPA2[155]	2011-2012 France	Cross-sectional survey among nationally representative sample of people living with HIV (random sample of HIV clinic outpatients). Results here for MSM only.	HIV-diagnosed for >12 months and with available VL data	N=2638 N MSM=1163 (44.1%)	• Past 12 months for stable partner • Most recent for casual partner	*Not shown*	"High risk transmission" (HRT) defined as ≥1 of: not on ART, or on ART and detectable VL, or on ART and suppressed VL for <12 mths, or on ART and suppressed VL for >12mths and ≥1 STI in 12mths. Versus "low risk transmission" (LRT) : on ART and suppressed VL for ≥12mths and no STI in past 12 mths	• CLS-D with stable partner was 18% among HRT MSM (p>0.1 for difference with LRT) ◊ • CLS-D with most recent casual partner was 10% among HRT MSM (p>0.1 for difference with LRT) ◊	Sexual behaviours and STIs assessed through face-to-face interviewing

Study / Data collection period / Country		Recruitment, population, study type	Eligibility criteria	N total N HIV-diagnosed MSM (%)	CLS-D recall period	Prevalence of CLS or CLS-D (all men and women* or MSM only◊)	Definition of CLS-D-HIV-risk	Prevalence of CLS-D-HIV-risk (all men and women* or MSM only◊)	Comments
ATN[177]	2009-2012 USA	Cross-sectional questionnaire study of young (12-26 years) HIV-diagnosed men receiving care in one of 20 HIV clinics. Results for MSM only.	Linked to care, reported anal sex with another male in past 3 months, on ART for >6 months.	N total= 2225 N MSM= 991 (44.5%)	Past 3 months	CLS-D: 31.3% ◊	CLS-D and latest VL≥200c/mL	18.9% (187/991) ◊	Excluded MSM on ART for ≤6 months (n=175). High prevalence of detectable VL even among on MSM on ART >6 months (55.4%)
Atlanta clinics[239]	2013-2014 USA	Questionnaire survey of HIV-diagnosed people attending for HIV care. Urine screening for recreational drug use and prospective text-message sexual behaviour diary for 28 consecutive days. Results examining association of detectable VL (>100c/mL) and condomless anal sex for men and women combined.		N total=1040 N MSM= Unknown	Subsequent 28 consecutive days of observation	CLS: 54.1% *	Defined as: any 'unprotected' vaginal or anal sex and most recent VL>100c/mL	16.7% (174/1040) *	Data not available for MSM. Majority black, low-income population in high HIV prevalence setting.

*Prevalence estimates shown in each study are for HIV-diagnosed MSM only ◊ or for men and women combined *; ART: antiretroviral therapy; ATN: Adolescent Medicine Trials Network for HIV/AIDS Interventions; CLS: condomless sex; CLS-D: condomless sex with HIV-serodifferent partners; HOPS: HIV Outpatient Study; HRT: high risk transmission; MMP: Medical Monitoring Project; SMART: Strategies for Management of Antiretroviral Therapy Trial; VL: viral load; RCT: randomised controlled trial; STI: sexually transmitted infection*

5.3 Methods

Analyses presented in this chapter include ASTRA MSM diagnosed with HIV for at least three months (N=2189).

5.3.1 Defining higher HIV risk CLS-D

In order to better reflect the prevalence of HIV transmission risk when the HIV-diagnosed partner is on virally suppressive ART,[24,242] various definitions for CLS-D with an appreciable risk of HIV transmission were examined. In the main definition, participants were required to report CLS-D in the past three months, plus one of the following two criteria:

- Study log (clinic-recorded) latest viral load>50c/mL, OR
- Not on ART at the time of the questionnaire (self-reported)

The following additional criteria were then incorporated into the main definition, one by one, and then all together (see Figure 5.1 for full details):

- Started ART <9 months ago (according to self-reported date of ART start), OR
- Non-adherent to ART (self-reported, missing ≥2 consecutive days of ART on ≥2 occasions in the past 3 months), OR
- Diagnosed STI in the past three months (self-reported, for the HIV-diagnosed participant only).

5.3.2 Statistical analysis

The prevalence (95%CIs) of CLS-D with an appreciable risk of HIV transmission was assessed among all MSM according to combinations of criteria (section 5.3.1.) The main definition of higher HIV risk CLS-D (CLS-D and: VL>50c/mL or not on ART) was then used to compare against MSM who had any other CLS-D (but not higher HIV risk CLS-D). Differences in socio-demographic characteristics, psychological symptoms, HIV-related factors, and other sexual behaviours, STIs, and attitudes were examined between the two groups reporting CLS-D, using chi-squared tests or Fisher's exact. All socio-demographic, HIV-related factors and sexual behaviours have been defined in sections 3.8 and 4.3.

5.3.2.1 Sensitivity analyses

Three sensitivity analyses were undertaken to examine the prevalence of higher HIV risk CLS-D according to other criteria. Firstly, a higher VL cut-off of >200c/mL was used in each definition (instead of >50c/mL). Secondly, the criterion of self-reported diagnosis of STIs in the past three months was restricted to STIs that present with genital ulcer disease (syphilis, lymphogranuloma venereum, new or recurrent genital herpes). Thirdly, the linked routine clinical data was used to include serial VL measurements in the six months preceding ASTRA questionnaire completion. Details of the consent rates for linkage of ASTRA questionnaire and routine clinical data are shown in section 3.10.2.5.The prevalence of higher HIV risk CLS-D was examined according to whether the participant had only one rebound (single VL>50c/mL) or more than one rebound (≥2 consecutive VL>50c/mL) during the six

months preceding ASTRA. No restriction was applied to the interval between consecutive VL measurements, as long as they were within the six month period under study.

5.4 Results

5.4.1 Prevalence of higher HIV risk CLS-D

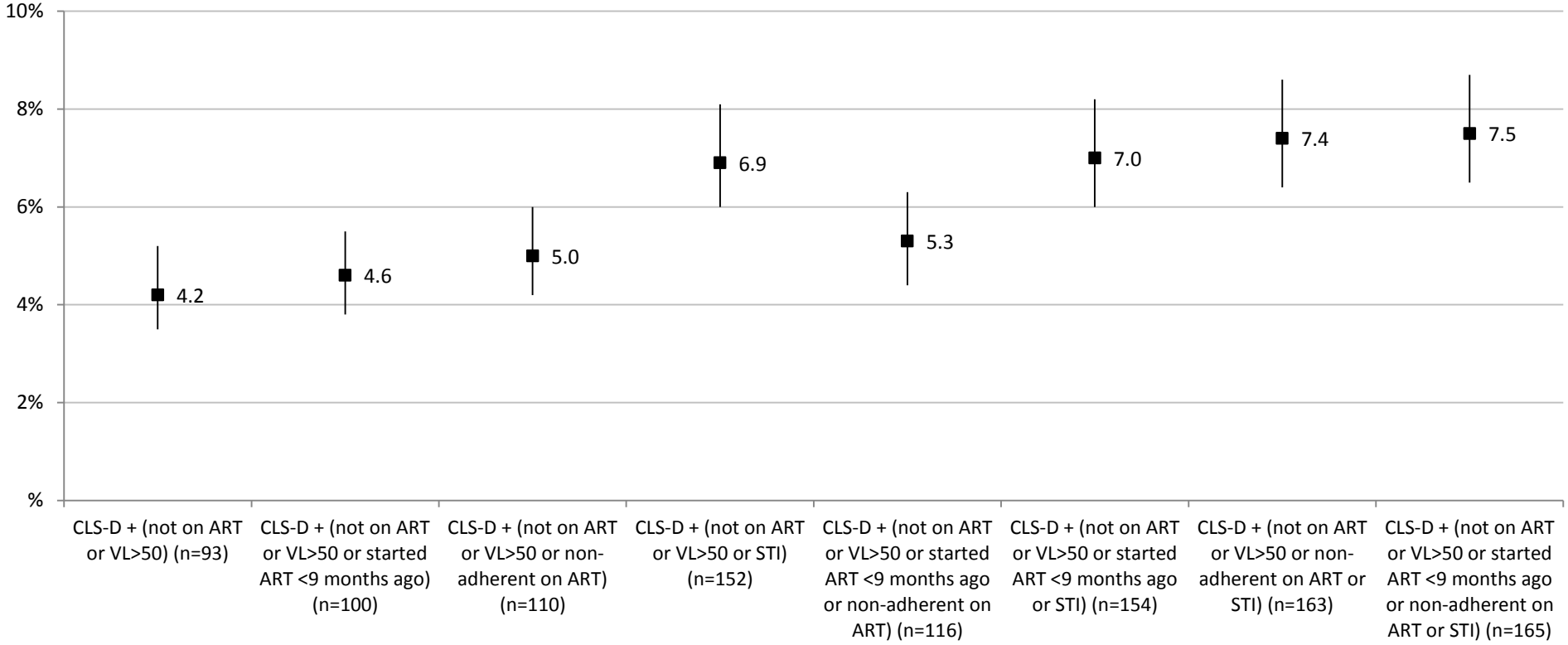
As shown in section 4.4.2, the overall prevalence of any CLS-D in the previous three months among all 2189 MSM was 16.3% (95%CI 14.8-17.9%, n=357). Using the main definition of higher HIV risk CLS-D (reporting CLS-D plus: not being on ART or having study log-recorded VL>50c/mL), 93 MSM were considered to have higher HIV risk CLS-D, yielding a prevalence of 4.2% (95%CI 3.5-5.2%) among 2189 MSM. Figure 5.1 also shows the prevalence of additional definitions of higher HIV risk CLS-D in the previous three months, according to various criteria incorporated (ART status, time since started ART, adherence to ART, and other diagnosed STIs). For example, 4.6% (n=100) of all HIV-diagnosed MSM were classified as having higher HIV risk CLS-D if they reported having CLS-D in the previous three months and either: were not on ART, or had latest VL>50c/mL, or started ART <9 months ago. Similarly, 7.5% (n=165) of all HIV-diagnosed MSM had higher HIV risk CLS-D if they reported having CLS-D in the previous three months and either: were not on ART, or had latest VL>50c/mL, or started ART <9 months ago, or reported non-adherence to ART, or another diagnosed STI. The footnote to the figure shows that prevalence estimates were similar when excluding 31 MSM who had CLS-D but did not specify their partners' HIV-serostatus ('CLS-unspecified', see section 4.3.3).

Among MSM *not* on ART, prevalence of higher HIV risk CLS-D (using the main definition) was 19.7% (57/290). Among MSM *on* ART with self-reported undetectable VL, prevalence of higher HIV risk CLS-D was 0.8% (13/1568), as these individuals had study log-recorded detectable VL despite reporting it as undetectable. Among MSM on ART with self-reported detectable VL, prevalence of higher HIV risk CLS-D was 7.7% (22/285).

5.4.2 Factors associated with higher HIV risk CLS-D

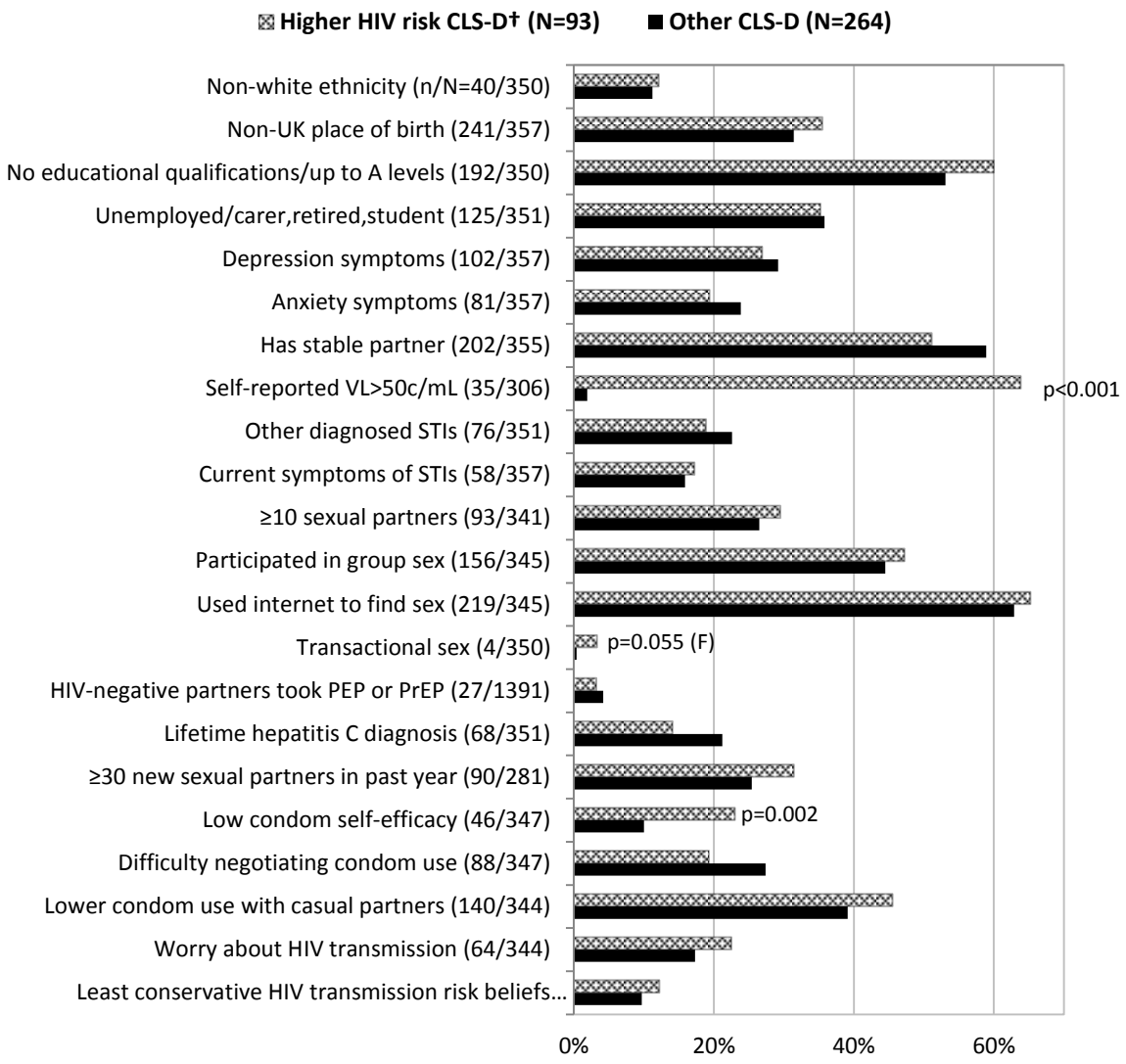
The main definition of higher HIV risk CLS-D was used in this analysis. Men who had higher HIV risk CLS-D according to this definition (n=93) were compared to men who had CLS-D but not higher HIV risk CLS-D (labelled 'other CLS-D', n=264).(Figure 5.2) MSM who had higher HIV risk CLS-D tended to be younger and diagnosed with HIV for a shorter period of time. There were few other significant differences between men in the two groups. Not surprisingly, men who had higher HIV risk CLS-D were more likely to report detectable VL (>50c/mL) compared to men who had other CLS-D (p<0.001). Prevalence of other sexual behaviours, STIs, and attitudes was similar between the two CLS-D groups, with the exception of low condom self-efficacy; this was much higher among the higher HIV risk CLS-D group compared to the other CLS-D group (23.0% vs 10.0%, p=0.002). There was weak evidence to suggest that transactional sex was more prevalent among MSM who had higher HIV risk CLS-D compared to MSM who had other CLS-D, although the sample size was small.

Figure 5.1: Prevalence (95%CI) of higher HIV risk CLS-D among 2189 MSM, according to specific definitions (incorporating ART status, viral load, time since started ART, ART non-adherence, and self-reported STI diagnosis)



ART: Antiretroviral therapy; CLS-D: condomless sex with HIV-serodifferent partners; non-adherent to ART: missed ≥2 consecutive days of ART on ≥2 occasions in the past 3 months; VL: latest clinic-recorded viral load (missing for n=30); STI: sexually transmitted infection (includes self-reported previous diagnosis of syphilis, gonorrhoea, chlamydia, LGV, new hepatitis B or C, new or recurrent genital herpes or warts, trichomonas, NSU/NGU). Excluding n=31 MSM who had CLS-unspecified, the prevalence (n, %) of each higher HIV risk CLS-D definition is: 1. Not on ART or VL>50: n=85 (3.9%); 2. Not on ART or VL>50 or on ART for <9 months: n=92 (4.2%); 3. Not on ART or VL>200 or non-adherent on ART: n=100 (4.6%); 4. Not on ART or VL>50 or STI: n=143 (6.5%); 5. Not on ART or VL>50 or on ART for <9 months or non-adherent on ART: n=106 (4.8%); 6. Not on ART or VL>50 or on ART for <9 months or STI: n=145 (6.6%); 7. Not on ART or VL>50 or non-adherent on ART or STI: n=152 (6.9%); 8. Not on ART or VL>50 or on ART for <9 months or non-adherent on ART or STI: n=154 (7.0%)

Figure 5.2: Prevalence of socio-demographic, psychological characteristics, and sexual behaviours of MSM who had higher HIV risk CLS-D† versus MSM who had 'other CLS-D' (CLS-D but not higher HIV risk CLS-D), N=357



P-values by chi-squared test or Fisher's exact test (F); †CLS-D plus not on ART or study log-recorded viral load>50c/mL; Three month recall unless otherwise specified; All factors shown have been defined in section 3.8. PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis

5.4.2.1 Sensitivity analyses

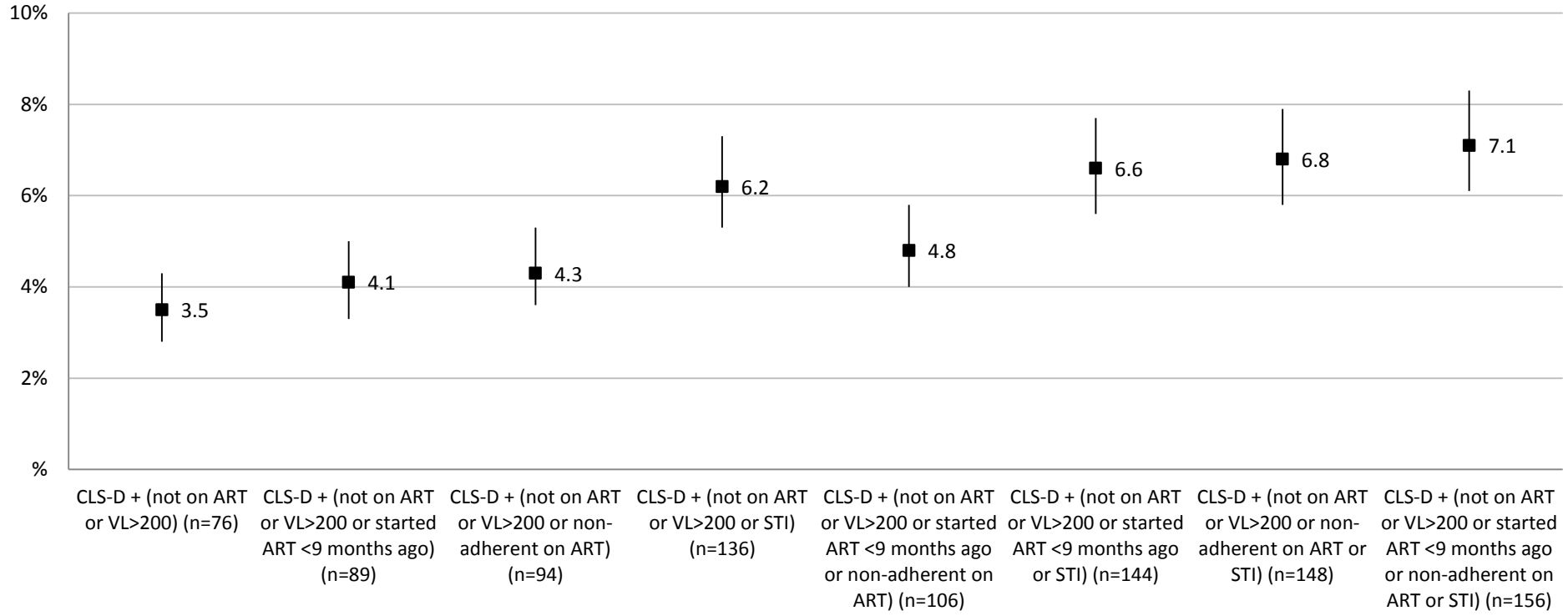
Prevalence of higher HIV risk CLS-D was assessed according to the same criteria, but with a higher VL cut-off of >200c/mL. (Figure 5.3) Over 17% of all MSM (n/N=386/2189) had study log-recorded VL>200c/mL, of whom 17.1% (66/386) had CLS-D in the past three months. The prevalence of higher HIV risk CLS-D was similar to that with a VL cut-off value of >50c/mL, ranging from 3.5% to 7.1% (Figure 5.3).

The prevalence of higher HIV risk CLS-D was then estimated using a reduced definition of self-reported previous diagnosis of STIs in the past three months, only including STIs that present with genital ulcer disease (GUD): syphilis, LGV, new or recurrent genital herpes.(Figure 5.4) Among 236 MSM who reported a diagnosis of STIs in the previous three months, 92 (38.9%) reported having GUD and were included in this criterion; 5.4% of 2189 MSM (n=118) had CLS-D plus were either not on ART or had VL>50c/mL or had GUD, as compared to 6.9% of MSM (n=152) who had the same criteria but any STIs instead of GUD (Figure 5.4).

In the third sensitivity analysis, the linked routine clinical data was used to examine the prevalence of higher HIV risk CLS-D incorporating serial VL measurements. Among 2189 MSM, 1810 had available linked VL data within six months preceding ASTRA completion. Of these MSM, 24.9% (n =452) had at least one rebound (single VL>50c/mL) during the six months prior to questionnaire completion. The prevalence of higher HIV risk CLS-D among 1810 MSM ranged from 4.5% (when defined as CLS-D preceded by one rebound) to 5.8% (when additionally considering ART status at questionnaire, ART non-adherence, and time since started ART). (Figure 5.5)

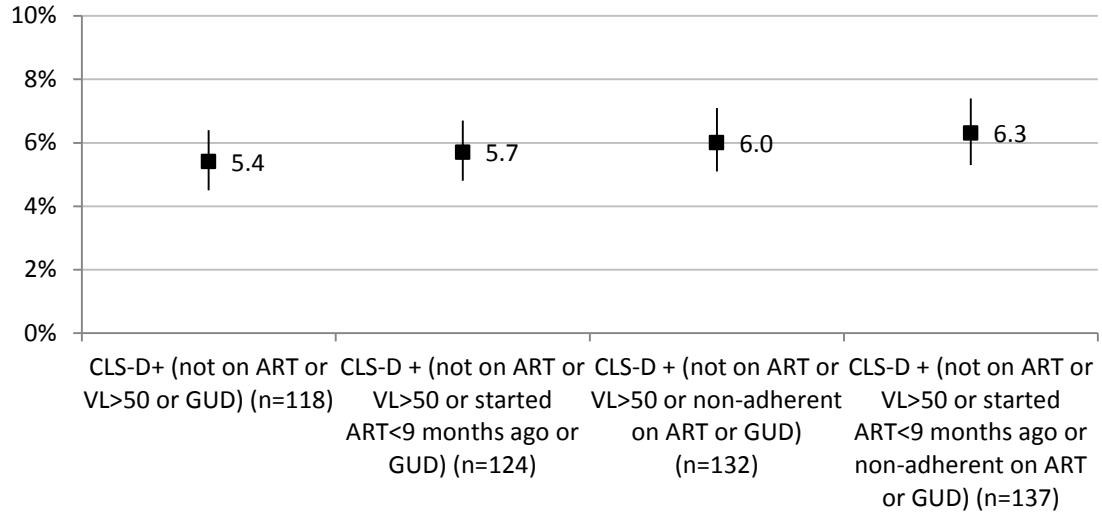
Over 21% (398/1810) of MSM had more than one rebound (≥2 consecutive VL>50c/mL) during the six months prior to questionnaire completion. The prevalence of higher HIV risk CLS-D among 1810 MSM ranged from 4.0% (when defined as CLS-D preceded by more than one rebound) to 5.6% (when additionally considering ART status at questionnaire, ART non-adherence, time since started ART). (Figure 5.5) Among those who had higher HIV risk CLS-D, median VL measurements were relatively high; those with one rebound had median VL 3.7 $\log_{10}$c/mL and those with more than one rebound had median 3.8 $\log_{10}$ c/mL.

Figure 5.3: Sensitivity analysis 1- Prevalence (95%CI) of higher HIV risk CLS-D among 2189 MSM, with viral load >200c/mL and additional criteria incorporated (ART status, time since started ART, ART non-adherence, and self-reported STI diagnosis)



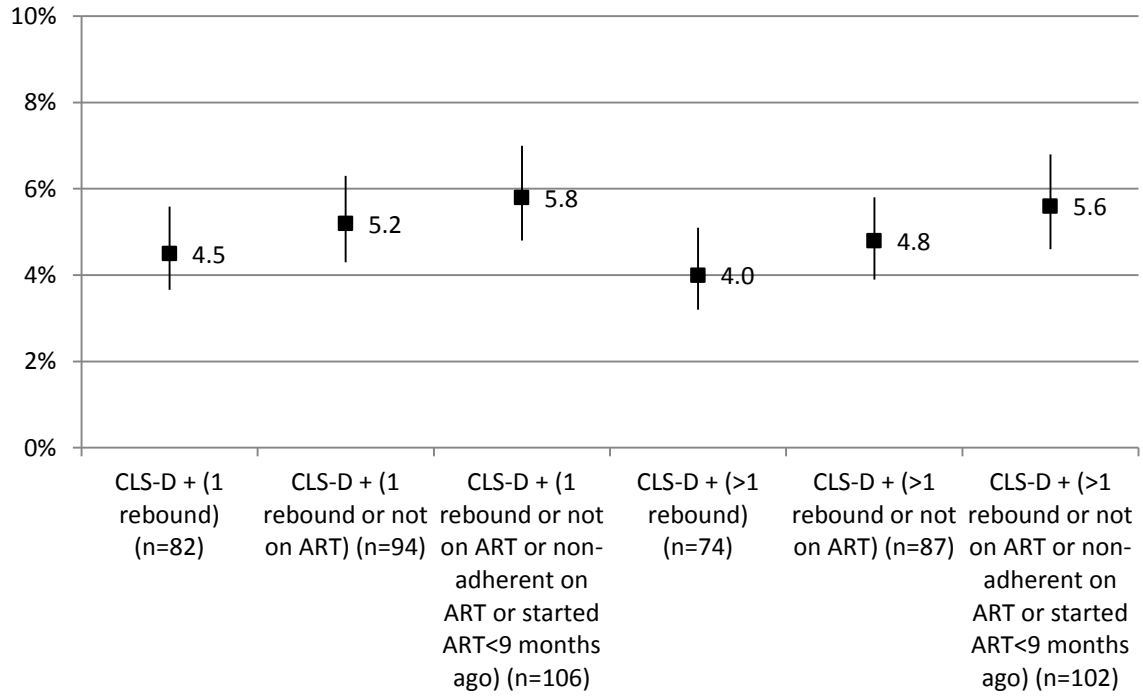
Excluding n=31 MSM who had CLS-unspecified, the prevalence of each higher HIV risk CLS-D definition is: 1. Not on ART or VL>50: n=60 (3.2%); 2. Not on ART or VL>50 or on ART for <9 months: n=83 (3.8%); 3. Not on ART or VL>200 or non-adherent on ART: n=86 (3.9%); 4. Not on ART or VL>50 or STI: n=129 (5.9%); 5. Not on ART or VL>50 or on ART for <9 months or non-adherent on ART: n=137 (4.8%); 6. Not on ART or VL>200 or started ART <9 months ago: n=137 (6.3%); 7. Not on ART or VL>200 or non-adherent on ART or STI: n=139 (6.3%); 8. Not on ART or VL>200 or started ART <9 months ago or non-adherent on ART or STI: n=146 (6.7%)

Figure 5.4: Sensitivity analysis 2 - Prevalence (95%CI) of higher HIV risk CLS-D according to criteria incorporating genital ulcer disease (GUD) (N=2189)



GUD includes self-reported syphilis, LGV, new or recurrent genital herpes in the past three months; Excluding n=31 MSM who had CLS-unspecified, the prevalence of each higher HIV risk CLS-D definition is: 1. Not on ART or VL>50 or GUD: n=110 (5.0%); 2. Not on ART or VL>50 or started ART <9 months ago or GUD: n=116 (5.3%); 3. Not on ART or VL>200 or non-adherent on ART or GUD: n=122 (5.6%); 4. Not on ART or VL>50 or started ART<9 months ago or non-adherent on ART or GUD: n=127 (5.8%)

Figure 5.5: Sensitivity analysis 3 - Prevalence (95%CI) of higher HIV risk CLS-D according to clinic-recorded viral load rebounds 6 months prior to ASTRA questionnaire completion (N=1801)



1 rebound: VL measurement>50c/mL in the six months prior to questionnaire; >1 rebound: two consecutive VL>50c/mL during same period; Higher HIV risk CLS-D as % of all 2189 MSM was: CLS-D + 1 rebound: 3.7%; CLS-D + (1 rebound or not on ART): 4.3%; CLS-D + (1 rebound or not on ART or non-adherent or started ART<9 months ago): 4.8%; CLS-D+ >1 rebound: 3.4%; CLS-D + (>1 rebound or not on ART): 4.0%; CLS-D + (>1 rebound or not on ART or non-adherent on ART or started ART<9 months ago): 4.7%

5.5 Discussion

5.5.1 Summary of findings

Among HIV-diagnosed MSM in ASTRA, prevalence of higher HIV risk CLS-D in the past three months ranged from 4.2% when considering CLS-D while not on ART or with viral load>50c/mL, to 7.5% when additionally considering time since ART initiation or non-adherence or other STI co-infections. Compared to the prevalence of any CLS-D in the past three months (16.3% of 2189 MSM), the prevalence of higher HIV risk CLS-D was lower by 53-74% in relative terms. MSM who had higher HIV risk CLS-D were very similar to those who had other CLS-D with regard to socio-demographic factors and most other markers of sexual behaviour.

5.5.2 Results in the context of other studies

Most studies (reviewed in Table 5.1) took a similar general approach to defining higher HIV risk CLS-D, incorporating current or recent detectable VL and, in some cases recent diagnosed STI, as additional criteria, at least one of which was necessary in addition to CLS-D. However, specific definitions varied, meaning prevalence estimates cannot easily be compared across studies.

In addition to differences in definitions, study eligibility criteria may influence estimates of the prevalence of CLS-D higher HIV risk, as they may introduce selection bias. For example, the French ANRS-VESPA2 and the US Medical Monitoring Project (MMP) had nationally representative random samples of HIV-diagnosed people and required participants to be diagnosed for at least 12 months (see Table 5.1).[155,158] This inclusion criterion may have masked an association of time since HIV diagnosis, use of ART, and prevalence of higher HIV risk CLS-D. ART use is likely to be lower among those recently diagnosed. Seroconversion cohorts have suggested that immediately following HIV diagnosis, MSM may reduce 'high risk behaviours' (such as CLS-D) and revert to stable levels within a year of testing positive.[152,243] It is possible that the prevalence of higher HIV risk CLS-D could be lower if recently diagnosed MSM were included in VESPA2 or MMP. In ASTRA and other studies,[180,241] MSM who were younger and diagnosed more recently tended to be report higher prevalence of higher HIV risk CLS-D compared to any other CLS-D. In SMART,[112] younger age and self-reported MSM status were also associated with higher HIV risk CLS-D. To date, there is no other evidence on the association between age, time since HIV diagnosis, and higher HIV transmission risk CLS-D from studies of HIV-diagnosed MSM. Conversely, studies that exclude participants who did not report CLS may also introduce bias as they are not representative of the underlying population, in which no sex or condom-protected sex may also be prevalent. For instance, both the USA Fenway Health and the international HPTN063 cohort studies included MSM "at the greatest risk for HIV transmission"(Table 5.1), which is likely to explain the high prevalence of higher HIV risk CLS-D in these studies compared to ASTRA (45% in the past 6 months, 34% in the previous three months, versus <8% in past three months, respectively).[174,180]

Finally, the method of survey administration is also crucial in studies of sensitive behaviours.[244] Sexual behaviour questionnaires administered via face-to-face interviewing (used in the ANRS-VESPA2 and

MMP studies)[155,158] or telephone interviewing (used in the HOPS study)[241] may be subject to social desirability bias; participants may underreport socially 'taboo' behaviours, such as CLS-D, especially with higher risk of HIV transmission. The prevalence of higher HIV risk CLS-D in studies that used interviewing for data collection (MMP[157,158], ANRS-VESPA[155]) was lower compared to studies using self-administered surveys (SMART[112], Fenway Health[180], HPTN063[174], ATN[177], Atlanta clinics[239], and ASTRA), although differences in definition also impact on this comparison.

5.5.3 Additional criteria for higher HIV risk CLS-D

More evidence is needed to understand whether factors additional to ART use and VL status should be incorporated in a definition of CLS-D with higher HIV transmission risk, particularly in the context of CLS-D with multiple partners. Such information is also important in refining current guidelines and helping HIV-diagnosed individuals and their partners make informed decisions on having CLS-D safely. Standardised definitions may be useful for epidemiological monitoring studies as well. The factors considered in this study (in addition to ART use and HIV plasma VL level) were length of time since ART initiation, self-reported diagnosis of co-infection with other STIs (for the HIV-positive partner only), and self-reported ART adherence.

5.5.3.1 Viral load (VL) cut-off

The VL cut-off considered when defining higher HIV risk CLS-D in ASTRA was set to 50c/mL. This was selected firstly, so as to be in line with BHIVA guidelines and other available evidence on transmission risk up until 2011 (when ASTRA began recruitment), and secondly, because this is the clinical treatment target for VL suppression used in the UK. The BHIVA guidelines, based on the Swiss Statement, stated that HIV transmission via vaginal sex is extremely low for individuals on effective ART, provided the HIV-positive partner has "sustained plasma VL below 50 HIV RNA c/mL for more than six months and that the VL is below 50 c/mL on the most recent test".[245] Higher VL cut-offs could additionally be considered in future research. Once viral suppression is achieved, intermittent episodes of detectable low-level viremia ('blips') can occur, typically between 50 and 1000c/mL.[246] HIV transmission studies have adopted higher VL thresholds (200c/mL in PARTNER and *Opposites Attract*)[25,247], possibly to account for isolated viral blips not associated with virological failure. In ASTRA, raising the viral load cut-off to 200c/mL in the definition of higher HIV risk CLS-D produced similar estimates as with a cut-off of 50c/mL (3.5% vs 4.2%, respectively). The Rakai study[8] found no instances of HIV transmission among the 51 heterosexual participants with VL≤1500 c/mL, but there are no transmission studies to date that incorporate such high VL thresholds when considering anal CLS-D among MSM.

5.5.3.2 Time since started ART

A minimum of nine months since ART started was used as one of the additional criteria in alternative definitions of higher HIV risk CLS-D in ASTRA. This threshold was chosen as VL suppression is usually achieved after three to six months on ART.[248] BHIVA guidelines also state that assurance of low infectiousness requires a six month period of viral suppression (see section 5.5.3.3).[245] In fact, the prospective Partners PREP study of 1592 HIV-serodifferent heterosexual couples showed that there is residual risk of HIV transmission during the first six months on ART (until viral suppression is achieved);

the HIV incidence rate during this period was close to that among couples where the HIV-diagnosed partner was not on ART (2.08 vs 1.79 per 100 person-years, based on 3 seroconversions).[249] In ASTRA, while self-reported dates of starting ART were used to ensure that participants had begun ART at least nine months prior to questionnaire completion, it was not possible to check whether participants were on ART continuously during those nine months; it may be that treatment discontinuations occurred during that period. This was accounted for to some extent when the ART non-adherence criterion was additionally used. Incorporating the length of time on ART when considering CLS-D may be important. Among people who are starting or have recently started ART, additional strategies are needed to reduce the risk of HIV transmission through CLS-D before viral suppression is achieved.

5.5.3.3 Time with viral suppression

It was not possible to incorporate time with viral suppression using the full ASTRA dataset, as only a single plasma VL measure was available in the study log for all participants. Sensitivity analyses using the routine clinical data incorporated serial VL measurements within six months before ASTRA questionnaire completion (among MSM who were HIV-diagnosed for at least three months). Viral 'blips' were not uncommon during this period. The prevalence of CLS-D three months prior to ASTRA among MSM with available clinical data was similar to that among MSM with one or more than one rebound. It is encouraging that only a small minority of HIV-diagnosed men who had episodes of detectable viremia also reported CLS-D. In addition, in the main definition of higher HIV risk CLS-D, no restriction was placed on the timing of the latest VL measure from the study log, although BHIVA guidelines state that VL testing should be undertaken regularly (every three to four months).[245] In ASTRA, for the majority of MSM the study log VL value was from a test done in the three month period prior to questionnaire completion (N=2175, 1.9% had study log VL measurement on the same day as questionnaire completion, 59.5% had a measurement ≤3 months ago, 29.0% 3-6 months, 9.2% more than 6 months ago, and 0.3% after). The study log VL aimed to be the most recent test that the participant had been informed of. Therefore, the VL value used in the definition of higher HIV risk CLS-D may not necessarily be the most relevant value for the duration of the three month recall period for sexual behaviour, but did occur during this period for the majority of participants. Incorporating these additional factors (time with viral suppression and timing of latest VL measure) would result in an increase in prevalence of CLS-D and a more conservative definition of higher risk HIV transmission sex.

5.5.3.4 ART adherence

Good adherence to ART is critical in ensuring continued VL suppression.[250] The prevalence of higher HIV risk CLS-D incorporating non-adherence varies according to the tools used to measure non-adherence (self-report, pill counts, or medication event monitoring systems). In ASTRA, clinically significant non-adherence was self-reported and defined as missing two or more consecutive days of ART on two or more occasions in the previous three months (prevalence 25.9%). Incorporating this measure of ART non-adherence into the definition of higher HIV risk CLS-D resulted in a marked increase in prevalence. This finding highlights the importance of supporting people on ART in remaining adherent to treatment, particularly if they are having CLS-D. Self-report is the most commonly used adherence measure and has

high specificity, but may have lower sensitivity.[251] To capture more accurate prevalence of higher HIV risk CLS-D when non-adherence is included in the definition, studies could use composite adherence measures (combining two or more methods) with higher validity, or take into account 'forgiving' ART regimens (that sustain viral suppression despite suboptimal adherence).[252] Importantly, there is a need for evidence on the effect of varying degrees of non-adherence on the likelihood of a viral rebound to a level that could significantly impact on HIV transmission risk. This evidence is important for epidemiological studies, but also for informing people living with HIV on the relative risk of CLS-D when specific doses of ART are missed.

5.5.3.5 STI co-infections

The role of STI co-infections on onward HIV transmission during CLS-D is discussed in detail in Chapter 8. Briefly, STIs may facilitate HIV shedding in mucosal membranes by hindering immunological response to ART.[245] The relevance of STIs in the context of viral suppression however remains unclear. When the criterion of other STI diagnosis was incorporated in the definition of higher HIV risk CLS-D, prevalence increased by 30-40% in relative terms, compared to only considering ART and VL status. This is driven by the underlying prevalence of STIs in the population. For example, in the HPTN 063 multi-cohort study, 44% of 200 MSM tested positive for either syphilis, gonorrhoea, and chlamydia at baseline; the resulting prevalence of higher HIV risk CLS-D (CLS-D and VL>50c/mL or STI diagnosis) was 34% in the previous three months.[174] This estimate is higher than that observed in ASTRA, where 10.9% of MSM had any self-reported STI in the previous three months and the resulting prevalence of higher HIV risk CLS-D was 6.9% (defined as CLS-D and: VL>50c/mL or not on ART or STI diagnosis).

In sensitivity analyses, only STIs that present with genital ulcer disease (GUD) were included in the definition of higher HIV risk CLS-D, and the prevalence was overall lower compared to including all STIs. Only self-reported STIs for the HIV-positive partner could be recorded in ASTRA. However, to ensure the extremely low risk of HIV transmission through vaginal CLS-D when the HIV-positive partner is on effective ART, BHIVA guidelines require that both partners do not have an STI, and further stress comprehensive STI screening of both partners.[245] The PARTNER study showed that acquisition of STIs during follow-up was not associated with risk of HIV transmission among HIV-serodifferent MSM couples, although power to detect a true effect was limited as there were no within-couple HIV transmissions.[9] To improve reliability of estimates of higher HIV risk CLS-D when the STI criterion is added, future studies of HIV-serodifferent couples (such as PARTNER and *Opposites Attract*) may benefit from STI testing of both partners concurrent to the CLS-D recall window (e.g. if the recall is in the previous three months, STI testing could be conducted within this period).

5.5.3.6 Plasma versus genital tract HIV RNA concentrations

The effect of ART on the genital tract is another factor which could be considered when discussing higher HIV transmission risk CLS-D. Overall, blood plasma HIV RNA concentrations are mirrored in the genital tract,[253] but a number of recent studies have shown that a minority of men (<10%) on ART with suppressed blood VL have detectable seminal VL, albeit low-level.[254–257] The extent to which discordance

between blood and genital viral suppression on ART impacts sexual transmission of HIV remains unclear, especially when compounded by genital inflammation caused by other STI co-infections (discussed in Chapter 8). For example, a US study of 101 HIV-diagnosed MSM clinic attendees on ART found a much higher prevalence of discordance between VL in blood and semen (25%) compared to other studies, which was attributed to the high prevalence of concomitant STIs and genital inflammation (9% and 24% respectively).[258] More research is needed on the role of seminal HIV shedding on transmission risk when blood VL is suppressed.

5.5.4 **Implications**

It is encouraging that the prevalence of higher HIV risk CLS-D in ASTRA is relatively low, ranging from 4.5% to 7.5% depending on criteria incorporated. This finding adds evidence to the hypothesis that transmission from HIV-diagnosed MSM is thought to contribute a minority of new HIV infections in the UK.

In addition, prevalence of higher HIV risk CLS-D was much lower among MSM on ART (versus those not on ART), and extremely low (<1%) among MSM on ART with self-reported undetectable VL. As ART use continues to expand, the prevalence of higher HIV transmission risk CLS-D is likely to remain far less prevalent among MSM on ART with self-reported undetectable VL, compared to those not on ART. With more HIV-diagnosed people initiating ART at diagnosis, the proportion of MSM who have higher HIV risk CLS-D with self-reported *detectable* VL on ART may also reach levels similar to those for MSM with self-reported undetectable VL (from 7.7% to 0.8%)

There are numerous challenges in defining CLS-D with higher HIV transmission risk, both in the clinical setting and for standardised use in epidemiological studies. In order for behavioural studies on HIV transmission to be representative of the developments in HIV prevention, there is a need to move away from the concept of 'unsafe' and 'risky' sex defined as CLS-D only. Instead, there is a need to examine other measures of CLS-D which have a greater potential for HIV transmission. Accounting for VL and ART status during CLS-D is one of the ways forward in adapting research to contemporary evidence.

Epidemiological studies of sexual behaviour among HIV-diagnosed MSM could also benefit from including higher HIV transmission risk CLS-D as a fifth category when grouping sexual behaviours into mutually exclusive categories (higher HIV transmission risk CLS-D, any other CLS-D, 'CLS-C without CLS-D', condom-protected sex, no anal or vaginal sex). This would allow for more detailed examination of the association of various factors with different sexual behaviours. Among HIV-diagnosed MSM, research measuring 'any CLS' still remains relevant for assessment of (non-HIV) STI transmission, but higher HIV risk CLS-D will be most relevant for assessment of HIV transmission risk.

Although ASTRA was conducted after the 2008 "Swiss statement", when expert opinion on reduced risk of HIV transmission with suppressed VL was widely publicised, it was conducted prior to the publication of conclusive results from HPT052 and PARTNER. The prevalence of higher HIV risk CLS-D may change as

ART is made available to everyone with HIV regardless of CD4 count.[17] In particular, as ART use expands, and prevalence of viral suppression increases among people with diagnosed HIV, this would tend to result in lower prevalence of higher HIV risk CLS-D. However, sexual behaviour patterns among MSM with HIV may also be changing, which could also impact on prevalence of higher HIV risk CLS-D. Future studies examining ongoing trends in sexual behaviour will remain important. Additionally, further follow-up from studies such as PARTNER and *Opposites Attract* will further clarify HIV transmission risk in the context of undetectable VL at most recent test but with suboptimal reported adherence, less frequent VL testing, or a recent STI.

5.6 Conclusions

The definitions of higher HIV transmission condomless sex with HIV-serodifferent partners (CLS-D) examined in this chapter show that the prevalence of higher HIV risk CLS-D is overall very low, and much lower than the prevalence of CLS-D overall. As the concept of 'high risk sex' for HIV transmission evolves, only considering CLS-D will no longer be the best measure of HIV transmission risk behaviour, especially when the HIV-positive partner is on virally suppressive ART. Incorporating viral load in the concept of higher risk CLS-D will thus become important both in future studies of sexual behaviour of HIV-diagnosed MSM, and in informing safer sexual practices between HIV-serodifferent partners.

6 Recreational drug use and condomless sex

6.1 Chapter aims

The main aim of this chapter is to examine the association of recreational drug use with sexual behaviours among HIV-diagnosed MSM. A review of literature will be undertaken from studies among HIV-diagnosed MSM in high-income countries (Western Europe, North America, Australia) between 1995 and 2016. The review will examine firstly, the prevalence of recreational drug use, secondly, any socio-demographic, psychological, HIV-related, lifestyle factors that have been identified as correlates of recreational drug use, and thirdly, associations between recreational drug use and sexual behaviours (mainly, condomless sex). While the focus of the review will be on HIV-diagnosed MSM, evidence from MSM who do not have HIV will also be reviewed to provide context. The aims of these analyses are to investigate, among ASTRA MSM: (i) the prevalence and factors associated with recent recreational drug use (including measures of polydrug use and chemsex associated drug use), (ii) the association of recreational drug use with measures of CLS, other sexual behaviours, and attitudes (iii) the relative association of recreational drug use to condom-protected sex compared to CLS, and to CLS-C compared to CLS-D, (iv) the association of specific drugs with CLS-C, CLS-D, and higher HIV risk CLS-D, (v) the association of measures of problematic alcohol use and sexual behaviours, accounting for recreational drug use, and (vi) the association of recreational drug use and problematic alcohol use with non-adherence to ART and viral load (VL) non-suppression.

6.2 Introduction

6.2.1 Recreational drugs studied

This chapter focuses on commonly used recreational drugs (summarised in Table 6.1), which are controlled and non-controlled under the UK Misuse of Drugs Act 1971. These include stimulants: 3,4-Methylenedioxymethamphetamine (MDMA, ecstasy), cocaine, methamphetamine (crystal meth), and mephedrone; hallucinogens: Lysergic acid diethylamide (LSD) and ketamine; depressants: opioids, gamma-hydroxybutyrate (GHB), gamma-butyrolactone (GBL), cannabis; and other substances: inhalants (poppers), drugs used in the treatment of erectile dysfunction (ED) taken without prescription (e.g. Viagra), and anabolic steroids. The term 'club drugs' refers to substances commonly or typically used in connection with attending nightclubs, bars, festivals, concerts, parties, or sex on premises venues to enhance sociality, enjoyment of music, or dancing.[259,260] This can encompass stimulants which trigger euphoric feelings and increase heart rate (cocaine, ecstasy, GHB/GBL, or mephedrone) as well as dissociatives which produce feelings of detachment from one's body and surroundings (ketamine and LSD).

In recent years, the UK has seen the emergence of new psychoactive substances (NPS), which mimic the effects of controlled drugs.[261] NPS does not refer to newly invented substances, rather to those which

are either newly available or misused.[262] These include substances recently controlled under the UK Misuse of Drugs Act, such as GHB/GBL (added in 2009), mephedrone (2010), khat (2014), and the dissociative methoxetamine (2013); substances which have been controlled for a number of years but available as newly modified chemical derivatives (e.g. the synthetic cannabinoid 'spice'); substances which have as yet not been regulated or are under temporary drug orders.[263] The UK is the single largest market of unregulated NPS.[264] The market is characterized by the speed with which suppliers circumvent drug controls by offering new alternatives to restricted products, advertising them as harmless everyday products (e.g. bath salts, room fresheners), and marketing them as 'legal highs' implying they are safe to use.[264] As of May 2016, all NPS are illegal to supply under the Psychoactive Substances Act 2016.

6.2.2 **Polydrug use**

Polydrug use refers to use of two or more recreational drugs either simultaneously (combining substances at the same time) or consecutively (within the same time period but not at the same time)[265]. An example of simultaneous polydrug use is inhalation of a mixture of ketamine and ecstasy. Consecutive polydrug use can be sequential, in order to induce differing physiological responses (e.g. use of cocaine while already under the influence of GHB) or refer to active use during a specific period (e.g. number of drugs used in the past three months). Polydrug use may be indicative of a more severe substance abuse problem. In addition, drug-drug interactions (DDIs) between recreational drugs can lead to severe adverse reactions; for example, co-administration of nitrites (poppers) and the ED drug Viagra can cause fatal hypotension and is thus contraindicated.[266,267]

Alcohol, being legal and freely available, is also commonly used alongside recreational drugs (particularly stimulants such as amphetamine and cocaine).[144,260,268,269] Problematic alcohol consumption (that increases the risk of or results in harmful consequences to the user or others) can be operationalised using a multitude of measures, usually involving number of units consumed over a period of time. Concomitant use of recreational drugs and alcohol can also be dangerous; for instance, alcohol has been shown to potentiate the sedative effects of GHB, leading to respiratory depression.[270]

Table 6.1: Commonly used recreational drugs: chemical and physiological characteristics, mode of administration, potential for drug interactions[267,270–276]

Name	Chemical classification	Related terms	Mode of administration	Behavioural and physiological effects	Drug-drug interactions (DDIs)/other health concerns
3,4-Methylenedioxymethamphetamine (MDMA)	Stimulant/ hallucinogen	Ecstasy, molly	swallowed, snorted, injected	• Mild hallucinogenic effects; increased empathy, euphoria, stimulation, and sexual arousal • Effects last 3-6 hours • Health risks: depression, anxiety, insomnia, impaired cognitive performance; ecstasy toxicity (increased body tempterature, dehydration, teeth grinding)	• Potential interaction with ATV/r, DRV/r, LPV/r
Alkyl nitrites	Smooth muscle relaxant	Poppers, amyls, TNT	inhaled nasally	• Rapid onset vasodilation, light-headedness, and euphoria; relaxation of sphincter muscles • Effects last a few minutes	• Concurrent exposure with sildenafil citrate (Viagra) is contraindicated • Potential interaction with PIs
Anabolic steroids	Synthetic androgen	Roids	injected, swallowed, applied to skin	• Improve sports endurance and performance, stimulate muscle growth • Health risks: kidney and liver damage; changes in cholesterol leading to increased risk of stroke or heart attack; anger, aggression	
Cannabis	Depressant	Marijuana, THC, weed	smoked, ingested (mixed in food)	• Enhanced sensory perception, euphoria, drowsiness/relaxation; increased heart rate and appetite • Effects last ≤10 minutes-4 hours (longer if ingested) • Health risks: problems with learning, memory, concentration; anxiety, panic attacks	• Potential interaction with ATV/r, EFV, ETV
Cocaine	Stimulant	Coke, crack	snorted, smoked, injected	• Increased euphoria, alertness, confidence; decrease need for food and sleep; hypersensitivity to sight, sound, touch; increased body temperature, heart rate, blood pressute • Effects last ≤30 minutes • Health risks: anxiety, heart attack, stroke, seizure; nasal damage	• High interaction with SQV/r • Potential interaction with ETV/r, DRV/r, LPV/r, EFV, ETV, NVP, RPV, and single-tablet regimens

Continued on next page

Name	Chemical classification	Related terms	Mode of administration	Behavioural and physiological effects	Drug-drug interactions (DDIs)/other health concerns
Erectile dysfunction drugs (EDDs)	Phosphodiesterase type 5 (PDE5) inhibitors	Viagra, caverject, cialis, kamagra	swallowed, sublingual	• Increase blood flow to penis resulting in erection • Effects last 15 minutes-2 hours • Health risks: headache; vision impairment and hearing loss; prolonged erection; severe low blood pressure; myocardial infarction, stoke	• High interaction with all PI's • Co-administration with amyl nitrites can lead to fatal cardiovascular events
Gammahydroxybutrate (GHB), gammabutyrolactone (GBL)	Depressant/ dissociative anaesthetic	Liquid ecstasy, G	swallowed (as liquid), injected	• Euphoria-inducing; increased sex drive, decreased inhibitions • Rapid onset (<20mins) and effects last up to 4 hours • Health risks: can cause coma-like state if combined with alcohol; narrow safety index: small increase in dosage can result in GHB toxicity (bradychardia, coma, respiratory depression)	• Associated with sexual assault/rape • Potential interaction with ATV/r, DRV/r, LPV/r, single-tablet regimens • High potential for dependence (and withdrawal syndromes upon abrupt discontinuation)
Ketamine	Hallucinogen/ dissociative anaesthetic	K, special K	swallowed, snorted, smoked, injected intramuscularly	• Distortion of time and space, analgesia, hallucinations, euphoria • Rapid onset (<30mins) and last up to 3 hours • Health risks: panic attack, depression; memory impairment; catatonia and delirium("k-hole"); bladder/kidney ulcers	• Regular use can cause severe ulcerative cystitis • Potential interaction with ATV/r, DRV/r, LPV/r, EFV, ETV, NVP, single-tablet regimens
Lysergic acid diethylamide (LSD)	Hallucinogen	Acid, microdotblotter	swallowed (tablet or liquid or tab: square of blotted paper), injected	• Intensification of sensory input, feelings of floating and dissociation • Effects last up to 2 hours • Health risks: LSD toxicity (paranoia, psychosis, flashbacks)	• Low potential for addiction • Potential interaction with ATV/r, DRV/r, LPV/r, single-tablet regimens
Mephedrone	Stimulant	Meph, M-CAT, bath salts, meow meow	snorted, ingested	• Increased motor activity, stimulated mood, sexual disinhibition • Rapid onset (15-45 minutes) and effects last 2-5 hours • Health risks: convulsions; mephedrone toxicity (agitation, tachycardia, hypertension)	• Potential interaction with ATV/r, DRV/r, LPV/r

Continued on next page

Name	Chemical classification	Related terms	Mode of administration	Behavioural and physiological effects	Drug-drug interactions (DDIs)/other health concerns
Methamphetamine	Stimulant	Crystal meth, yaba, Tina, ice	swallowed, snorted, injected, smoked, rectal suppository, rubbed into gums	• Increased energy, alertness, decreased appetite; decreased inhibition, increased sexual confindence • Effects last 10-12 hours • Health risks: severe dental disease; insomnia; psychosis; stroke, damage to lungs and kindneys; excessive skin picking and scratching	• Potential interactions with ATV/r, DRV/r, LPV/r predicted to be of of weak intensity • Methamphetamine can mask signs of alcohol intoxication (sedation) leading to increased consumption of alcohol
Opioids	Depressant/ analgesic	Codeine, morphine, heroin (china white, smack), opium, oxycodone	ingested, injected, smoked, snorted, suppository	• Euphoria; warm flushing of skin; relaxation and drowsiness; analgesia • Rapid onset (≤5 minutes) and lasting 3-7 hours • Health risks: constipation; collapsed veins; respiratory depression; endocarditis; pneumonia	•Highly physically dependent and addictive • Potential interaction between codeine, morphine, oxycodone and ATV/r, DRV/r, LPV/r • Potential interaction between heroin and ATV/r, DRV/r, LPV/r, EFV, ETV predicted to be of weak intensity

PI: protease inhibitor; ATV/r: ritonavir-boosted atazanavir; DRV/r: ritonavir-boosted darunavir; EFV: efavirenz; ETV: etravirine; EVG/c: cobicistat-boosted elvitegravir; FTC: emtricitabine; NVP: nevirapine; SQV/r: ritonavir boosted-Saquinair; TDF: tenofovir; single-tablet regimens containing EVG/cobicistat/FTC/TDF

6.2.3 Prevalence of recreational drug use in the UK

6.2.3.1 General UK population

Information on extent and trends in drug use is available from the Crime Survey for England and Wales (CSEW), an annual, nationally representative sample of individuals aged 16-59 years resident in England and Wales.[277] In 2014/2015, one in 12 adults had used recreational drugs in the past year and one in 20 used a drug in the past month. The most commonly used drugs in the past year were cannabis (6.5%), cocaine (2.2%), and ecstasy (1.5%). Polydrug use remains an understudied phenomenon in the general population in the UK.

6.2.3.2 All MSM

Research conducted over the past twenty years has demonstrated that a higher proportion of MSM in the UK and abroad use recreational drugs compared to age-comparable non-MSM populations.[278–282] Population-wide surveys, such as the CSEW, do not routinely include questions on sexual orientation and so cannot monitor drug use among MSM as a distinct group. Hence, data on drug use among MSM is derived from studies of convenience samples (online, gyms, clinics, nightclubs, sex-on-premises venues). Patterns and prevalence of drug use among MSM have been comprehensively documented in literature from Australia and the USA, showing that recreational drug use is common.[283–288] In the UK, various estimates have been reported; prevalence of any drug use in the past year was 55.6% among all MSM in the 2002 London Gyms study[289] (N=653) and 59.9% among MSM in the 2005 GMSS[290] (N=3913). Prevalence of drug use in the past month was 40% among MSM surveyed in the Midlands[291] between 2009 and 2011 (N=1843), compared to 16.3% in Brighton, 13.2% in London, and 4.1% in the rest of the UK in the 2010 European MSM Internet Survey (EMIS)[292] (N=13983). The most commonly used drugs in the GMSS (2005, 2007, and 2010) have consistently been shown to be nitrites, cannabis, cocaine, and ecstasy (all prevalence ≥20% in the past year).[260,290,292]

Approximately 5% of MSM from the UK partaking in EMIS 2010 reported ever having injected drugs.[293] In the most recent wave of the GMSS (2014), 1.8% of over 15000 MSM indicated injection drug use (IDU) other than anabolic steroids or prescribed medicines in the last 12 months.[144] Among them, 1.8% had injected GHB/GBL, 2.8% heroin, 6.4% amphetamine, 9.9% ketamine, 59.9% crystal methamphetamine, and 60.6% mephedrone.

6.2.3.3 HIV-diagnosed MSM

MSM are not a homogeneous group with regards to recreational drug use. Studies from the USA and Australia show that drug use is more prevalent among HIV-positive compared to HIV-negative men.[282,287,294–299] There is a limited number of studies on drug use conducted among large representative samples of HIV-diagnosed MSM in the UK, although cross-sectional community-based surveys of MSM of mixed HIV-serostatus (such as the GMSS and GMSHS, see Table 2.2) as well as nationally representative surveys (such as Natsal-3) also corroborate the difference in prevalence by HIV-serostatus, with higher drug use apparent among HIV-positive MSM.[281,300–302] Most venue and internet-

based behavioural surveys, however, report on drug use as a secondary finding with limited information on the types, combinations, and context of drugs used.[303] Findings from such samples are also likely to have limited generalizability.

Behavioural surveys recruiting HIV-diagnosed MSM from outpatient clinics are more representative of all MSM living with HIV, and are summarised in Table 6.2. It can be seen that prevalence of drug use was high (above 50%) in all studies. In terms of the four UK studies, prevalence of any drug use was: in the past 12 months: 53.6% in the 2002 'London Gyms' study[289] and 55.8% in the GMSS; in the past three months: 46.8% in the 2004 Internet & HIV study[151] and 71.4% in the 2004 Guys and St.Thomas' clinic.[304] Prevalence estimates of specific drugs used also varies and direct comparisons are not always possible due to different recall periods. (Table 6.2) Of note, none of the studies reviewed in Table 6.2 (conducted in high-income countries between 1996 and 2016) have examined the prevalence of mephedrone use among HIV-diagnosed MSM.

Injection drug use among HIV-diagnosed MSM is also understudied in the UK. (Table 6.2) Of the almost 2% of MSM who injected drugs in the past 12 months in the 2014 GMSS, 11.3% were HIV-diagnosed MSM, and 14.4% were HIV-diagnosed MSM living in London (0.3% of all GMSS participants).[144] By comparison, in the 2002 'London Gyms' study prevalence of IDU in the past year was 1.3% among HIV-diagnosed clinic attendees.[289] There is some evidence of a significant increase in the prevalence of IDU among HIV-diagnosed MSM in the Sydney Gay Community Periodic Surveys (from 14.2% in the past six months in 2011 to 20.2% in 2015), but it is unclear whether this is also the case in the UK.[287]

6.2.4 Prevalence of polydrug use among HIV-diagnosed MSM

Simultaneous polydrug use (see section 6.2.2) is generally understudied due to difficulties in data collection and accuracy. More commonly, polydrug use is classified as consecutive use of a number of substances (usually two or more) over a period of time.[265,289,290] Polydrug use is prevalent in cross-sectional surveys of MSM attending clubs in the USA[265,305,306] but evidence on its extent among MSM in the UK is limited. (Table 6.2) Among recreational drug users in the 2005 GMSS, polydrug use was the norm; of the 9% of MSM who used ketamine in the past year, 89% also used ecstasy, 80% cocaine, and 23% also used crystal methamphetamine.[281,290] In the earlier 'London Gyms' study, the most common combination of drugs in the past three months among HIV-diagnosed clinic outpatient MSM was ecstasy and cocaine, followed by ketamine and ecstasy.[289]

As in the case of recreational drug use, alcohol use is more prevalent among MSM compared to non-MSM populations, and among HIV-positive people compared to HIV-negative.[301,307] The prevalence of harmful/hazardous alcohol use among HIV-diagnosed MSM is understudied, especially among those who also use recreational drugs.

Table 6.2: Prevalence of recreational drugs used in studies of HIV-diagnosed MSM in high-income countries (1996-2016)*

Study/ Recruitment period/ Country			N of HIV+ MSM	Recall period	Prevalence (% of HIV-diagnosed MSM participants)												
					Any	Cannabis	Cocaine	Ecstasy	EDDs	GHB/GBL	Ketamine	LSD	Meth	Nitrites	Opioids	IDU	Polydrug use (%)
MACS[308]	1998-2008	USA	57	Past 6 months	66.7	-	-	-	14.0	-	-	-	-	45.6	-	-	≥2 drugs:21.0
SUMIT [309,310]	2000-01	USA	1168	Past 3 months	-	-	-	-	12.3	-	-	-	-	-	-	-	≥2 drugs:9.1 ≥3 drugs:2.2
Project BUMPS[311]	2001-02	USA	166	Past 4 months	-	-	84.9	60.8	-	24.7	46.4	-	67.5	-	-	-	-
London Gyms[289,312]	2002-03	UK	116 (gyms)	Past 12 months	72.4	-	-	-	-	-	-	-	-	-	-	-	-
				≥1 x week	-	-	5.2	5.2	-	-	7.8	-	1.7	-	-	-	-
				≤2 x month	-	-	17.2	27.6	-	-	19.0	-	7.8	-	-	-	-
			338 (clinic)	Past 12 months	53.6	-	-	-	-	-	-	-	-	-	-	1.3	-
				≥1 x week	-	-	3.4	2.8	-	-	2.8	-	0.5	-	-	-	-
				≤2 x month	-	-	14.4	14.4	-	-	10.1	-	3.1	-	-	-	-
Internet & HIV[151]	2002-03	UK	547	Past 3 months	46.8	-	-	-	-	-	-	-	-	-	-	-	-
Guys & St.Thomas' clinic[304]	2002-04	UK	98	Past 3 months	71.4	-	-	-	-	-	42.9	-	-	-	-	-	-
Sex and Love Project[297]	2002-07	USA	743	Past 3 months	-	-	15.8	11.5	-	7.0	7.4	-	15.4	38.9	-	-	≥2 drugs:13.4
Positive Health[313]	2004-05	Australia	274	Past 6 months: at least monthly	83.9	12.0	1.5	1.8	-	1.1	-	0.7	5.5	17.2	1.8	4.4	-
Positive Connections[314]	2004-09	USA	669	Past 3 months	-	41.0	30.0	-	26.0	-	-	-	-	32.0	-	-	-
GMSS[290,315]	2005	UK	507	Past 12 months	55.8	-	50.0	49.4	-	19.0	41.3	11.0	-	60.8	-	-	-
German HIV clinics[316]	2009-10	Germany	445	≤3 x week	-	11.0	2.0	-	9.4	-	-	1.8	0.7	21.4	0	-	-
				>3 x week	-	8.1	1.3	-	2.0	-	-	0	0	5.0	1.1	-	-
GCPS Sydney[287]	2011	Australia	352	Past 6 months	-	41.2	-	32.1	40.6	-	-	-	27.6	52.3	-	14.2	≥3 drugs:44.0

EDD: Erectile Dysfunction proprietary drugs such as Viagra(sildenafil), Cialis(tadalafil), or similar; GCPS: Gay Community Periodic Survey; GMSS: Gay Men's Sex Survey; IDU: injection drug use; LSD: lysergic acid diethylamide; MACS: Multicenter AIDS Cohort Study; Meth: methamphetamine; Nitrites: poppers; Opioids: codeine, heroin, methadone, morphine, opium; Polydrug use refers to use in respective recall period.SUMIT: Seropositive Urban Men's Intervention Trial. Note no information on mephedrone in studies included.

* Studies have been described in literature review (section 2.5)

6.2.4.1 Recreational drug use and HIV: drug-drug interactions (DDIs)

In the case of HIV, drug use (and polydrug use) further presents issues of interactions with ART leading to toxicity[317] and potential neurological and cardiovascular consequences.[318] (I have previously published results on the prevalence of possible DDIs among ASTRA MSM who use recreational drugs, according to type of ART regimen.[319]) The primary mechanism of ART elimination is mediated through the hepatic cytochrome p450 (CYP) complex of proteins. This pathway is also shared by recreational drugs, which can either induce CYP activity, leading to decrease of ART concentration to sub-therapeutic levels, or inhibit it, resulting in toxic drug accumulation.[320] Not all drugs have high potential for harm arising from DDIs; potential for interaction of ART is lowest with alcohol, cannabis, opioids, and nitrites; moderate with methamphetamine, ecstasy, and mephedrone; and highest between protease inhibitors, EDDs, ketamine.[321] Despite a substantial increase in the number of GHB-associated deaths in London between 2010 and 2015 (n=61, a third of whom were HIV-positive)[322], the potential for interaction between GHB and ART remains unknown.

6.2.5 Factors associated with recreational drug use among HIV-diagnosed MSM

6.2.5.1 Socio-demographic factors

Few consistent associations between socio-demographic characteristics and drug use have been shown across different studies. There is some evidence that certain drugs are more commonly used by different socio-demographic sub-groups, and therefore results may vary according to study location, recruitment, and sample. The most consistent finding relates to age; a number of studies have found that, among HIV-diagnosed MSM, younger age is associated with higher prevalence of any recreational drug[292,323,324] and polydrug use.[305] However, specific drugs may be more commonly used by MSM of different age groups. For HIV-diagnosed MSM in Project BUMPS (N=166), a US cohort study of MSM using 'club drugs' recruited from gay venues and websites, younger age (<30 years) was significantly associated with using GHB and/or ketamine, while older age (≥30 years) was associated with using cocaine and/or methamphetamine.[311] In addition, men aged 30-39 were more likely to use ecstasy compared to those in their 20's, but not compared to those over 40 years.[311] In the SUMIT trial (see Table 2.2), MSM who were older (>45 years) were more likely to use Viagra.[309]

There is mixed evidence on patterns of drug use by race/ethnicity. For example, in the US Positive Connections study[314] (see Table 6.2), white HIV-diagnosed MSM were more likely to report use of nitrites in the past three months compared to black MSM, but the pattern was reversed for all other drugs. Other studies, including the SUMIT trial,[325] have not found any association between ethnicity and drug use.[323,326]

Three studies showed that higher educational attainment was associated with any drug use (specifically with ecstasy and EDDs) in unadjusted analyses,[290,309,310,314] while four other studies found no significant association after adjustment for confounders.[323–325,327,328] Another US study of 261 HIV-diagnosed MSM (EDGE Project)[329,330] enrolled in a sexual risk reduction intervention for active methamphetamine users

found that 'heavy' polydrug users (using methamphetamine, cocaine, heroin, hallucinogens, and ketamine in the past two months) were less educated compared to 'light' polydrug users (using methamphetamine, cannabis, and nitrites). It might be expected that employment (and consequently, higher disposable income) is associated with recreational drug use; this was corroborated in the 2014 GMSS[327] as well as two earlier North American studies of HIV-diagnosed MSM[314,323] but not in the SUMIT trial.[309]

6.2.5.2 HIV-related factors

There is limited information on associations of HIV-related factors and recreational drug use. In the SUMIT trial, MSM who were diagnosed with HIV for longer were more likely to report anabolic steroid use; being on ART was also associated with use of Viagra or steroids.[310] However, results from this study are hard to interpret as no adjustment was conducted for participant's age. Project BUMPS did not find any association between length of time diagnosed with HIV and recreational drug use, despite adjustment for age.[311]

6.2.5.3 Lifestyle factors

Associations of alcohol misuse and recreational drugs are to be expected, as both frequently co-occur in the same social settings.[324,328,331,332] Although most HIV-diagnosed MSM report some recent alcohol use (79–89%), only a minority (8–16%) report frequent and heavy alcohol use.[288,333,334] The extent of hazardous/harmful alcohol use among HIV-diagnosed MSM in the UK is understudied, particularly among those who also use drugs.

6.2.6 Recreational drug use and sexual behaviour among HIV-diagnosed MSM

Cross-sectional studies from the USA and Australia document strong associations between drug use, CLS, and high number of partners among MSM, across all age groups and regardless of HIV-serostatus.[96,286,295,311,324,335,336] In prospective studies of HIV-negative MSM, use of nitrites (poppers), methamphetamine, and/or erectile dysfunction drugs (EDDs) has been significantly associated with HIV seroconversion, through their association with CLS-D.[308,337–340] Predictive mathematical models[338] and cohort studies[341,342] also show that recent use of methamphetamine is an independent predictor of HIV seroconversion. The association of drug use and CLS among HIV-diagnosed MSM could be causal or correlational.[294] (Further discussed in section 6.5.4)

While there are numerous studies on the association of recreational drug use and sexual behaviour among all MSM in high income countries, there are fewer studies among *HIV-diagnosed* MSM. In this population, a number of cross-sectional US studies have shown that use of crystal methamphetamine, GHB, and/or ketamine, are associated with CLS-D,[309,310,343,344] including insertive CLS-D.[286](Table 6.3) Baseline results from the START trial of over 2500 ART-naïve HIV-diagnosed MSM also showed significant associations of any drug use in the past month and reporting CLS-D, after adjustment for socio-demographic, lifestyle, and HIV-related factors.[156] In the 2002 'London Gyms' study,[289] HIV-diagnosed MSM recruited from clinics who used methamphetamine and/or EDDs reported significantly higher prevalence of CLS-D with casual partners compared to those who did not use any drug in the past

three months (p<0.001, unadjusted); this estimate however, was based on a limited sample size (≤50 MSM). There has since been little information on patterns of recreational drug use, the extent of polydrug use, or on any association of different drugs with types of CLS from large, representative samples of HIV-diagnosed MSM in the UK. Patterns of drug use may be changing, and there are no studies in the UK to date that examine the association of drug use and CLS-D with higher risk of HIV transmission.

6.2.7 **Emerging trends in recreational drug use**

Since 2013, health care services and community organisations in the UK have reported shifting trends in popularity and use of specific drugs among MSM,[345,346] suggesting, firstly, an increase in prevalence of 'club drug' use overall, and secondly, the emergence of 'chemsex', meaning sex between men that occurs under the influence of methamphetamine, mephedrone, and/or GHB/GBL.[259] These drugs are associated with increased feelings of sexual arousal, enabling sexual longevity, and high partner turnover. Evidence relating to the extent of chemsex use is limited to a qualitative report (2013) of 30 chemsex-using MSM (13 HIV-diagnosed) in South London[259]. The report suggested that chemsex occurs in a range of settings but most commonly in private homes and that polydrug use is the norm during chemsex. A third of men in this study had injected methamphetamine or mephedrone, and the majority of HIV-positive men reported chemsex in the context of predetermined decisions to have CLS with partners they believed were also HIV-positive. Therefore, it is unclear the extent to which chemsex use may be associated with HIV-transmission risk behaviour. Recent Public Health England investigations into outbreaks of other STIs (such as *S.flexneri* and *E.coli*) have also found that cases are more likely to be HIV-positive MSM who engaged in chemsex.[148,346–350] While there are reports from STI clinics and community organisations about the link between chemsex and CLS, there is no robust quantitative evidence to date.[351]

Table 6.3: Prevalence of condomless sex (CLS) among HIV-diagnosed MSM who use recreational drugs in studies from high-income countries (1996-2016)

Study /Location/Data collection period			Study setting and recruitment*	N HIV+ MSM	Recall period	Prevalence of recreational drug use (% of HIV+ MSM)	Prevalence of CLS (% of HIV+ MSM using drugs)
MACS [308]	USA	1998-2008	Ongoing prospective study of HIV seroconversion with biannual questionnaire. Here showing data for MSM who seroconverted only.	57	At current or previous 6-month visit	66.7%	42.1% of MSM who used any drug had any receptive CLS (12% had ≥5 receptive CLS partners)
SUMIT trial [309,310]	USA	2000-2001	Baseline results of multisite RCT on HIV-positive MSM. Here focus on MSM who used Viagra.	1168	Past 3 months	12.3% used Viagra	Of MSM who used Viagra: •34.3% had CLS-C insertive •26.1% had CLS-D insertive
London Gyms [289,312]	UK	2002-2003	Here showing data for HIV-diagnosed MSM recruited from HIV outpatient clinic only.	388	Past 12 months	• Any drug use: 53.6% • Methamphetamine use: 12.6%	Of MSM who used methamphetamine: • 34.7% had CLS-D • 18.4% had CLS-C Of MSM who used other drug but not methamphetamine: • 18.9% had CLS-D • 9.4% had CLS-C
Internet & HIV[139,151]	UK	2002-2003	Here showing combined data for HIV-diagnosed MSM recruited from HIV outpatient clinic and online.	547	Past 3 months	46.8%	Of MSM used any drug: • 7.0% had CLS-D • 12.1% had CLS-C
Guys & St.Thomas' clinic [352]	UK	2002-2004	MSM with primary HIV infection (positive test within 6 months of documented negative) recruited from sexual health services and enrolled in ART intervention.	98	Past 3 months (at 12 week follow-up after seroconversion)	71.4%	Of MSM used any drug: 19.4% had CLS-D with a regular partner and/or CLS with a casual partner
Positive Health[167,313]	Australia	2004	Observational cohort of HIV-diagnosed MSM recruited from gay community events, organisations, HIV clinics, online, with interviewer-administered questionnaire.	274	Less than monthly or at least monthly	83.9%	•41.2% of MSM who used any drug less than monthly had any CLS •25.8% of MSM used at least monthly had any CLS

Study /Location/Data collection period			Study setting and recruitment*	N HIV+ MSM	Recall period	Prevalence of recreational drug use (% of HIV+ MSM)	Prevalence of CLS (% of HIV+ MSM using drugs)
START trial [156]	International	2009-2013	ART-naïve HIV-diagnosed MSM enrolled in international RCT on deferred or immediate ART initiation. Results from MSM at baseline pre-randomisation survey across all recruitment regions.	2559	<1 day or ≥1 day per week in past month	• <1 day/week: 11.6% • ≥1 day/week: 3.1%	• Of MSM who used drugs <1 day/week 26.2% had CLS-D • Of MSM who used drugs ≥1 day/week 29.1% had CLS-D
Scotland GMSHS[301]	UK	2011	Anonymous self-completed questionnaire in gay commercial venues in 2 cities with oral fluid HIV antibody testing. Here showing results for MSM who tested HIV-positive.	24	Always or sometimes using drugs during CLS in past 12 months	-	54.2%

ART: antiretroviral therapy; CLS: condomless sex; CLS-D: CLS with HIV-serodifferent partners; CLS-C: CLS with HIV-seroconcordant partners; GMSHS: Gay Men's Sexual Health Survey; MACS: Multicenter AIDS Cohort Study; RCT: randomised controlled trial; START: Strategic Timing of AntiRetroviral Treatment; SUMIT: Seropositive Urban Men's Intervention Trial

*Studies described in literature review (section 2.5)

6.3 Methods

This chapter includes MSM participating in the ASTRA study who were diagnosed with HIV for ≥3 months (N=2189).

6.3.1 Recreational drug use

Participants were asked if they had used recreational drugs in the past three months and if so which ones, listing the following 18 drugs as phrased here; acid/LSD/magic mushrooms, anabolic steroids, cannabis (marijuana), cocaine (coke), crack, codeine, crystal meth (methamphetamine), ecstasy (E), GHB (liquid ecstasy), heroin, ketamine (K), Khat (chat), mephedrone, morphine, opium, poppers (amyl nitrites), speed (amphetamine), Viagra, and 'other (please specify)'.(Appendix I) The term opioid was used to combine heroin, morphine, and opium. Free-text responses in the 'other (please specify)' category included slang names or other proprietary medications; these were examined case-by-case and recoded to the above categories if applicable, as in Table 6.4. Other drugs used in the treatment of erectile dysfunction (ED) were combined with Viagra and classified as ED drugs (EDDs). Use of one or more of the following three drugs: methamphetamine, GHB/GBL, or mephedrone was defined as use of a 'chemsex-associated drug'.[259] Of note, the ASTRA questionnaire did not explicitly enquire about chemsex use (any of the three substances used before or during sex specifically), and so the term chemsex-'associated' drugs is used instead. Use of one or more of the following four drugs: GHB/GBL, mephedrone, ketamine, or ecstasy was defined as use of a 'club drug'. Polydrug use was assessed by the number of different drugs used during the previous three months.

Table 6.4: Coding of responses in 'other (please specify)' recreational drug use category (N=40)

Slang or proprietary name	Frequency	Recoded to drug category
Caverject, Cialis, Kamagra, or 'herbal Viagra'	12	ED drugs
DMT	1	Acid/LSD/magic mushrooms
GBL	2	GHB
'hello kitty'	1	Cocaine
MDMA or 'benzo fury'	11	Ecstasy
'meow meow', NRG, energy, or MCAT	4	Mephedrone
Methadone	2	Opioids
Methoxetamine, MXE, 'moxxy'	2	Ketamine
Poppers	3	Nitrites (poppers)
Not classifiable	2	-

ED drugs; erectile dysfunction

Participants were asked also whether they had injected recreational drugs in the past three months, and if so, whether they shared needles, syringes, or 'works' (cotton, cooker, spoon, etc.) with an HIV-serodifferent person after injecting themselves.

6.3.2 Other factors and sexual behaviours

All socio-demographic, psychological, other lifestyle, and HIV-related factors examined in this chapter have been defined in section 3.8. Sexual behaviours (including definitions of CLS variables) are defined in section 4.3.

6.3.3 Statistical analysis

The prevalence of any recreational drug use, use of 1, 2, 3, 4, ≥5 types of drugs, and injection drug use (IDU) was assessed in the past three months. Patterns of drug use were examined according to number of drugs used and injection drug status (whether injected drugs or not).

6.3.3.1 Factors associated with recreational drug use

Associations were examined of socio-demographic, psychological, lifestyle, and HIV-related factors with:

(i.) any recreational drug use in the past three months among all MSM;

(ii.) polydrug use (for the purposes of this analysis defined as use of ≥4 drugs versus 1-3 drugs) among MSM who used drugs in the past three months;

(iii.) use of chemsex-associated drugs (use of one or more of: GHB/GBL, mephedrone, or crystal methamphetamine versus use of any other drugs) among MSM who used drugs in the past three months.

Unadjusted and adjusted modified Poisson regression models were used with robust error variances. In multivariable analyses, two adjustment strategies were used (see section 3.9.5). Firstly, each factor was adjusted separately for core factors, and secondly, any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in the multivariable model in addition to clinic; correlated variables were assessed and excluded accordingly (specifics for each model are discussed in sections 6.4.2, 6.4.3.)

6.3.3.2 Association of recreational drug use with sexual behaviours

Associations were then examined, among all MSM, of recreational drug use, polydrug use (0, 1, 2, 3, 4, ≥5 drugs), and chemsex-associated drug use with the following sexual behaviours:

(i.) In the past three months: any anal or vaginal sex, condomless sex (CLS), CLS with HIV-seroconcordant partners (CLS-C), CLS with HIV-serodifferent partners (CLS-D), higher HIV risk CLS-D (CLS-D plus not on ART or latest study log-recorded VL>50c/mL, see section 5.3.1), self-reported other STI diagnosis, participation in group sex, use of the internet to find sex;

(ii.) In the past year: having 10 or more new sex partners;

(iii.) No recall period: low condom self-efficacy, difficulty negotiating condom, lower condom use with casual partners, and worry about HIV transmission (all defined in section 4.3).

As in section 6.3.3.1, unadjusted and adjusted modified Poisson regression was used with robust error variances. Models were adjusted for core factors. As some recreational drugs are reported to be used solely in a sexual context,[348,349] the analysis of associations of polydrug use and measures of condomless sex (any CLS, CLS-C, CLS-D, and higher HIV risk CLS-D) was repeated in the subgroup of MSM who reported any anal and/or vaginal sex in the past three months. In this analysis, models were adjusted for

core variables only; the model with higher HIV risk CLS-D as the dependent variable did not include adjustment for ART status.

Unadjusted multinomial logistic regression (MNL) was used to examine associations of recreational, polydrug, and chemsex-associated drug use with reporting different sexual behaviours according to the single four-category variable of sexual behaviour (see section 4.3.3). All MSM were classified into one of the following mutually exclusive groups based on sex in the past three months:

1. Condomless sex with HIV-serodifferent partners (CLS-D)
2. Condomless sex with HIV-seroconcordant partners only ('CLS-C without CLS-D')
3. Condom-protected sex only
4. No anal or vaginal sex

In examining associations with drug use variables, firstly, MSM who did not report any anal or vaginal sex (group 4) were the reference group, compared to each of the other three categories. Secondly, MSM who reported no anal or vaginal sex in the past three months were excluded, and MSM who had CLS-D (group 1), and those who had 'CLS-C without CLS-D' (group 2) were compared to those who had condom-protected sex only (group 3, used as the reference category).

In order to assess any differential effect of specific drugs on different types of CLS, associations were examined between use of particular drugs with any CLS-D, CLS-C, or higher HIV risk CLS-D among the subgroup of MSM who reported any anal and/or vaginal sex in the past three months. Modified Poisson models were used with adjustment for core factors. For each drug, the reference category was no recreational drug use, and the remaining two categories were use of; the specific drug, and of any other recreational drug.

In the last main analysis, the aim was to examine, among MSM who used recreational drugs, which drugs were more strongly associated with having CLS-C only (a proxy for HIV-serosorting) compared to having CLS-D. This analysis included only MSM who had CLS *and* used any recreational drug in the previous three months. MSM were thus classified into two mutually exclusive categories (either 'CLS-C without CLS-D' or CLS-D, the reference group). Unadjusted modified Poisson regression was used due to the smaller sample size.

6.3.3.3 Association of alcohol misuse, recreational drug use, and sexual behaviours

As alcohol is commonly used with recreational drugs, the aim of this analysis was to examine any independent associations between alcohol misuse and sexual behaviours (shown in section 6.3.3.2, (i)), accounting for recreational drug use. Two measures of problematic alcohol use were used: 'higher alcohol consumption' (defined as a score ≥6 on the first two questions of the WHO-AUDIT-C questionnaire[213]), and 'evidence of alcohol dependency' (defined as a score ≥2 on the CAGE questionnaire[353], see section 3.8.2 for both). For each measure of alcohol misuse, separate models were

conducted, firstly only adjusting for the alcohol measure and secondly, additionally adjusting for core factors plus recreational drug use in the past three months.

6.3.3.4 Association of recreational drug use, alcohol misuse, and ART outcomes

It was hypothesized that recreational drug use and alcohol misuse might impact adherence to ART, which in turn could lead to viral load (VL) non-suppression on ART. As this was the hypothesised direction of association, it was deemed appropriate to not include factors relating to treatment outcomes (such as non-adherence) when examining factors associated with drug use (as described in section 6.3.3.1), but rather to separately assess the association of drug use (as the independent variable) with ART adherence and VL non-suppression (as the dependent variables). This analysis examines, among MSM who were on ART only, associations of recreational drug use, polydrug use (1, 2-4, ≥5 drugs) in the past three months, higher alcohol consumption, evidence of alcohol dependency with:

(i.) Non-adherence to ART (missed ≥2 consecutive days of ART on ≥2 occasions in the past 3 months)

(ii.) VL non-suppression (study log-recorded VL>50c/mL among MSM who started ART ≥6 months ago)

Unadjusted and adjusted modified Poisson regression was used. Models were adjusted for core factors (as in section 6.3.3.1), excluding ART status.

6.3.3.5 Sensitivity analyses

In the first sensitivity analysis, the aim was to examine associations of recreational drug use and sexual behaviours accounting for factors not already included in the set of core variables that were associated with CLS in earlier analyses (section 4.4.5), as these could be considered as potential confounding factors. These factors (defined in section 3.8) were: employment status (employed full or part-time, unemployed or other), education (no qualifications or up to A levels, university degree or higher), and identifying as religious (yes, no). Associations between polydrug use, chemsex-associated drug use and measures of sexual behaviour (described in section 6.3.3.2) were examined in two modified Poisson regression models adjusted for core factors, clinic and:

1. employment plus religion
2. education plus religion

Employment and education were not mutually adjusted for in a single model as they are collinear. The second sensitivity analysis aimed at allowing for valid comparisons of the magnitude of associations of a single independent variable (polydrug use) across a number of dependent binary variables of varying prevalence (CLS, CLS-D, CLS-C, higher HIV risk CLS-D). (Discussed in section 3.9.4.3) This was done by presenting associations of polydrug use and sexual behaviours as odds ratios rather than prevalence ratios using logistic regression with adjustment for core variables only.

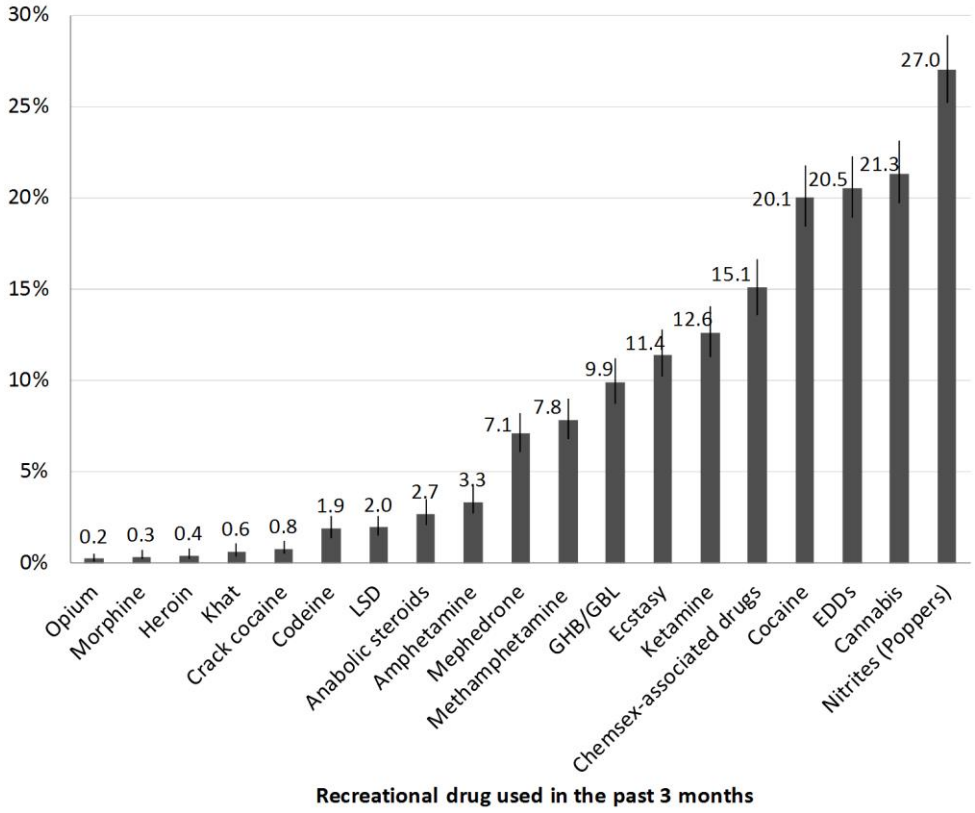
6.4 Results

6.4.1 Prevalence of recreational drug use

Among 2189 MSM who were diagnosed with HIV for ≥3 months, the prevalence of any recreational drug use was 50.8% (95%CI 48.7-52.8%, n=1111) in the previous three months.

The most commonly used drugs (prevalence ≥10%) were nitrites (27.0%, 95%CI 25.2-28.9%), cannabis (21.3%, 19.7-23.1%), erectile dysfunction drugs, EDDs, (20.5%, 18.9-22.3%), cocaine (20.1%, 18.4-21.8%), ketamine (12.6%, 11.3-14.1%), ecstasy (11.4%, 10.2-12.8%), and GHB/GBL (9.9%, 8.7-11.2%). (Figure 6.1) A total of 330 MSM (15.1%, 13.6-16.6%) had used any chemsex-associated drug (methamphetamine, mephedrone, and/or GHB/GBL) in the previous three months. When excluding 831 MSM who used nitrites and EDDs (which are not illegal in the UK), the prevalence of any recreational drug use in the past three months was 38.0% (36.0-40.0%).

Figure 6.1: Prevalence of recreational drug use in the past three months (N=2189 HIV-diagnosed MSM)



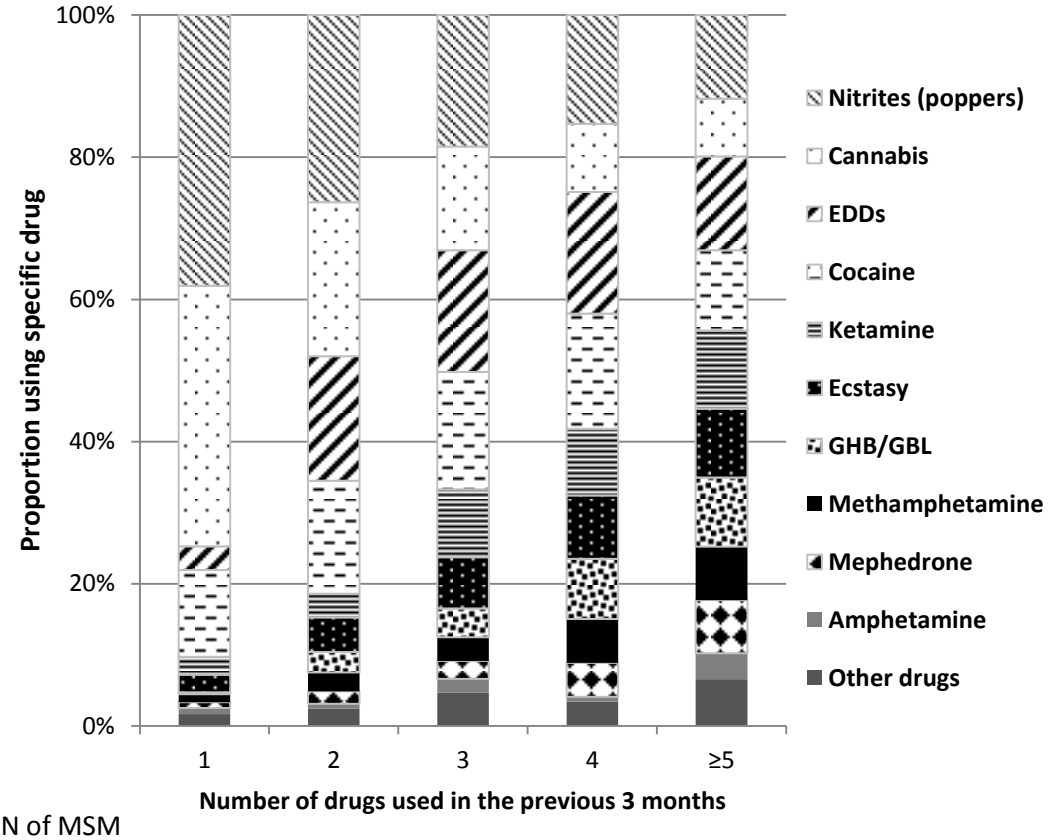
Bars and lines represent prevalence with 95% CI
Chemsex-associated drugs include GHB/GBL, mephedrone, and/or methamphetamine; EDD: erectile dysfunction drugs

6.4.1.1 Polydrug use

Among 1111 MSM who had used drugs in the previous three months, 363 (32.7%, 95%CI 30.0-35.5%) used one drug, 229 (20.6%, 18.3-23.1%) used two, 173 (15.6%, 13.6-17.8%) used three, 111 (10.0%, 8.4-11.9%) used four, and 235 (21.2%, 18.8-23.7%) used five or more. Figure 6.2 shows the proportion of responses for each drug used as a percentage of the total number of responses, according to number of

drugs taken in the previous three months. Among MSM who used only one drug in the past three months, 38.1% used nitrites (poppers), 36.7% cannabis, and 12.2% cocaine only. Of the recreational drugs reported among MSM who used two drugs, 26.3% of responses were for nitrites, 21.7% were for cannabis, 17.5% for EDDs, and 15.9% for cocaine. As the number of drugs taken increased, so did the proportion of responses for EDDs, chemsex-associated drugs, ketamine, and ecstasy. For example, among MSM using only one drug, 0.2% used GHB/GBL, whereas GHB/GBL accounted for 9.8% of responses among MSM using five or more drugs. Similarly, the corresponding percentages for ketamine were 2.5% and 11.0%, for ecstasy 2.5% and 9.7%, and for methamphetamine 1.1% and 7.5%.

Figure 6.2: Type of drug according to number of drugs used in the past three months among 1111 HIV-diagnosed MSM using one or more drugs.



N of MSM (N=1111)	363	229	173	111	235
N of responses (N=3241)	360	452	514	438	1477

Other drugs includes opium, morphine, heroin, khat, crack cocaine, codeine, LSD, and anabolic steroids; EDDs: erectile dysfunction drugs

6.4.1.2 Injection drug use

Injection drug use was reported by 66 MSM (3.0%, 95%CI 2.4-3.8%) in the past three months, of whom 4 (6.1%) reported sharing needles, syringes, or 'works' with an HIV-serodifferent person. Among 1111 MSM who used any drug in the past three months, use of specific drugs was compared between injection (n=66) and non-injection drug users (n=1045). (Table 6.5) MSM who reported IDU were more

likely to be polydrug users than MSM who reported non-injection drug use only (93.8% versus 65.7% used ≥4 drugs, p<0.001). Over 90% of injection drug users reported use of chemsex-associated drugs, compared to 12.8% of non-injection drug users. For example, methamphetamine was used by 84.6% of MSM who also injected any drugs compared to 11.1% of MSM who did not inject any drugs (p<0.001). Use of each specific drug was significantly higher among injection compared to non-injection drug users, with the exception of amphetamines and nitrites (p>0.05).

Table 6.5: Use of specific recreational drugs among injection and non-injection drug users in the previous three months (N=1111)

		Injection drug use *		
		Yes (n=66)	No (n=1045)	
Use in the past three months	**row N**	**col %**	**col %**	**p-value**
Nitrites (Poppers)	592	46.2	53.7	0.235
EDDs	449	76.9	38.1	<0.001
Cocaine	439	55.4	38.5	0.007
Chemsex-associated drugs	330	90.8	25.9	<0.001
Ketamine	276	46.2	23.5	<0.001
GHB/GBL	216	64.6	16.6	<0.001
Methamphetamine	171	84.6	11.1	<0.001
Mephedrone	155	32.3	12.8	<0.001
Amphetamine	73	7.7	6.5	0.707
Anabolic steroids	59	15.4	4.7	<0.001
Crack cocaine	17	6.2	1.2	0.001 (F)
Opioids	53	24.6	3.5	<0.001
Polydrug use	346	75.4	28.4	<0.001

p-values by chi-squared test or Fisher's exact (F)
**Note: not showing injection of specific drug. P-values for each drug shown for comparison of injection versus non-injection drug users; Chemsex-associated drugs: mephedrone, GHB/GBL, and/or methamphetamine; EDDs: erectile dysfunction drugs; Opioids: opium, morphine, heroin, codeine. Polydrug use: ≥4 recreational drugs in the previous 3 months.*

6.4.2 Factors associated with recreational drug use

6.4.2.1 Any recreational drug use

Table 6.6 shows the associations of socio-demographic, psychological, lifestyle, and HIV-related factors with any recreational drug use in the past three months. Although prevalence of drug use was high across most demographic groups, in unadjusted analysis recreational drug use was strongly associated with younger age, more recent HIV diagnosis, not identifying with a religion, being employed, evidence of harmful alcohol drinking, having an HIV-positive stable partner, and not being on ART. Drug use was not significantly associated with ethnicity, place of birth, education, financial hardship, social support, depression, or anxiety.

In the first multivariable analyses (models 1, Table 6.6), each factor was adjusted for core variables in a separate model. The following factors remained associated with recreational drug use (p<0.05) with little or no attenuation in magnitude of associations: younger age (a significant inverse trend was observed with lower drug use prevalence at older ages, such that MSM under 30 years had more than twice the prevalence of drug use compared to those 60 or older), not being religious, higher alcohol

consumption, alcohol dependency, and having an HIV-positive stable partner; MSM who had an HIV-serodifferent stable partner and those who did not have a stable partner had approximately 20% and 10% lower prevalence of recreational drug use respectively compared to MSM with an HIV-positive stable partner. Associations with shorter time since HIV diagnosis, employment, and not being on ART were not significant in the core-adjusted models, primarily due to adjustment for age.

In the second multivariable model, any factor with p<0.10 at unadjusted analysis was a candidate for inclusion in the multivariable model, in addition to clinic. (model 2, Table 6.6) These were: age, time since HIV diagnosis, religion, employment, higher alcohol consumption, stable partner status, ART status, and ART status/self-reported VL. As the last two variables included categories of the other, ART status was excluded from the model. After mutual adjustment, while some associations were slightly attenuated, the same factors as in model 1 remained significantly associated with recreational drug use.

6.4.2.2 Polydrug use

Associations were examined of socio-demographic, psychological, lifestyle, HIV-related factors and polydrug use (use of 4 or more drugs compared to 1-3 drugs) among 1111 MSM who used drugs in the previous three months. (Table 6.7) In unadjusted analysis, polydrug use was more prevalent among MSM who were younger, recently diagnosed, did not identify as religious, had a university degree, were employed, had an HIV-positive stable partner, and were not on ART.

After adjustment for core factors (models 1, Table 6.7), the following factors remained significantly associated with polydrug use with some attenuation (p<0.05): younger age (with prevalence particularly elevated in the <30 year age group), university degree, employment, and having an HIV-positive stable partner. Time since HIV diagnosis, ART status, and ART status/self-reported VL were no longer significantly associated with polydrug use in multivariable analysis. There remained a weak association between not being religious and polydrug use (p=0.07).

In model 2, the following factors were candidates for inclusion in the multivariable model in addition to clinic (model 2, Table 6.7): age, time since HIV diagnosis, religion, education, employment, stable partner status, ART status, and ART status/self-reported VL. Education and employment were highly correlated and so only one could be retained in the model; it was deemed more relevant in this case to examine the effect of early socio-economic factors, such as education, on polydrug use. ART status was excluded from the model as it was included in the ART status/self-reported VL variable. Hence, after adjustment for age, time since HIV-diagnosis, religion, education, stable partner status, ART status/self-reported VL, and clinic, the same variables were found to be significantly associated with polydrug use as in model 1 (p<0.05). The prevalence of polydrug use was two-fold higher among MSM under 30 years compared to those 60 or older, 22% higher in relative terms among those with a university degree compared to those with lower qualifications, and approximately 50% higher in relative terms among MSM with a HIV-positive stable partner compared to those with an HIV-serodifferent partner. There was some evidence of an association of not being religious and polydrug use (p=0.07).

Table 6.6: Association of socio-demographic, psychological, lifestyle, and HIV-related factors with recreational drug use in the previous three months (n/N=1111/2189 HIV-diagnosed MSM)

	Recreational drug use (n/N=1111/2189)							
	n used drugs/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=2167)								
<30	61/96	63.5	2.2 [1.6,2.9]		2.1 [1.6,2.9]		2.1 [1.5,2.8]	
30-39	300/487	61.6	2.1 [1.6,2.8]		2.1 [1.6,2.8]		2.0 [1.5,2.7]	
40-49	484/929	52.1	1.8 [1.4,2.3]		1.8 [1.4,2.3]		1.7 [1.3,2.3]	
50-59	210/503	41.7	1.4 [1.1,1.9]		1.4 [1.1,1.9]		1.4 [1.0,1.8]	
≥60	44/152	28.9	1.0	<0.001(T)	1.0	<0.001(T)	1.0	<0.001(T)
Ethnicity (N=2154)								
White	984/1928	51.0	1.0		1.0		-	
All other (black, Asian, Mixed, other)	109/226	48.2	0.9 [0.8,1.1]	0.435	0.9 [0.8,1.0]	0.189		
Years since HIV diagnosis (N=2177)								
≤2	111/184	60.3	1.0		1.0		1.0	
2-5	183/338	54.1	0.9 [0.8,1.0]		0.9 [0.8,1.1]		0.9 [0.8,1.0]	
5-10	275/550	50.0	0.8 [0.7,1.0]		0.9 [0.7,1.0]		0.8 [0.7,1.0]	
10-15	230/461	49.9	0.8 [0.7,1.0]		0.9 [0.8,1.1]		0.9 [0.8,1.0]	
>15	304/644	47.2	0.8 [0.7,0.9]	0.001(T)	0.9 [0.8,1.1]	0.827(T)	0.9 [0.8,1.1]	0.951(T)
Place of birth (N=2189)								
UK	762/1502	50.7	1.0		1.0			
Outside the UK	349/687	50.8	1.0 [0.9,1.1]	0.976	1.0 [0.9,1.1]	0.378	-	
Religious (N=2152)								
Yes	414/919	45.0	1.0		1.0		1.0	
No	679/1233	55.1	1.2 [1.1,1.3]	<0.001	1.2 [1.1,1.3]	<0.001	1.1 [1.0,1.2]	0.004
Education (N=2149)								
University degree or above	480/950	50.5	1.0		1.0			
No qualifications or up to A levels	615/1199	51.3	1.0 [0.9,1.1]	0.724	1.0 [0.9,1.1]	0.588	-	

	Recreational drug use (n/N=1111/2189)							
	n used drugs/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Employment (N=2142)								
Employed	700/1318	44.3	1.0		1.0		1.0	
Unemployed or other(carer, student, retired)	389/824	39.9	0.9 [0.8,1.0]	0.011	1.0 [0.9,1.1]	0.822	1.0 [0.9,1.1]	0.582
Money for basic needs (N=2158)								
Always	560/1114	50.3	1.0		1.0			
Mostly	302/596	50.7	1.0 [0.9,1.1]		1.0 [0.9,1.1]			
Sometimes	137/275	49.8	1.0 [0.9,1.1]		1.0 [0.8,1.1]		-	
Never	100/173	57.8	1.1 [1.0,1.3]	0.198(T)	1.1 [1.0,1.3]	0.415(T)		
Social support (N=2170) ‡								
High	640/1286	49.8	1.0		1.0			
Medium	349/666	52.4	1.1 [1.0,1.2]		1.0 [0.9,1.1]		-	
Low	118/218	54.1	1.1 [1.0,1.2]	0.138(T)	1.1 [1.0,1.3]	0.126(T)		
Depression symptoms (N=2189) ‡								
No	793/1590	49.9	1.0		1.0		-	
Yes	318/599	53.1	1.1 [1.0,1.2]	0.174	1.1 [1.0,1.2]	0.227		
Anxiety symptoms (N=2189) ‡								
No	491/1110	44.2	1.0		1.0		-	
Yes	109/263	41.4	1.0 [0.9,1.1]	0.678	0.9 [0.8,1.1]	0.832		
Higher alcohol consumption(N=2189) ‡								
No	898/1823	49.3	1.0		1.0		1.0	
Yes	213/366	58.2	1.2 [1.1,1.3]	0.001	1.2 [1.1,1.3]	0.002	1.2 [1.1,1.3]	0.003
Evidence of alcohol dependency (N=2188) ‡								
No	869/1768	49.2	1.0		1.0		-	
Yes	241/420	57.4	1.2 [1.0,1.2]	0.001	1.1 [1.0,1.2]	0.009		

	Recreational drug use (n/N=1111/2189)							
	n used drugs/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Stable partner's HIV-serostatus (N=2189)								
HIV-positive	294/510	57.6	1.0		1.0		1.0	
HIV-negative or unknown status	314/694	45.2	0.8 [0.7,0.9]		0.8 [0.7,0.9]		0.8 [0.7,0.9]	
No stable partner	503/985	51.1	0.9 [0.8,1.0]	<0.001	0.9 [0.8,1.0]	0.001	0.9 [0.8,1.0]	0.002
ART status (N=2178)								
On ART	941/1888	49.8	1.0		1.0		-	
Not on ART	167/290	57.6	1.2 [1.0,1.3]	0.009	1.0 [0.9,1.2]	0.682		
ART status/self-reported VL (N=2143)								
On ART, reports undetectable VL	770/1568	49.1	1.0		1.0		1.0	
On ART, does not report undetectable VL†	155/285	54.4	1.1 [1.0,1.2]		1.0 [0.9,1.2]		1.1 [0.9,1.2]	
Not on ART	167/290	57.6	1.2 [1.0,1.3]	0.010	1.0 [0.9,1.2]	0.788	1.0 [0.9,1.1]	0.564

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, ART status. Denominators vary due to missing data in each model.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic. In both cases, model for 'ART status/self-reported VL' omits variable on ART due to collinearity. †Self-reported viral load (VL)>50c/mL or "don't know"; Alcohol consumption by WHO-AUDIT-C, alcohol dependency by CAGE questionnaire*

‡ For variable definitions see section 3.8

Table 6.7: Association of socio-demographic, psychological, lifestyle, and HIV-related factors with polydrug use (≥4 drugs versus 1-3 drugs) in the previous three months (N=1111 HIV-diagnosed MSM used drugs)

	Polydrug use (n/N=346/1111)							
	polydrug use/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=1099)								
<30	34/61	55.7	2.0 [1.2,3.5]		1.8 [1.1,3.2]		2.0 [1.1,3.7]	
30-39	104/300	34.7	1.3 [0.8,2.1]		1.2 [0.7,2.1]		1.2 [0.7,2.2]	
40-49	143/484	29.5	1.1 [0.7,1.8]		1.1 [0.7,1.8]		1.2 [0.7,2.0]	
50-59	50/210	23.8	0.9 [0.5,1.5]		0.9 [0.5,1.5]		0.9 [0.5,1.7]	
≥60	12/44	27.3	1.0	<0.001(T)	1.0	0.002(T)	1.0	0.002(T)
Ethnicity (N=1093)								
White	303/984	30.8	1.0		1.0		-	
All other (black, Asian, Mixed, other)	37/109	33.9	1.1 [0.8,1.5]	0.492	1.1 [0.8,1.4]	0.583		
Years since HIV diagnosis (N=1103)								
≤2	43/111	38.7	1.0		1.0		1.0	
2-5	67/183	36.6	0.9 [0.7,1.3]		1.0 [0.7,1.3]		0.9 [0.7,1.2]	
5-10	87/275	31.6	0.8 [0.6,1.1]		0.9 [0.7,1.2]		0.9 [0.6,1.2]	
10-15	59/230	25.7	0.7 [0.5,0.9]		0.8 [0.6,1.1]		0.7 [0.5,1.0]	
>15	87/304	28.6	0.7 [0.6,1.0]	0.007(T)	0.9 [0.7,1.3]	0.421(T)	0.9 [0.6,1.2]	0.309(T)
Place of birth (N=1111)								
UK	234/762	30.7	1.0		1.0			
Outside the UK	112/687	32.1	1.0 [0.9,1.3]	0.643	1.0 [0.8,1.2]	0.973	-	
Religious (N=1093)								
Yes	116/414	28.0	1.0		1.0		1.0	
No	226/679	33.3	1.2 [1.0,1.4]	0.072	1.2 [1.0,1.5]	0.066	1.2 [1.0,1.4]	0.075
Education (N=1095)								
University degree or above	171/480	35.6	1.0		1.0		1.0	
No qualifications or up to A levels	171/615	27.8	0.8 [0.7,0.9]	0.006	0.8 [0.6,0.9]	0.004	0.8 [0.7,1.0]	0.004

	Polydrug use (n/N=346/1111)							
	polydrug use/N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Employment (N=1089)								
Employed	240/700	34.3	1.0		1.0		-	
Unemployed or other(carer, student, retired)	102/389	26.2	0.8 [0.6,0.9]	0.007	0.8 [0.7,1.0]	0.038		
Money for basic needs (N=1099)								
Always	189/560	33.8	1.0		1.0			
Mostly	82/302	27.2	0.8 [0.6,1.0]		0.8 [0.6,1.0]			
Sometimes	44/137	32.1	1.0 [0.7,1.2]		0.9 [0.7,1.2]		-	
Never	28/100	28.0	0.8 [0.6,1.2]	0.208(T)	0.8 [0.6,1.1]	0.129(T)		
Social support (N=1107) ‡								
High	203/640	31.7	1.0		1.0			
Medium	110/349	31.5	1.0 [0.8,1.2]		1.0 [0.8,1.2]		-	
Low	31/118	26.3	0.8 [0.6,1.1]	0.350(T)	0.8 [0.6,1.2]	0.367(T)		
Depression symptoms (N=1111) ‡								
No	245/793	30.9	1.0		1.0		-	
Yes	101/318	31.8	1.0 [0.8,1.2]	0.778	1.0 [0.8,1.2]	0.971		
Anxiety symptoms (N=1111) ‡								
No	273/880	31.0	1.0		1.0		-	
Yes	73/231	31.6	1.0 [0.8,1.3]	0.865	1.0 [0.8,1.2]	0.868		
Higher alcohol consumption (N=1111) ‡								
No	276/898	30.7	1.0		1.0		-	
Yes	70/213	32.9	1.1 [0.9,1.3]	0.543	1.1 [0.9,1.3]	0.494		
Evidence of alcohol dependency (N=1110) ‡								
No	278/869	32.0	1.0		1.0		-	
Yes	68/241	28.2	0.9 [0.7,1.1]	0.271	0.9 [0.7,1.1]	0.325		

	Polydrug use (n/N=346/1111)							
	polydrug use/N	**row %**	**unadjusted PR [95%CI]**	**p-value**	**Models 1: aPR [95%CI]**	**p-value**	**Model 2: aPR [95%CI]**	**p-value**
Stable partner's HIV-serostatus (N=1111)								
HIV-positive	114/294	38.8	1.0		1.0		1.0	
HIV-negative or unknown status	79/314	25.2	0.6 [0.5,0.8]		0.7 [0.5,0.9]		0.7 [0.5,0.9]	
No stable partner	153/503	30.4	0.8 [0.6,1.0]	0.001	0.8 [0.6,0.9]	0.003	0.8 [0.7,1.0]	0.005
ART status (N=1108)								
On ART	278/941	29.5	1.0		1.0		-	
Not on ART	66/167	39.5	1.3 [1.1,1.7]	0.007	1.1 [0.9,1.4]	0.478		
ART status/self-reported VL (N=1092)								
On ART, reports undetectable viral load	227/770	29.5	1.0		1.0		1.0	
On ART, does not report undetectable viral load[1]	45/155	29.0	1.0 [0.8,1.3]		0.9 [0.7,1.2]		1.0 [0.7,1.3]	
Not on ART	66/167	39.5	1.3 [1.1,1.7]	0.024	1.1 [0.8,1.4]	0.625	1.1 [0.8,1.4]	0.818

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression: ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, ART status. Denominators vary due to missing data in each model.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic. In both cases, model for 'ART status/self-reported VL' omits variable on ART due to collinearity. †Self-reported viral load (VL)>50c/mL or "don't know"; Alcohol consumption by WHO-AUDIT-C, alcohol dependency by CAGE questionnaire.*

‡ For variable definitions see section 3.8

6.4.2.3 Chemsex-associated drug use

Among 1111 MSM who used drugs in the previous three months, associations were examined of socio-demographic, psychological, lifestyle, HIV-related factors with chemsex-associated drug use (GHB/GBL, mephedrone, and/or crystal methamphetamine versus any other drug).(Table 6.8) In unadjusted analysis, chemsex-associated drug use was more prevalent among MSM who were younger (<30 years), diagnosed with HIV more recently (≤2 years), born outside the UK, university educated, employed, always had money for basic needs, had lower alcohol consumption, had an HIV-positive stable partner, and were not on ART. Ethnicity, being religious, social support, alcohol dependency, depression, anxiety were not associated with chemsex-associated use.

After adjustment for core factors (models 1, Table 6.8), the following factors remained independently associated with chemsex-related drug use ($p<0.05$): younger age (with a trend of decreasing prevalence of chemsex with older age), non-UK place of birth, university degree, employment, no financial hardship, and having an HIV-positive stable partner (to a lesser extent, those with no stable partner had higher prevalence of chemsex-associated drug use than those with an HIV-negative/unknown status stable partner). There was a weak suggestion that more recent time since HIV diagnosis was associated with chemsex-associated drug use ($p=0.07$). Associations with lower alcohol consumption and not being on ART did not remain after adjustment for core factors.

In model 2, the following factors were candidates for inclusion in the multivariable model ($p<0.10$ at unadjusted analysis): age, time since HIV diagnosis, place of birth, education, employment, money for basic needs, higher alcohol consumption, stable partner, ART status, and ART status/self-reported VL. (Table 6.8) ART status was excluded from the model as it was included in the ART status/self-reported VL variable. Education, employment, and money for basic needs were highly correlated; it was decided to only retain education so as to examine the effect of early socio-economic factors. Hence after adjustment for age, time since HIV diagnosis, place of birth, education, higher alcohol consumption, stable partner, ART status/self-reported VL, and clinic, chemsex-associated drug use remained associated ($p<0.05$) with younger age, more recent HIV diagnosis, and having an HIV-positive stable partner, or no stable partner.

Table 6.8: Association of socio-demographic, psychological, lifestyle, and HIV-related factors with chemsex-associated drug use (GHB/GBL, mephedrone, and/or methamphetamine versus any other drug) in the previous three months (N=1111 HIV-diagnosed MSM used drugs)

	Chemsex-associated drug use (n/N=330/1111)							
	n used chemsex drugs/row N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=1084)								
<30	33/59	55.9	3.3 [2.3,4.6]		4.3 [2.8, 6.7]		4.3 [2.8, 6.6]	
30-39	116/296	39.2	2.3 [1.7, 3.1]		3.2 [2.3, 4.6]		3.0 [2.1, 4.3]	
40-49	131/477	27.5	1.6 [1.1,2.1]		2.0 [1.5, 2.8]		2.0 [1.4, 2.8]	
≥50	43/252	17.1	1.0	<0.001(T)	1.0	<0.001(T)	1.0	<0.001(T)
Ethnicity (N=1093)								
White	294/984	29.9	1.0		1.0		-	
All other (black, Asian, Mixed, other)	31/109	28.4	1.0 [0.7,1.3]	0.757	0.8 [0.5,1.1]	0.107		
Years since HIV diagnosis (N=1103)								
≤2	45/111	40.5	1.0		1.0		1.0	
2-5	65/183	35.5	0.8 [0.6,1.2]		0.8 [0.6,1.2]		0.7 [0.5,1.0]	
5-10	98/275	35.6	0.8 [0.7, 1.2]		0.9 [0.7,1.2]		0.8 [0.6,1.1]	
10-15	58/230	25.2	0.6 [0.4,0.8]		0.8 [0.5,1.1]		0.7 [0.5,1.0]	
≥15	61/304	20.1	0.5[0.4,0.7]	<0.001(T)	0.7 [0.5,1.0]	0.073(T)	0.6 [0.4,0.9]	0.026(T)
Place of birth (N=1111)								
UK	206/762	27.0	1.0		1.0		1.0	
Outside the UK	124/349	35.5	1.3 [1.1,1.6]	0.003	1.2 [1.0,1.5]	0.042	1.0 [0.8,1.3]	0.781
Religious (N=1093)								
Yes	122/414	29.5	1.0		1.0		-	
No	204/679	30.0	1.0 [0.8,1.2]	0.840	1.1 [0.9,1.4]	0.330		
Education (N=1095)								
University degree or above	166/480	34.6	1.0		1.0		1.0	
No qualifications or up to A levels	161/615	26.2	0.8 [0.6,0.9]	0.003	0.8 [0.6,0.9]	0.006	0.9 [0.7,1.1]	0.301
Employment (N=1093)								
Employed	238/700	34.0	1.0		1.0		-	
Unemployed or other(carer, student, retired)	89/396	22.5	0.7 [0.5,0.8]	<0.001	0.8 [0.6,1.0]	0.030		

	Chemsex-associated drug use (n/N=330/1111)							
	n used chemsex drugs/row N	row %	unadjusted PR [95%CI]	p-value	Model 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Money for basic needs (N=1099)								
Always	183/560	32.7	1.0		1.0		-	
Mostly	84/302	27.8	0.9 [0.7,1.1]		0.8 [0.6,1.0]			
Sometimes/never	60/237	25.3	0.8 [0.6,1.0]	0.054(T)	0.8 [0.6,1.0]	0.048(T)		
Social support (N=1107) ‡								
High	193/640	30.2	1.0		1.0		-	
Medium/low	135/467	28.9	1.0 [0.8,1.2]	0.227(T)	1.0 [0.8,1.2]	0.739(T)		
Depression symptoms (N=1111) ‡								
No	240/793	30.3	1.0		1.0		-	
Yes	90/318	28.3	0.9 [0.8,1.1]	0.520	0.9 [0.8,1.2]	0.626		
Anxiety symptoms (N=1111) ‡								
No	269/880	30.6	1.0		1.0		-	
Yes	61/231	26.4	0.9 [0.7,1.1]	0.227	0.8 [0.6,1.1]	0.170		
Higher alcohol consumption (N=1111) ‡								
No	279/898	31.1	1.0		1.0		1.0	
Yes	51/213	23.9	0.8 [0.6,1.0]	0.048	0.9 [0.7,1.2]	0.426	1.0 [0.8,1.3]	0.914
Evidence of alcohol dependency (N=1110) ‡								
No	268/869	30.8	1.0		1.0			
Yes	62/241	25.7	0.8 [0.7,1.1]	0.133	0.9 [0.7,1.2]	0.573	-	
Stable partner's HIV-serostatus (N=1111)								
HIV-positive	107/294	36.4	1.0		1.0		1.0	
HIV-negative or unknown status	65/314	20.7	0.6 [0.4,0.7]		0.5 [0.4,0.7]		0.5 [0.4,0.7]	
No stable partner	158/503	31.4	0.9 [0.7,1.1]	<0.001	0.8 [0.6,1.0]	<0.001	0.8 [0.6,1.0]	<0.001

	Chemsex-associated drug use (n/N=330/1111)							
	n used chemsex drugs/row N	**row %**	**unadjusted PR [95%CI]**	**p-value**	**Model 1: aPR [95%CI]**	**p-value**	**Model 2: aPR [95%CI]**	**p-value**
ART status (N=1108)								
On ART	259/941	27.5	1.0		1.0		-	
Not on ART	69/167	41.3	1.5 [1.2,1.8]	<0.001	1.2 [0.9,1.5]	0.207		
ART status/self-reported VL (N=1092)								
On ART, reports undetectable viral load	216/770	28.1	1.0		1.0		1.0	
On ART, does not report undetectable viral load†	41/155	26.5	0.9 [0.7,1.3]		0.9 [0.6,1.2]		1.0 [0.7,1.4]	
Not on ART	69/167	41.3	1.5 [1.2,1.8]	<0.001	1.1 [0.9,1.5]	0.366	1.1 [0.9,1.5]	0.614

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression models: ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, and ART status. Denominators vary due to missing data in each model.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, in addition to clinic. In both cases, model for 'ART status/self-reported VL' omits variable on ART due to collinearity. †Self-reported viral load (VL)>50c/mL or "don't know". Alcohol consumption by WHO-AUDIT-C, dependency by CAGE.*

‡ For variable definitions see section 3.8

6.4.3 Recreational drug use and sexual behaviour

This section describes associations of recreational drug use, polydrug use, chemsex-associated drug use (as well as measures of alcohol misuse) with various measures of sexual behaviour, firstly, among all 2189 MSM, and secondly, among 1392 MSM who reported having any anal or vaginal sex in the past three months.

6.4.3.1 Drug use and sexual behaviour among all HIV-diagnosed MSM

In unadjusted analyses, compared to MSM who did not use drugs in the previous three months (n=1078), MSM who used drugs (n=1111) were more likely to report any anal and/or vaginal sex, any CLS (including CLS-C, CLS-D, and higher HIV risk CLS-D), group sex, using the internet to find sex in the previous three months, and having 10 or more new sexual partners in the past year ($p<0.001$ for all, Table 6.9) Recreational drug use was also significantly more prevalent among MSM who had low condom self-efficacy and those who reported lower condom use with casual partners ($p<0.05$ for both, Table 6.10. No significant association was observed between recreational drug use and difficulty negotiating condom use or worry about HIV transmission ($p>0.05$ for both, Table 6.10, Figure 6.4).

With increasing number of recreational drugs used there were striking increases in the prevalence of CLS and all other sexual behaviour outcomes in unadjusted models ($p<0.05$ for all, Table 6.9) Polydrug use was also significantly more prevalent among MSM with low condom self-efficacy and lower condom use with casual partners in unadjusted analyses. ($p<0.05$ for both). After adjustment for core factors, polydrug use remained significantly associated with all sexual behaviours. ($p<0.001$ trend, Figure 6.3) For most measures, there was a trend of increasing prevalence with increasing number of drugs; this trend was particularly marked for group sex and having 10 or more new partners. The range of adjusted prevalence ratios (PR) for MSM using from 1 to ≥5 drugs, compared to MSM using no drugs, respectively was: 1.3 to 1.7 for any anal or vaginal sex; 1.3 to 2.7 for any CLS; 1.3 to 3.2 for CLS-C; 1.4 to 2.9 for CLS-D; 1.3 to 2.9 for other STIs; 1.9 to 6.2 for group sex; 1.2 to 2.8 for using the internet to find sex; and 1.5 to 3.9 for ≥10 new sexual partners in the past year.(Figure 6.3) Categories were combined for higher HIV risk CLS-D due to the lower prevalence of this measure, so that the range of PRs for MSM using from 1 to ≥4 drugs was 2.2 to 2.6. Polydrug use also remained significantly associated with low condom self-efficacy and lower condom use with casual partners after adjustment for core factors ($p<0.001$ trend for both, Figure 6.4). There was no statistically significant association of polydrug use with difficulty negotiating condom use or with worry about HIV transmission ($p>0.05$ trend for both, Figure 6.4).

In unadjusted analyses, compared to MSM who did not use chemsex-associated drugs (n=1859), MSM who used chemsex-associated drugs (n=330) were more likely to report higher prevalence of all sexual behaviours ($p<0.05$ for all), low condom self-efficacy, and low condom use with casual partners ($p<0.01$ for both, Table 6.10). There was no significant association of chemsex use and difficulty negotiating condom use or worry about HIV transmission.

Table 6.9: Unadjusted associations of any recreational drug use, polydrug use, and chemsex-associated drug use with sexual behaviours in the past three months (N=2189 MSM)

		Any anal and/or vaginal sex (N=1392)		Condomless sex (CLS) (N=836)		Condomless sex with HIV-seroconcordant partner (CLS-C) (N=628)		Condomless sex with HIV-serodifferent partner (CLS-D) (N=357)		Higher HIV risk CLS-D (N=93)		Diagnosed with another STI (N=235)		Had group sex (N=796)		Used internet to find sexual partners (N=796)		≥10 new sexual partners in past year (N=586)	
	Total N†	row %	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]	%	PR [95%CI]
Recreational drug use																			
No	1078	48.6	1.0	24.0	1.0	16.5	1.0	10.5	1.0	2.1	1.0	6.9	1.0	9.5	1	24.5	1.0	5.7	1.0
Yes	1111	78.1	1.6 [1.5,1.7]	51.9	2.2 [1.9,2.4]	40.5	2.5 [2.1,2.9]	22.0	2.1 [1.7,2.6]	6.3	3.0 [1.9,4.7]	14.8	2.1 [1.7,2.8]	32.5	3.4 [2.8,4.2]	49.3	2.0 [1.8,2.3]	7.5	2.6 [2.2,3.0]
p-value			<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
Polydrug use																			
None	1078	48.6	1.0	24.0	1.0	16.5	1.0	10.5	1.0	2.1	1.0	6.9	1.0	9.5	1.0	24.5	1.0	14.9	1.0
1	363	64.2	1.3 [1.2,1.5]	32.8	1.4 [1.1,1.6]	21.8	1.3 [1.0,1.7]	14.9	1.4 [1.0,1.9]	4.4	2.1 [1.1,3.9]	9.0	1.3 [0.9,2.0]	17.6	1.9 [1.4,2.5]	29.7	1.2 [1.0,1.5]	22.9	1.5 [1.2,1.9]
2	229	79.9	1.6 [1.5,1.8]	48.0	2.0 [1.7,2.4]	33.6	2.0 [1.6,2.6]	23.1	2.2 [1.6,3.0]	7.9	3.7 [2.0,6.7]	13.2	1.9 [1.3,2.9]	26.3	2.8 [2.1,3.7]	48.7	2.0 [1.7,2.4]	32.8	2.2 [1.7,2.8]
3	173	79.2	1.6 [1.5,1.8]	53.2	2.2 [1.9,2.6]	41.6	2.5 [2.0,3.1]	23.1	2.2 [1.6,3.0]	6.4	3.0 [1.5,6.0]	16.3	2.4 [1.6,3.6]	28.3	3.0 [2.2,4.0]	47.4	1.9 [1.6,2.3]	38.7	2.6 [2.0,3.3]
4	111	89.2	1.8 [1.7,2.0]	66.7	2.8 [2.3,3.3]	52.3	3.2 [2.5,4.0]	29.7	2.8 [2.0,4.0]	7.2	3.4 [1.9, 5.9]	16.4	2.4 [1.5,3.8]	45.9	4.8 [3.7,6.4]	71.8	2.9 [2.5,3.4]	49.5	3.3 [2.6,4.2]
≥5	235	91.9	1.9 [1.8,2.0]	77.4	3.2 [2.8,3.7]	69.8	4.2 [3.6,5.0]	27.2	2.6 [2.0,3.4]		*	23.2	3.4 [2.4,4.7]	58.1	6.1 [4.9,7.6]	70.9	2.9 [2.5,3.3]	61.7	4.1 [3.5,4.9]
p-value(T)			<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
Chemsex-associated use																			
No	1859	58.8	1.0	31.8	1.0	22.2	1.0	14.8	1.0	3.7	1.0	8.5	1.0	15.4	1.0	30.9	1.0	20.9	1.0
Yes	330	90.6	1.5 [1.5,1.6]	74.2	2.3 [2.1,2.6]	65.2	2.9 [2.6,3.3]	24.8	1.7 [1.4,2.1]	7.3	2.0 [1.2,3.1]	24.5	2.9 [2.3,3.7]	53.6	3.5 [3.0,4.0]	72.4	2.3 [2.1,2.6]	60.0	2.9 [2.5,3.3]
p-value			<0.001		<0.001		<0.001		<0.001		0.003		<0.001		<0.001		<0.001		<0.001

*P-values by chi-squared test and, for polydrug use, by test for trend (T); † Denominators vary due to missing values. Three month recall unless otherwise specified; HIV-serodifferent: HIV-negative or unknown status partner; CLS-D includes n=31 MSM who reported having CLS but not their partners' HIV-serostatus; Higher HIV risk CLS-D: CLS-D plus either not on ART or latest study log-recorded viral load>50c/mL; *Showing prevalence of higher HIV risk CLS-D for MSM who used ≥4 drugs (rather than ≥5) due lower prevalence of this measure; Chemsex-associated drug use: GHB/GBL, mephedrone, and/or crystal methamphetamine; STI: sexually transmitted infection*

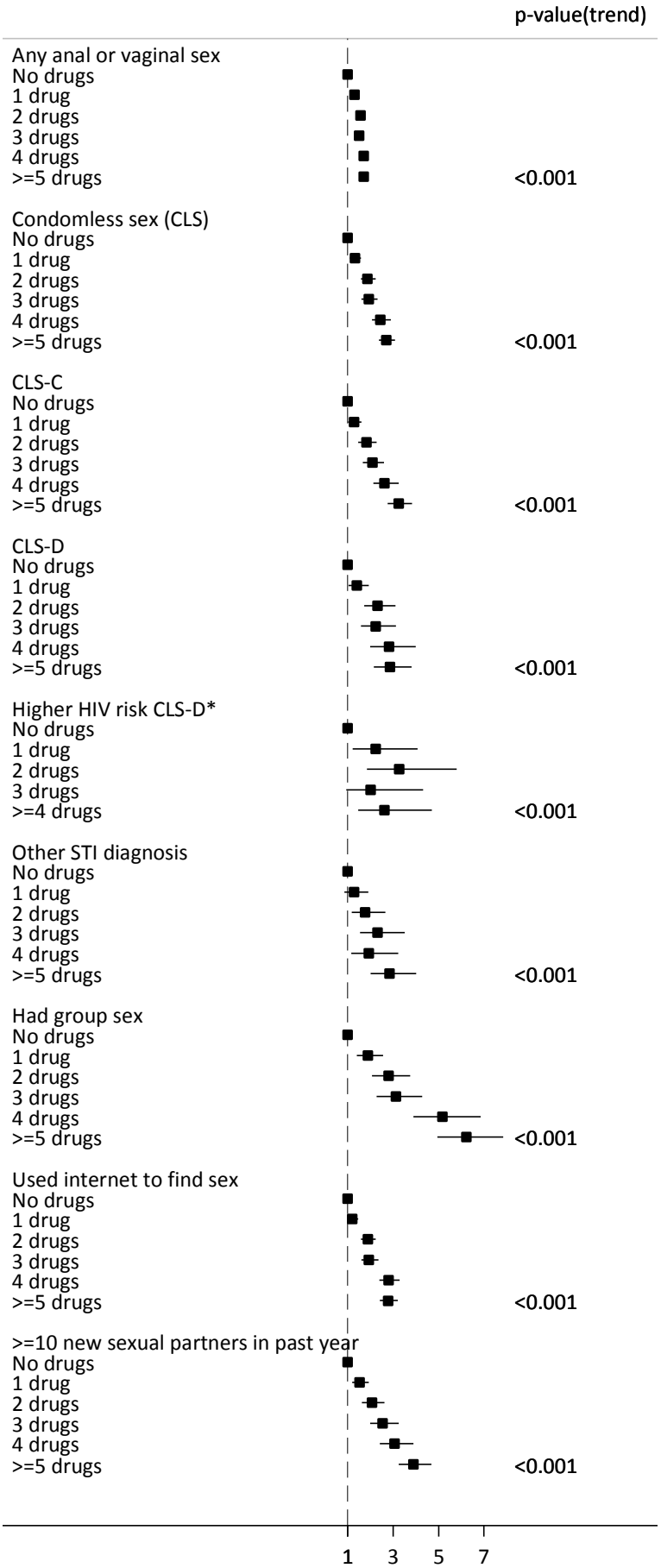
Table 6.10: Unadjusted associations of any recreational drug use, polydrug use, and chemsex-associated drug use with level of agreement to statements on low condom self-efficacy, difficulty negotiating condom use, lower condom use with casual partners, and worry about HIV transmission* (N=2189 MSM)

		Low condom self-efficacy (N=139)		Difficulty negotiating condom use (N=319)		Lower condom use with casual partners (N=355)		Worry about HIV transmission (N=141)	
	Total N†	row %	PR [95%CI]	row %	PR [95%CI]	row %	PR [95%CI]	row %	PR [95%CI]
Recreational drug use						(%)			
No	1055	4.6	1.0	14.2	1.0	12.6	1.0	5.7	1.0
Yes	1092	8.2	1.8 [1.3,2.5]	15.5	1.1 [0.9,1.3]	20.6	1.6 [1.3,2.0]	7.5	1.3 [1.0,1.8]
p-value		<0.001		0.401		<0.001		0.094	
Polydrug use									
None	1055	4.6	1.0	14.2	1.0	12.6	1.0	5.7	1.0
1	357	6.4	1.4 [0.9,2.2]	15.5	1.1 [0.8,1.5]	15.7	1.2 [0.9,1.7]	6.8	1.2 [0.7,1.9]
2	224	6.3	1.3 [0.8,2.4]	15.9	1.1 [0.8,1.6]	16.8	1.3 [1.0,1.9]	6.3	1.1 [0.6,1.9]
3	172	6.4	1.4 [0.7,2.6]	12.1	0.9 [0.6,1.3]	19.3	1.5 [1.1,2.2]	9.4	1.6 [1.0,2.8]
4	110	10.9	2.3 [1.3,4.3]	17.1	1.2 [0.8,1.9]	24.5	1.9 [1.4,2.8]	10.9	1.9 [1.1,3.4]
≥5	229	13.1	2.8 [1.8,4.3]	16.9	1.2 [0.9,1.6]	30.7	2.4 [1.9,3.1]	6.9	1.2 [0.7,2.1]
p-value (T)		<0.001		0.369		<0.001		0.071	
Chemsex-associated drug use									
No	1824	5.6	1.0	14.5	1.0	14.5	1.0	6.4	1.0
Yes	323	11.5	2.0 [1.4,2.9]	17.3	1.2 [0.9,1.6]	29.2	2.0 [1.6,2.5]	7.7	1.2 [0.8,1.8]
p-value		<0.001		0.180		<0.001		0.385	

No recall period for statements; P-values by Wald test and, for polydrug use, by test for trend (T); † Denominators vary due to missing values; PR: unadjusted prevalence ratio; Chemsex-associated drug use: GHB/GBL, mephedrone, and/or crystal methamphetamine in the previous three months.

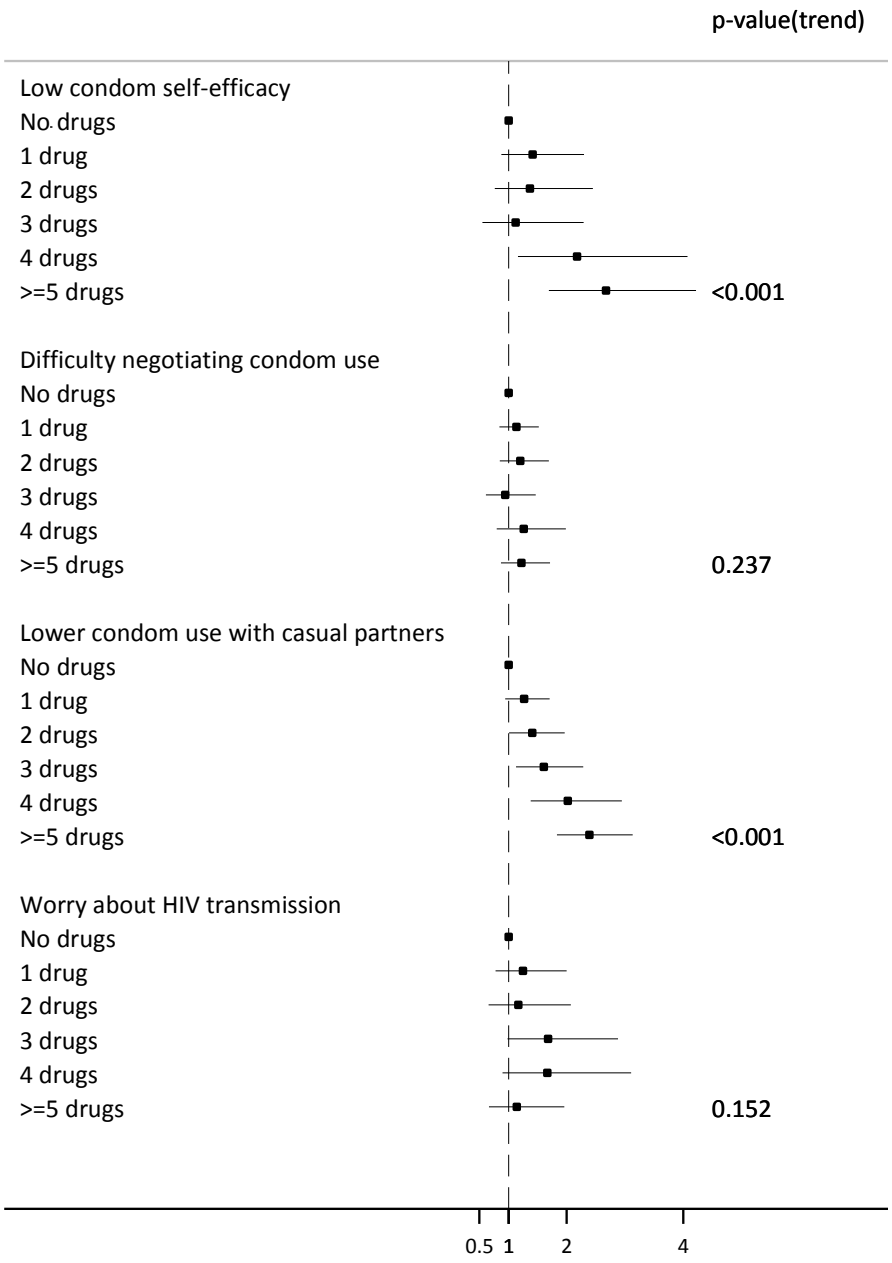
**All statements defined in section 4.3.5*

Figure 6.3: Adjusted prevalence ratios [95%CI] for the association of polydrug use in the past three months with sexual behaviours (N=2189 MSM) †



Prevalence Ratios [95%CIs] by modified Poisson regression models adjusted for core factors. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partners; CLS-D: CLS with HIV-serodifferent partners; Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL, *collapsed drug use categories due to lower prevalence of this measure. This model does not include adjustment for ART status; STI: sexually transmitted infection.†For denominators see Table 6.9*

Figure 6.4: Adjusted prevalence ratios [95%CI] for the association of polydrug use and level of agreement to statements on low condom self-efficacy, difficulty negotiating condom use, lower condom use with casual partners, and worry about HIV transmission (N=2189 MSM)†



†All statements defined in section 4.3.5. For denominators see Table 6.10; Prevalence Ratios [95%CIs] by modified Poisson regression models adjusted for core factors.

6.4.3.2 Drug use, alcohol misuse, and sexual behaviour among all HIV-diagnosed MSM

Associations of alcohol misuse, measured by two tools (higher alcohol consumption by WHO-AUDIT-C and evidence of alcohol dependency by CAGE questionnaire), and sexual behaviours were assessed by unadjusted (Table 6.11) and adjusted modified Poisson regression models (Figure 6.5, Figure 6.6). In unadjusted analysis, no significant association was observed between higher alcohol consumption (using the WHO-AUDIT-C) with any sexual behaviours, with the exception of CLS-D and higher HIV risk CLS-D, the prevalence of both being significantly higher among MSM with higher compared to lower alcohol consumption ($p<0.05$ for both, Table 6.11). These associations were attenuated but remained significant after adjustment for core factors and additional adjustment for recreational drug use in the past three months. (Figure 6.5)

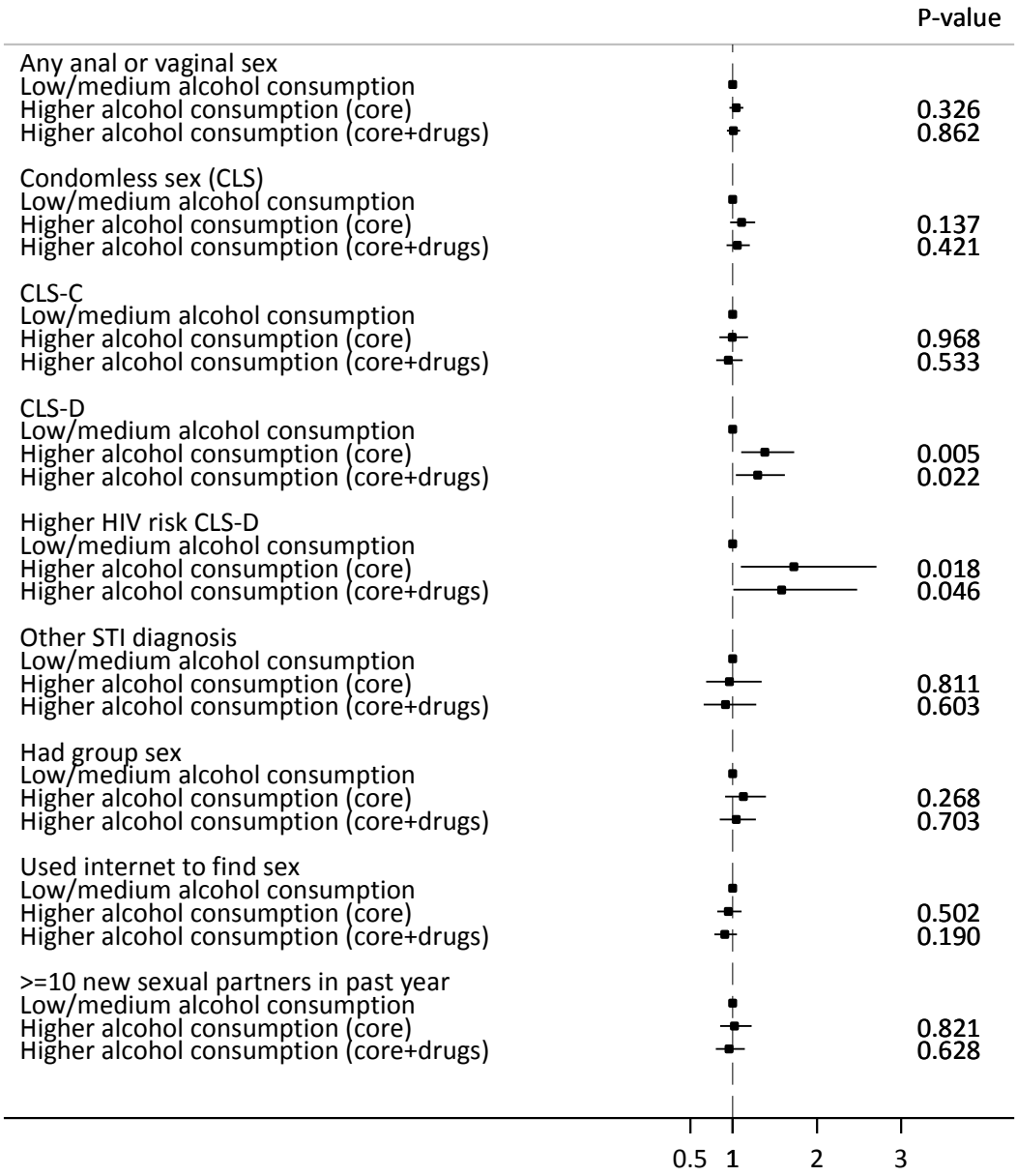
Alcohol dependency (by CAGE) was not associated with any sexual behaviour in unadjusted or adjusted analyses. ($p>0.05$ for all, Table 6.11, Figure 6.6)

Table 6.11: Associations of higher alcohol consumption (by WHO-AUDIT-C), evidence of alcohol dependency (by CAGE questionnaire) with sexual behaviours (N=2189, unadjusted)

		Any anal and/or vaginal sex (N=1392)		Condomless sex (CLS) (N=836)		CLS-C (N=628)		CLS-D (N=357)		Higher HIV risk CLS-D (N=93)		Diagnosed with another STI (N=235)		Had group sex (N=453)		Used internet to find sexual partners (N=796)		≥10 new partners in past year (N=586)	
	Total N◊	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]	row %	PR[95%CI]
Higher alcohol consumption†																			
No	1823	63.0	1.0	37.5	1.0	28.9	1.0	15.2	1.0	3.7	1.0	11.0	1.0	20.7	1.0	37.4	1.0	26.5	1.0
Yes	366	66.4	1.1 [1.0,1.1]	41.5	1.1 [1.0,1.3]	27.9	1.0 [0.8,1.2]	21.6	1.4 [1.1,1.8]	7.1	1.9 [1.2,3.0]	10.2	0.9 [0.7,1.3]	23.3	1.1 [0.9,1.4]	35.6	0.9 [0.8,1.1]	27.9	1.0 [0.9,1.3]
p-value			0.208		0.141		0.705		0.002		0.003		0.658		0.263		0.503		0.601
Evidence of alcohol dependency‡																			
No	1768	63.7	1.0	38.1	1.0	28.8	1.0	15.8	1.0	4.0	1.0	10.8	1.0	21.4	1.0	37.1	1.0	26.3	1.0
Yes	420	63.1	1.0 [0.9,1.1]	38.6	1.0 [0.9,1.2]	28.1	1.0 [0.8,1.2]	18.3	1.2 [0.9,1.5]	5.0	1.2 [0.8,2.0]	11.0	1.0 [0.8,1.4]	20.0	0.9 [0.8,1.2]	37.5	1.0 [0.9,1.2]	28.6	1.1 [0.9,1.3]
p-value			0.821		0.848		0.761		0.199		0.366		0.891		0.538		0.879		0.340

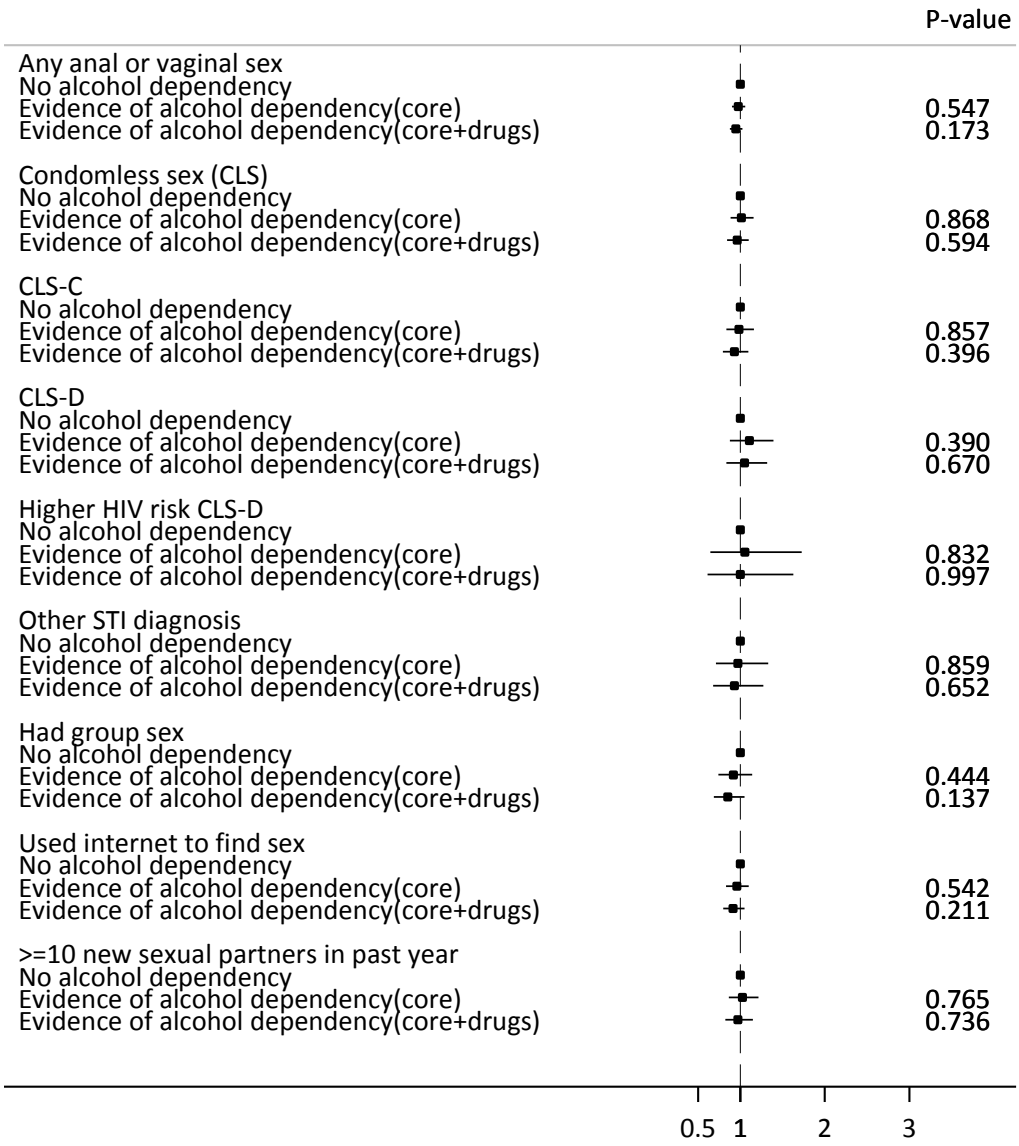
p-values by chi-squared test; Three month recall unless otherwise specified. ◊ Denominators vary due to missing values; † WHO-AUDIT-C score ≥6 on first two questions only; ‡ CAGE questionnaire score ≥2; CLS-C: CLS with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; Higher HIV risk CLS-D: CLS-D plus either not on ART or latest study log-recorded VL>50c/mL; PR: unadjusted prevalence ratio; STI: sexually transmitted infection

Figure 6.5: Associations of higher alcohol consumption (by WHO-AUDIT-C) and sexual behaviours, adjusted for recreational drug use (N=2189)



Prevalence ratios [95%CI] by modified Poisson regression; p-value by Wald test; Three month recall for sexual behaviours unless otherwise specified. Reference group is low/medium alcohol consumption versus higher alcohol consumption (score <6 versus ≥6 on WHO-AUDIT-C first two questions); Core: adjusted for core factors (age, ethnicity, time since HIV diagnosis, stable partner status, ART status); Core+drugs: adjusted for core factors and recreational drug use. Model for Higher HIV risk CLS-D does not include adjustment for ART status.

Figure 6.6: Associations of evidence of alcohol dependency (by CAGE questionnaire) and sexual behaviours, adjusted for recreational drug use (N=2189)



Prevalence ratios [95%CI] by modified Poisson regression; p-value by Wald test; reference group is no evidence of alcohol dependency (score <2 on CAGE questionnaire) versus evidence of alcohol dependency (score ≥2 on CAGE); Core: adjusted for core factors (age, ethnicity, time since HIV diagnosis, stable partner status, ART status); Core+drugs: adjusted for core factors and recreational drug use; Three month recall for sexual behaviours unless otherwise specified. Model for higher HIV risk CLS-D does not include adjustment for ART status.

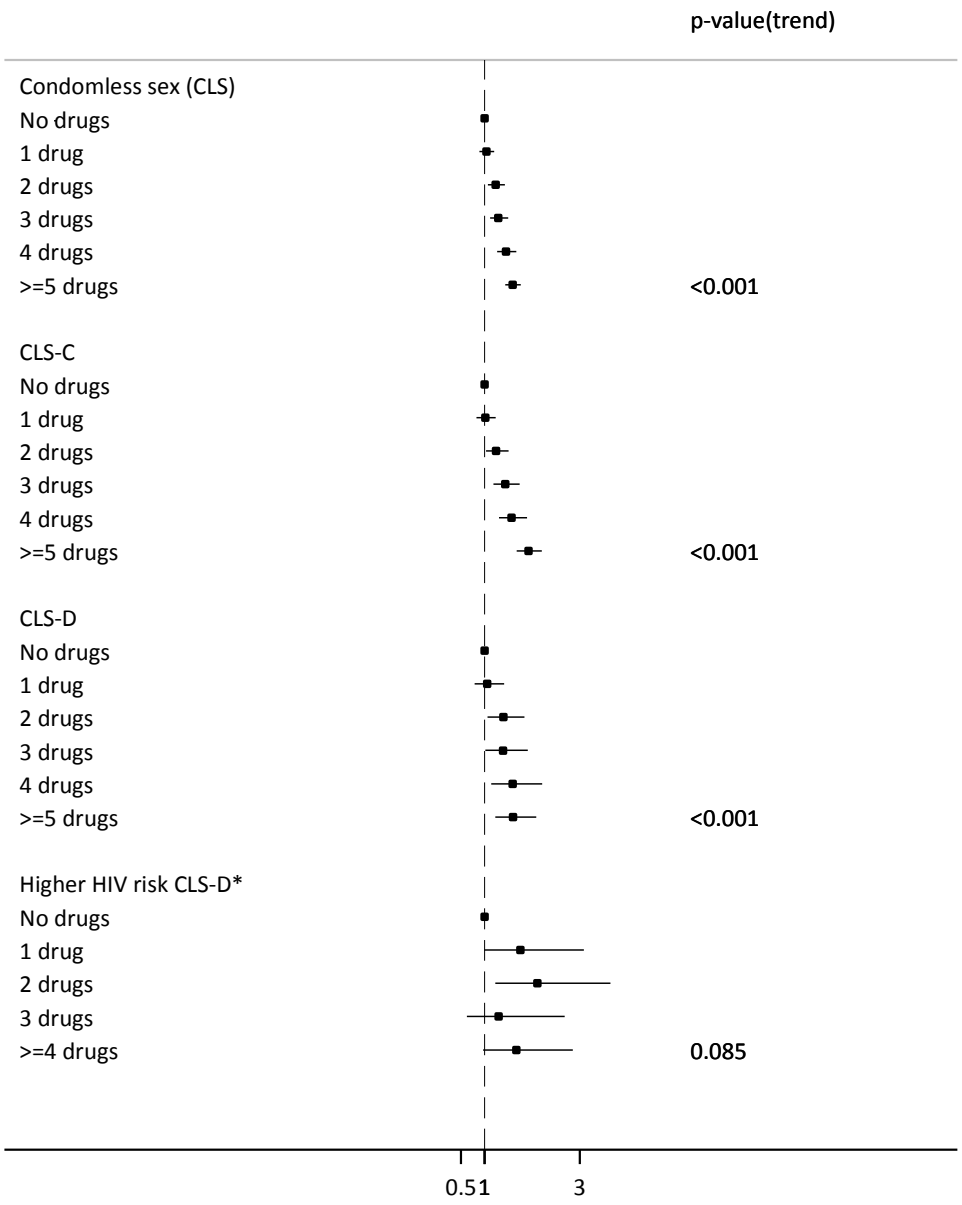
6.4.3.3 Drug use and sexual behaviour among HIV-diagnosed MSM who had sex in the past three months

Only MSM who reported any anal or vaginal sex in the past three months were included in analyses described in this section (N=1392). The aim of the first analysis was to examine the effect of polydrug use on CLS among those who reported having sex. After adjustment for core factors, the associations of polydrug use with CLS, CLS-C, CLS-D remained significant ($p<0.001$ trend, Figure 6.7), but not for higher HIV risk CLS-D. For higher HIV risk CLS-D, the last two polydrug use categories were collapsed into one category (≥4 drugs) due to lower prevalence of this measure.

Associations were then examined between specific drugs and CLS-C, CLS-D, and higher HIV risk CLS-D among MSM who reported any sex in the past three months. (Figure 6.8) After adjustment for core factors, significant associations were observed for specific drugs and CLS-C ($p<0.05$ for all); compared to MSM who did not use drugs, those who used methamphetamine had the highest prevalence of CLS-C (PR=2.0, 1.8-2.3), followed by those who used EDDs (1.8, 1.6-2.1), or chemsex-associated (1.6, 1.4-1.9) (Figure 6.8). Compared to MSM not using drugs, MSM who used EDDs had the highest prevalence of CLS-D in the past three months (PR=1.7, 95%CI 1.4-2.1), followed by similar prevalence of CLS-D for MSM who used methamphetamine (1.5, 1.1-2.1), nitrites (1.5, 1.2-1.9), 'club drugs' (1.5, 1.2-1.9), or chemsex-associated drugs (1.3, 1.1-1.6). The prevalence of higher HIV risk CLS-D was, relative to MSM who did not use drugs, highest for MSM who used nitrites (2.0, 1.3-3.2) or methamphetamine (2.0, 1.0-3.9), followed by those who used chemsex-associated drugs (1.8, 1.2-2.8), or cocaine (1.9, 1.2-3.1).

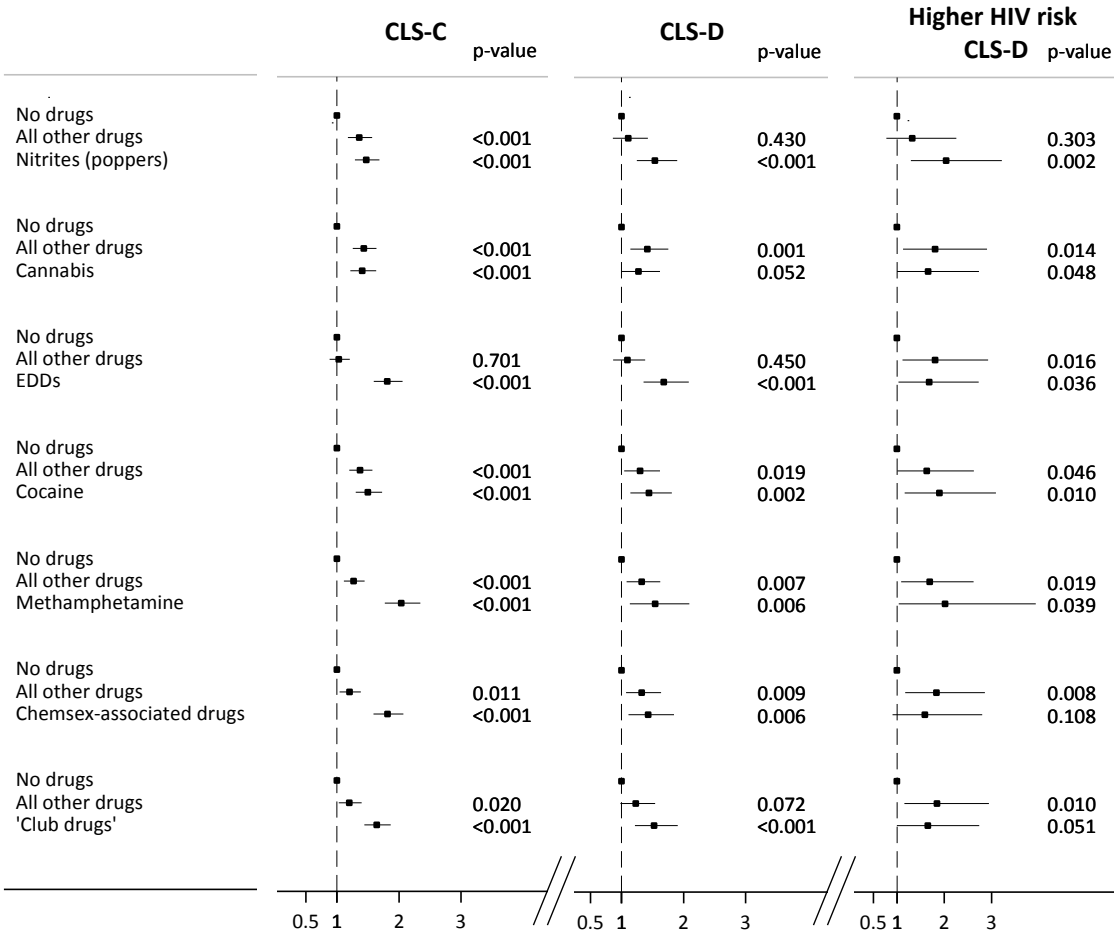
The last analysis in this section aimed at examining which specific drugs were associated with reporting 'CLS-C without CLS-D' compared to CLS-D.(Figure 6.9) Only MSM who reported having CLS *and* using recreational drugs in the past three months were included (N=557). In unadjusted modified Poisson regression, use of chemsex-associated drugs was significantly associated with higher prevalence of 'CLS-C without CLS-D' compared to CLS-D (PR=1.3, 95%CI 1.1-1.5); when examining methamphetamine separately (versus any other drug) only the association with CLS-C remained robust (1.2, 1.1-1.4). The prevalence of 'CLS-C without CLS-D' (versus CLS-D) was lower among MSM who used nitrites (poppers) compared to those who used any other drug (0.8, 0.7-0.9). There were no significant differences in reporting 'CLS-C without CLS-D' versus CLS-D among MSM who used EDDs, cocaine, or cannabis ($p>0.05$ for all).

Figure 6.7: Adjusted prevalence ratios [95%CI] for the association of polydrug use and types of condomless sex in the previous three months (N=1392 MSM reported any anal or vaginal sex only)



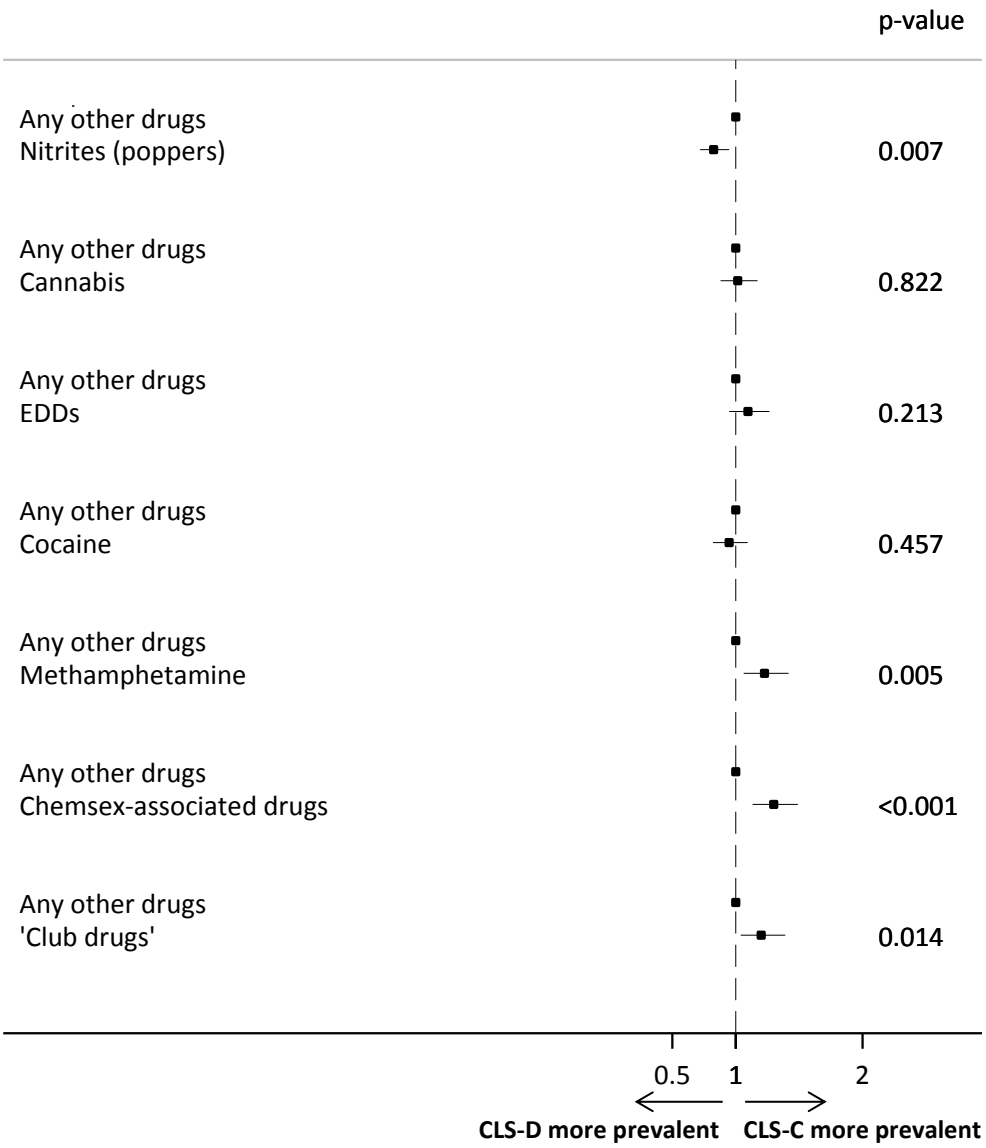
*Prevalence Ratios [95%CIs] by modified Poisson regression models adjusted for core factors. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partners; CLS-D: CLS with HIV-serodifferent partners; *Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL; Collapsed drug use categories due to lower prevalence of this measure. This model does not include adjustment for ART status.*

Figure 6.8: Adjusted prevalence ratios [95%CI] for the association of use of specific drugs and reporting CLS-C, CLS-D, or higher HIV risk CLS-D in the past three months (N=1392 MSM reported any anal or vaginal sex)



Prevalence Ratios [95%CIs] by modified Poisson regression adjusted for core factors. CLS-C: condomless sex(CLS) with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL (This model does not include adjustment for ART status); EDD: erectile dysfunction drugs; Chemsex-associated drugs: methamphetamine, mephedrone, GHB/GBL; 'Club drugs': ketamine, ecstasy, GHB/GBL, mephedrone

Figure 6.9: Unadjusted associations between use of specific drugs and reporting condomless sex with HIV-seroconcordant partners only (CLS-C) versus with HIV-serodifferent partners (CLS-D) among 557 MSM who reported any CLS and using drugs in the past three months.



Prevalence Ratios [95%CIs] by modified Poisson regression. EDDs: erectile dysfunction drugs; Chemsex-associated drugs: methamphetamine, mephedrone, GHB/GBL; 'Club drugs': ketamine, ecstasy, GHB/GBL, mephedrone

6.4.3.4 Drug use and the four-category variable of sexual behaviour

In this analysis, all 2189 MSM were classified into one of the following mutually exclusive groups of sexual behaviour in the past three months (as described in section 4.4.7):

1. CLS-D (n=357)
2. 'CLS-C without CLS-D' (n=479)
3. Condom-protected sex only (n=556)
4. No anal or vaginal sex (n=797)

Unadjusted multinomial logistic regression was used to examine the effect of recreational drug use on the three categories of sexual behaviour (1-3) compared to no sex (category 4) (Table 6.12 panel A) and on the two CLS categories (1 and 2) compared to condom-protected sex (category 3) (Table 6.12 panel B). Relative to MSM who did not have any anal or vaginal sex, prevalence of CLS-D and 'CLS-C without CLS-D' was five-fold higher for drug users compared to MSM who did not use drugs, while prevalence of condom-protected sex was higher by more than twofold.(Table 6.12 panel A) Strong trends were also observed between polydrug use and higher prevalence in each of the two CLS categories: as the number of drugs used increased, so did the prevalence of having 'CLS-C without CLS-D' and CLS-D relative to not having any sex in the past three months ($p<0.001$ trend for both). The association with polydrug use was strongest for 'CLS-C without CLS- D', followed by CLS-D, and was less strong for condom-protected sex. A similar pattern was observed for chemsex-associated drug use ($p<0.001$ for all, Table 6.12).

After excluding MSM who did not have sex in the past three months (Table 6.12 panel B), the magnitude of associations attenuated but remained strong; the prevalence of 'CLS-C without CLS-D' relative to condom-protected sex was twice as high among MSM who used recreational drugs compared to those who did not, and over four times higher among MSM who used chemsex-associated drugs compared to MSM who did not. Similar findings were observed for CLS-D relative to condom-protected sex. Polydrug use was also strongly associated with increasing prevalence of both CLS-C and CLS-D, relative to condom-protected sex ($p<0.001$ trend for both).

Table 6.12: Unadjusted associations (by multinomial logistic regression) of recreational drug use, polydrug use, chemsex-associated drug use with sexual behaviours in past three months among: (A.) all MSM (N=2189) and (B.) among MSM who reported any anal or vaginal sex (N=1392).

(A.)	No anal or vaginal sex (n=797)	Condom-protected sex (n=556)		CLS-C without CLS-D (n=479)		CLS-D (n=357)	
		OR [95%CI]	p-value	OR [95%CI]	p-value	OR [95%CI]	p-value
Recreational drug use							
No	ref	1.0		1.0		1.0	
Yes		2.5 [2.0,3.2]	<0.001	5.2 [4.1,6.7]	<0.001	5.0 [3.8,6.5]	<0.001
Polydrug use							
1		1.0		1.0		1.0	
2		1.8 [1.2,2.8]		2.5 [1.5,4.0]		2.8 [1.7,4.6]	
3	ref	1.4 [0.9,2.4]		2.9 [1.7,4.9]		2.7 [1.5,4.6]	
4		2.4 [1.1,4.9]		6.8 [3.4,13.9]		6.6 [3.2,13.8]	
≥5		2.2 [1.2,4.1]	0.002(T)	13.1 [7.4,23.4]	<0.001(T)	8.6 [4.6,15.8]	<0.001(T)
Chemsex-associated drug use							
No	ref	1.0		1.0		1.0	
Yes		2.7 [1.7,4.2]	<0.001	12.7 [8.5,19.1]	<0.001	7.4 [4.8,11.4]	<0.002

(B.)	Condom-protected sex (n=556)	CLS-C without CLS-D (n=479)		CLS-D (n=357)	
		OR [95%CI]	p-value	OR [95%CI]	p-value
Recreational drug use					
No	ref	1.0		1.0	
Yes		2.1 [1.6,2.7]	<0.001	2.0 [1.5,2.6]	<0.001
Polydrug use					
1		1.0		1.0	
2		1.4 [0.9,2.2]		1.5 [0.9,2.5]	
3	ref	2.0 [1.2,3.3]		1.9 [1.1,3.2]	
4		2.9 [1.6,5.2]		2.8 [1.5,5.1]	
≥5		5.9 [3.6,9.6]	<0.001(T)	3.9 [2.3,6.5]	<0.001(T)
Chemsex-associated drug use					
No	ref	1.0		1.0	
Yes		4.8 [3.4,6.7]	<0.001	2.8 [1.9,4.0]	<0.001

ref: reference (baseline) category; p-values by Wald test and, for polydrug use, test for trend (T); OR: odds ratio; Mutually exclusive categories of sexual behaviour; CLS-D: condomless sex with HIV-serodifferent partners; CLS-C: condomless sex with HIV-seroconcordant partners only (no CLS-D partners); chemsex-associated drugs: GHB/GBL, mephedrone, and/or crystal methamphetamine.

6.4.4 **Recreational drug use, alcohol misuse, and ART outcomes**

Among 1888 MSM who were on ART, associations were examined between recreational drug use, polydrug use (1, 2-4, ≥5 drugs) in the past three months, higher alcohol consumption (≥6 on the modified WHO-AUDIT-C), evidence of alcohol dependency (≥2 on CAGE questionnaire) and:

(i.) Non-adherence to ART (prevalence 9.7%, 95%CI 8.4-11.1%, n/N=183/1888)

(ii.) Viral load (VL) non-suppression among MSM who started ART ≥6 months ago (9.8%, 8.5-11.3%, n/N=172/1744)

Significant associations were observed between recreational drug use, higher alcohol consumption, alcohol dependency, and non-adherence to ART after adjustment for age, ethnicity, time since HIV diagnosis, and stable partner status.($p<0.05$ for all, Table 6.13) There was also evidence of a positive trend between polydrug use and non-adherence to ART ($p<0.001$). Recreational drug use and polydrug use were not significantly associated with VL non-suppression on ART in unadjusted or adjusted analyses. This was also the case for higher alcohol consumption and evidence of alcohol dependency. The magnitude of associations between each measure of alcohol misuse (WHO-AUDIT-C versus CAGE) and non-adherence to ART was similar.

Table 6.13: Associations of recreational drug use, polydrug use, higher alcohol consumption, evidence of alcohol dependency and non-adherence to ART and VL non-suppression (N=1888 MSM on ART)

	Non-adherence to ART (n/N=183/1888)†				Viral load non-suppression* (n/N=172/1744)			
	row N	row %	PR [95%CI]	aPR[95%CI]	row N	row %	PR [95%CI]	aPR[95%CI]
Recreational drug use								
No	947	6.8	1.0	1.0	880	9.0	1.0	1.0
Yes	941	12.6	1.9 [1.4,2.5]	1.7 [1.2,2.2]	864	10.8	1.2 [0.9,1.6]	1.1 [0.8,1.4]
p-value			*<0.001*	*0.001*			*0.212*	*0.690*
Polydrug use								
No drugs	947	6.8	1.0	1.0	880	9.0	1.0	1.0
1 drug	320	10.0	1.5 [1.0,2.2]	1.3 [0.8,1.9]	291	9.6	1.1 [0.7,1.6]	1.0 [0.7,1.5]
2-4 drugs	435	13.3	2.0 [1.4,2.8]	1.8 [1.3,2.6]	407	9.6	1.1 [0.7,1.5]	0.9 [0.6,1.3]
≥5 drugs	186	15.6	2.3 [1.5,3.5]	2.0 [1.3,3.1]	166	15.7	1.7 [1.2,2.6]	1.6 [1.0,2.4]
p-value(T)			*<0.001*	*<0.001*			*0.055*	*0.266*
Higher alcohol consumption (WHO AUDIT-C)‡								
No	1581	8.6	1.0	1.0	1468	9.4	1.0	1.0
Yes	307	15.3	1.8 [1.3,2.4]	1.8 [1.3,2.5]	276	12.3	1.3 [0.9,1.9]	1.3 [0.9,1.9]
p-value			*<0.001*	*<0.001*			*0.133*	*0.109*
Evidence of alcohol dependency (CAGE)◊								
No	1540	8.7	1.0	1.0	1411	9.2	1.0	1.0
Yes	348	14.1	1.6 [1.2,2.2]	1.6 [1.1,2.1]	332	12.3	1.3 [1.0,1.9]	1.3 [0.9,1.8]
p-value			*0.002*	*0.004*			*0.082*	*0.174*

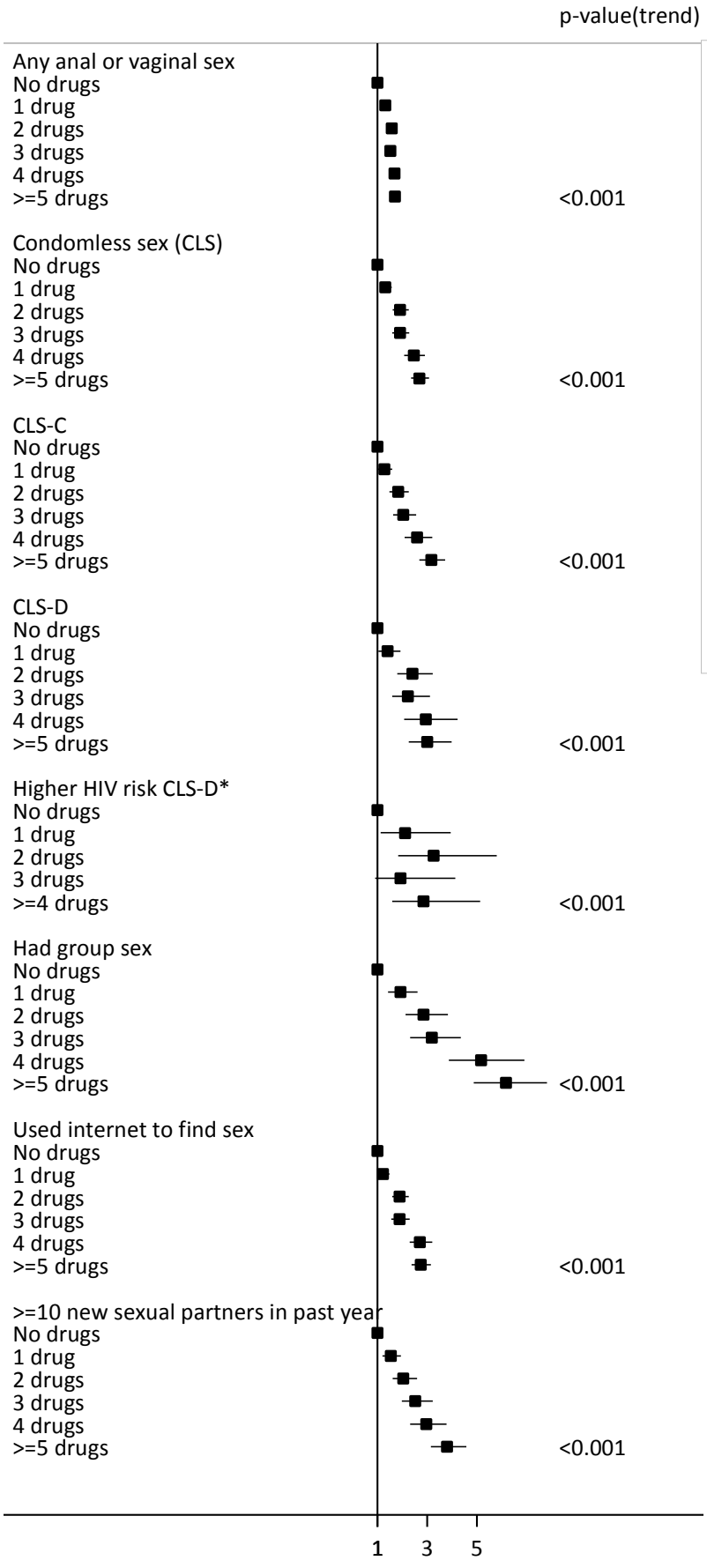
*†Missed ≥2 consecutive days of ART on ≥2 occasions in the past three months; *Study log-recorded VL>50c/mL among MSM on ART for≥6 months; ‡ modified WHO-AUDIT score ≥6 (first two questions only); ◊ CAGE questionnaire score ≥2; p-values by Wald test and, for polydrug use, by test for trend; PR: prevalence ratios; aPRs: adjusted for age, ethnicity, time since HIV diagnosis, stable partner status.*

6.4.5 **Sensitivity analyses**

In sensitivity analysis 1, the association between polydrug use and measures of sexual behaviour was examined in models adjusted for core factors, clinic, employment, and religion. (Figure 6.10) The range of adjusted PRs for MSM using 1 to ≥5 drugs compared to MSM who did not use any drugs was very similar to those observed in the main analysis adjusted for core factors only (Figure 6.3). In sensitivity analysis 2, the association between polydrug use and sexual behaviours was examined in models adjusted for core factors, clinic, education, and religion. (Figure 6.11) The range of adjusted PRs for MSM using 1 to ≥5 drugs was identical to those observed in sensitivity analysis 1.

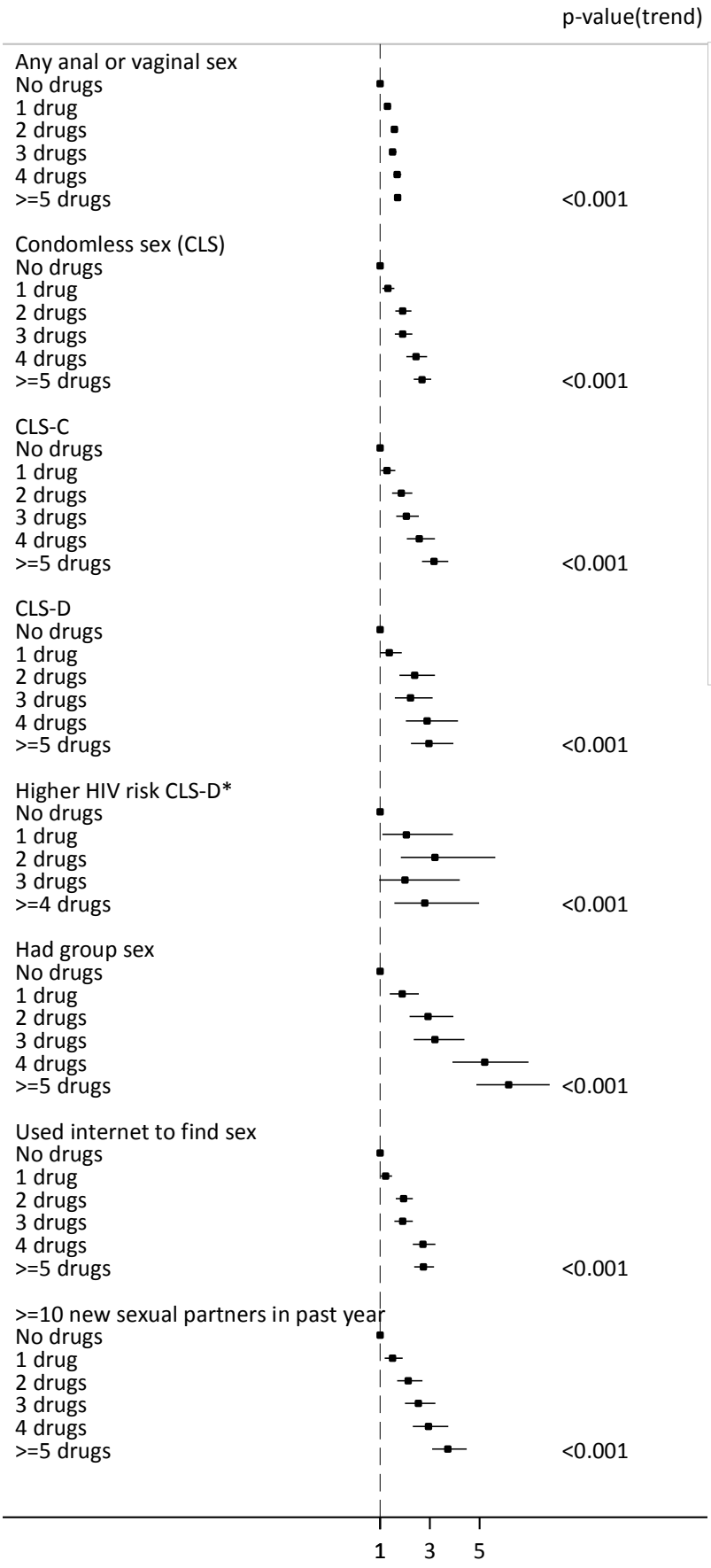
In sensitivity analysis 3 the aim was to examine the magnitude of associations of polydrug use and sexual behaviours using logistic regression to derive odds ratios (ORs), rather than prevalence ratios. (Figure 6.12) From this figure, it is more meaningful to compare the magnitude of associations between the different sexual behaviour measures. Increasing polydrug use was more strongly associated with CLS-C, group sex, use of the internet to find sex, and >=10 new sexual partners, compared to CLS-D, higher HIV risk CLS-D and other STI diagnosis. After adjustment for core factors the range of ORs for MSM using 1 to ≥5 drugs compared to MSM who did not use drugs was: 2.0 to 10.3 for any anal or vaginal sex; 1.6 to 9.4 for any CLS; 1.4 to 11.4 for CLS-C; 1.5 to 3.8 for CLS-D; (from 1 to ≥4 drugs) 2.5 to 3.1 for higher HIV risk CLS-D; 1.3 to 3.5 for other STIs; 2.1 to 13.7 for group sex; 1.3 to 7.9 for use of the internet to find sex; and 1.7 to 9.1 for ≥10 new sex partners in the past year.

Figure 6.10: Sensitivity analysis 1: Associations of polydrug use in the past three months and sexual behaviours, adjusted for core factors, employment, religion, and clinic (N=2189 MSM).



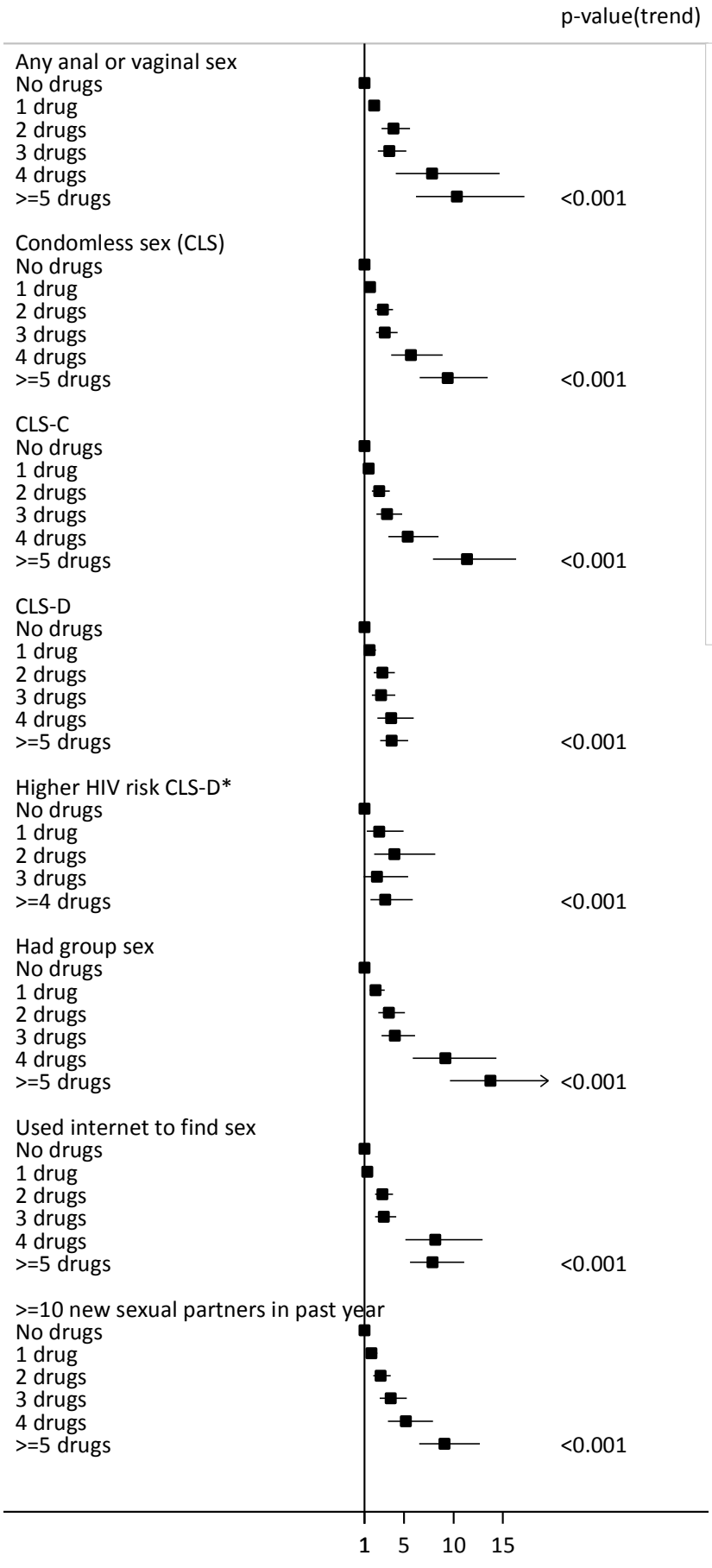
*Prevalence Ratios [95%CIs] by modified Poisson regression models adjusted for age, ethnicity, time since HIV diagnosis, stable partner status, ART status, employment, religion, and clinic. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partners; CLS-D: CLS with HIV-serodifferent partners; *Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL; Collapsed drug use categories due to lower prevalence of this measure; Model for higher HIV risk CLS-D does not include adjustment for ART. STI: sexually transmitted infection.*

Figure 6.11: Sensitivity analysis 2: Associations of polydrug use in the past three months and sexual behaviours, adjusted for core factors, education, religion, and clinic (N=2189 MSM).



Prevalence Ratios [95%CIs] by modified Poisson regression models adjusted for age, ethnicity, time since HIV diagnosis, stable partner status, ART status, education, religion, and clinic. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partners; CLS-D: CLS with HIV-serodifferent partners; Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL; Collapsed drug use categories due to lower prevalence of this measure; Model for higher HIV risk CLS-D does not include adjustment for ART. STI: sexually transmitted infection.*

Figure 6.12: Sensitivity analysis 3: Odds ratios [95%CIs] for associations of polydrug use in the past three months with sexual behaviours (N=2189 MSM) †



Odds Ratios [95%CIs] by logistic regression models adjusted for age, ethnicity, time since HIV diagnosis, stable partner status, ART status. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partners; CLS-D: CLS with HIV-serodifferent partners; Higher HIV risk CLS-D: CLS-D plus not on ART or latest study log VL>50c/mL; Collapsed drug use categories due to lower prevalence of this measure; Model for higher HIV risk CLS-D does not include adjustment for ART status. STI: sexually transmitted infection. †For denominators see Table 6.9*

6.5 Discussion

6.5.1 Summary of findings

In this large, multicentre cross-sectional study of 2189 HIV-diagnosed MSM, half of the men surveyed had used recreational drugs and almost a quarter had used at least three types of drugs in the past three months. Over 15% of MSM had used chemsex-associated drugs and less than 3% injected drugs. Drug use and polydrug use were significantly associated with younger age, higher educational attainment, current employment, higher alcohol consumption, and having an HIV-positive stable partner. In particular, among MSM who used drugs, use of chemsex-associated drugs was more prevalent among MSM who were younger, employed, had university degree, and an HIV-positive stable partner. There were strong and consistent associations between increasing numbers of drugs used and increasing prevalence of all types of CLS (including with HIV-serodifferent or HIV-seroconcordant partners) as well as with higher HIV transmission risk CLS-D, group sex, high partner numbers, low condom self-efficacy, and lower condom use with casual partners. Among MSM who reported any anal or vaginal sex in the past three months, increasing polydrug use remained significantly associated with higher prevalence of any CLS, CLS-C, and CLS-D; the association with higher HIV risk CLS-D was attenuated. Compared to MSM having condom-protected sex, polydrug use was most prevalent among MSM who had 'CLS-C without CLS-D', as well as those who had CLS-D. Chemsex-associated drugs were more prevalent among MSM who had CLS-C, while nitrites were more prevalent among those who had CLS-D. Higher alcohol consumption was associated with higher prevalence of CLS-D and of higher HIV risk CLS-D, independently of recreational drug use. While drug and polydrug use, higher alcohol consumption, and evidence of alcohol dependency were significantly associated with non-adherence to ART, there was no significant association with VL non-suppression.

6.5.2 Prevalence and patterns of recreational drug use among HIV-diagnosed MSM

Almost 51% of MSM in ASTRA had used any recreational drug in the past three months, similar to estimates from earlier UK HIV clinic studies (Internet & HIV[151] and Guys and St.Thomas' clinic[352]), which measured prevalence during the same recall window. Direct comparison to other studies (Table 6.2) is not straightforward due to different recall periods, but there is evidence of a substantial prevalence of drug use from all studies of HIV-diagnosed MSM, ranging from 55.8% to 66.5% in the past year[290,341] and as high as 83.9% in the past six months.[313]

The pattern of most commonly used drugs in ASTRA mirrors that observed in earlier studies of HIV-diagnosed MSM from the USA, Western Europe, and Australia,[287,290,297,301,308,313,315,316] with nitrites, cannabis, EDDs, and cocaine being most prevalent, and opioids being least prevalent. However, ASTRA is the only UK study to date to report on mephedrone, used by 7.1% of all MSM (14% of all drug-using MSM). Evidence regarding this particular drug began to accumulate in 2015/2016 (more than three years after ASTRA concluded recruitment), when qualitative studies and community organisations reported use of mephedrone among MSM in sexual settings (chemsex).[278,321,354] In the 2014 GMSS, prevalence of mephedrone use among all MSM (mixed HIV-serostatus) in the past month was 5.3%.[144]

By comparison, among 1484 HIV-negative or undiagnosed MSM recruited to the AURAH study from GUM clinics in the UK (2013-14), prevalence of mephedrone use was 19.1% in the past three months.[355] Previous comparable data on specific drugs used among HIV-diagnosed MSM in the UK derive predominantly from the 2002-2003 'London Gyms' study, which surveyed HIV-negative and HIV-positive MSM at gyms and outpatient clinics (see Table 2.1); prevalence of recreational drug use in the previous year in the HIV-diagnosed outpatient sample (N=388) was 54%.[289] It is possible to informally compare use of specific drugs in the previous three months among ASTRA MSM from London clinics only (N=1482) to drug use in the past month ('once-twice per month') among MSM in the 'London Gyms' HIV outpatient sample. Prevalence of the following drugs was higher in ASTRA compared to 'London Gyms': methamphetamine (10% versus 4%), cocaine (23% versus 18%), and IDU (in the past 12 months: 4% versus 1%); prevalence was similar for ketamine (12% versus 13%) and amphetamine (3% versus 2%); and prevalence of ecstasy use was lower in ASTRA (11% versus 17%).[289] The 'London Gyms' study did not collect information on GHB/GBL and mephedrone. This may suggest changing patterns of drug use among HIV-diagnosed MSM, with possible increases in methamphetamine and IDU, which would be consistent with anecdotal reports of patterns in drug use, and an increase in use of chemsex drugs. Overall, comparisons are not straightforward due to different recall periods for drug use, potential confounding factors in the comparison, and lack of data from other comparable studies in the UK.

Over a third of MSM in ASTRA reported using two or more drugs (almost a quarter used three or more) in the past three months. Estimates on prevalence of polydrug use also range widely due to different definitions and locations of recruitment. Four studies from the USA and Australia have reported on prevalence of polydrug use among HIV-positive MSM (Table 6.2); only one recruited MSM attending for HIV care in clinics (SUMIT trial),[309,310] while the rest recruited HIV-positive MSM from gay venues,[287,297,308] which tend to over-represent MSM who report 'sensitive' behaviours (such as polydrug use and CLS).[356] For instance, polydrug use (defined here as using three or more drugs) was reported by 2.2% of SUMIT participants in the past three months and by 44.0% of Sydney Gay Community Periodic Survey (GCPS) participants in the past six months.[287] There are even fewer studies of polydrug use among representative samples of HIV diagnosed MSM in the UK. Polydrug use was common among men who used recreational drugs in the 'London Gyms' study; over 90% of the 49 HIV-diagnosed MSM who used methamphetamine during the previous year had used at least one other drug during this time, and over 80% of the 162 cocaine users had used other drugs.[289] In ASTRA, although there is no information on the timing of use of different drugs, the high prevalence of polydrug use in the previous three months (over a fifth of MSM were using five or more drugs) is concerning, especially in light of potential drug-drug interactions (DDIs) between recreational drugs (e.g. EDDs and nitrites[357]), with alcohol (e.g. GHB and alcohol[317]), and the potential for polydrug use to interfere with the effectiveness of antiretroviral drugs.[318]

Injection drug use (IDU) was overall low in ASTRA (3%), but higher than that observed among HIV-diagnosed clinic attendees in the 'London Gyms'.[289] Prevalence of IDU was much higher in the past six

months in the Australian Positive Health[313] and GCPS surveys compared to ASTRA (4.4% and 14.2% respectively).[296] Although the ASTRA questionnaire did not enquire about injection of specific drugs, significant associations were observed between any IDU and use of chemsex-associated drugs (especially methamphetamine), EDDs, and polydrug use.

6.5.3 Factors associated with recreational drug use

In ASTRA, recreational drug use was more prevalent among MSM who were younger (particularly those under 30 years), a finding also observed in two previous studies in Australia[313,324] and the USA.[311] This was also the case for EDDs (27.1% of MSM under 30 years used EDDs compared to 14.5% of those 60 or older), which were also more prevalent among older MSM (over 45 years) in the SUMIT trial.[310] In ASTRA, polydrug use was highest in the under 30's group. The prevalence of any drug use mirrors that observed in the general UK population, whereby young adults have three times the prevalence of last year drug use compared to older adults (≤25 versus >25 years).[277,358]

Alcohol misuse was also strongly associated with recreational drug use. This finding was expected, as drug and alcohol use frequently co-occur. High prevalence of 'excessive' alcohol use is commonly reported among MSM, but estimates vary considerably due to different modes of reporting. In ASTRA, 17% of MSM were classified as having higher alcohol consumption (score of ≥6 on the first two questions on the WHO-AUDIT-C) and 19% as having alcohol dependency (≥2 on the CAGE questionnaire). The reported prevalence of alcohol drinking among HIV-diagnosed individuals varies widely, from 40% to 82% for any and 3% to 35% for severe/harmful alcohol consumption.[331,359–362] Definitions of alcohol misuse are usually based on units of alcohol consumed, which also vary by county (e.g. one unit is equivalent to 14g of pure alcohol in the US compared to 8g in the UK). Despite the difference in prevalence, there was a significant association between both measures of alcohol misuse and recreational drug use, which has also been observed in previous studies.[313,360,363–365]

In addition, MSM who had a stable HIV-positive partner were more likely to report any drug use and polydrug use in ASTRA. This finding has not been previously reported, as earlier studies reported on partner status (casual or long-term) rather than incorporate stable partners' HIV-serostatus. For instance, in the Australian Positive Health cohort[313] (2004-05) HIV-diagnosed MSM were more likely to have used drugs in the past six months if they were not in a monogamous relationship, compared to being in an open relationship or having casual partners only.

Markers of socio-economic status (SES), such as higher educational attainment and current employment were not associated with any drug use. However, among MSM who used drugs, higher SES was independently associated with polydrug use and chemsex drug use. Two US studies of HIV-diagnosed MSM found that use of EDDs and nitrites was higher among those with higher education,[309,310,314] but no associations have been reported yet with polydrug use. Studies of all MSM (regardless of HIV-serostatus), such as the GMSS, have also reported that university degree and full-time employment are associated with any drug use.[327] The opposite effect was observed in the UK AURAH study, as HIV-

negative or undiagnosed MSM with lower SES (lower educational attainment and higher financial instability) were more likely to report polydrug and chemsex-associated drug use in the past three months.[355] It is unclear whether the association of higher SES and polydrug use would be observed in smaller or suburban gay populations compared to the large populations with a vibrant 'gay scene' concentrated in London, Brighton, and Manchester, which recruited men to ASTRA. Polydrug use may require higher disposable income due to the high cost of multiple drugs, which could explain the association with higher SES.

Symptoms of depression and anxiety were not associated with drug use.[313,366] In the Australian Positive Health survey there was also no association of drug use with measures of "mental or emotional wellbeing".[313] On the other hand, in the AURAH study of HIV-negative or undiagnosed MSM, polydrug and chemsex-associated drug use were significantly more prevalent among MSM with symptoms of depression and anxiety compared to those without.[355] Overall, drug use is more prevalent among MSM than age-comparable non-MSM populations, which has been hypothesized to be in part due to complex reasons associated with emotional wellbeing. These include coping with interpersonal prejudice or discrimination (minority stress) or HIV-related stress and stigma[190], internalised homophobia or negative feelings of self-worth with deeper sources[259], as well as the positive effect of drugs on displacing anxieties on self-esteem and body image by boosting confidence[367]. In our study, drug use was not incompatible with good mental health, which may indicate that drug use is perceived as a positive way to engage with the gay and HIV-positive community. However, any such hypothesis could not be extrapolated from our data and qualitative studies are best suited to generate theories on motivations behind drug use.

6.5.4 **Recreational drug use and sexual behaviour**

In this study, recreational drug use and particularly polydrug use were associated with being sexually active and more strongly associated with all measures of CLS, independently of socio-demographic and HIV-related factors. Drug use was also strongly associated with other STIs, group sex, greater numbers of sexual partners, and low condom self-efficacy. Although a minority of HIV-diagnosed MSM reported CLS-D (16.3%) and even fewer fulfilled criteria for CLS-D that could confer a higher risk of HIV transmission (4.3%), increasing polydrug use was independently associated with an increasing trend in prevalence of both CLS-D measures. Among MSM who had any anal or vaginal sex in the past three months, use of methamphetamine, EDDs, and nitrites was strongly associated with CLS-D (including higher HIV risk CLS-D) and CLS-C, and MSM who used these drugs had higher prevalence of CLS-D than MSM using other common drugs (such as cannabis and cocaine). Previous cross-sectional studies have found associations between use of methamphetamine and CLS-D among HIV-diagnosed MSM in the USA[283,305,329,330,340,366,368,369] and the UK,[289,300,351] but none have incorporated VL level in their measures.

Trends of increasing prevalence of sexual behaviour measures with increasing polydrug use were strongest for CLS-C, group sex, and higher number of new partners. Among MSM who used drugs and had any CLS in the past three months, chemsex-associated drug use (and particularly

methamphetamine) was more prevalent among MSM who had CLS-C compared to those who had CLS-D; the opposite pattern was observed for nitrites. Use of odds ratios allowed for comparison of the magnitude of associations between polydrug use and multiple sexual behaviours, showing that the odds of having CLS-C and group sex were 11-fold and 13-fold greater respectively among MSM who used five or more drugs compared to those who did not; these odds ratios were considerably greater than those associated with CLS-D measures. Similarly associations of chemsex drug use were stronger for CLS-C than CLS-D. Coupled with evidence that, among drug users, chemsex-associated drug use was linked to having an HIV-positive stable partner and not being on ART, it could be hypothesized that some HIV-positive MSM may engage in group chemsex sessions and CLS with other HIV-positive partners. This may be circumstantial, a sexual preference, or a decision to reduce HIV transmission risk to HIV-negative partners (serosorting). The strong link between chemsex and CLS-C is in line with the qualitative chemsex study in London (2013), in which two thirds of men who had chemsex were HIV-diagnosed and had made pre-determined decisions to have CLS-C.[259] While there is no risk of HIV transmission during CLS-C, such seroadaptive practices facilitate transmission of other STIs, as evidenced by recent outbreaks of other STI epidemics among HIV-diagnosed MSM who report chemsex with other HIV-positive partners (discussed in chapter 8).[370]

The difficulties in attributing a causal relationship to the associations between recreational drug use and higher risk sexual behaviours in cross-sectional studies have been well documented. Evidence from prospective studies suggests a causative link between methamphetamine use and HIV seroconversion. Certain case-control[367] and cohort studies[341,371,372] have accounted for increasing number of CLS partners in the association of methamphetamine use and HIV seroconversion. For example, in the MACS study[341], a joint dose-response relationship of methamphetamine use and increasing number of CLS receptive partners was observed (relative hazard of HIV seroconversion ranged from 2.7 for recent methamphetamine users with one partner to 13.6 for ≥5 partners), which is not surprising. However, the 2.7-fold increased risk of HIV seroconversion associated with methamphetamine use with *only one* CLS receptive partner is noteworthy, as it shows that methamphetamine use increases the risk of HIV acquisition over and above the risk of increasing numbers of CLS partners. A retrospective analysis of recreational drug use among HIV-negative MSM enrolled in an HIV screening programme in the USA (2008-14) showed that men who started using methamphetamine between visits (and had never used it previously) were significantly more likely to report higher prevalence of receptive CLS with HIV-positive partners and overall increased number of sex partners.[371] The temporal relationship shown in this study provides strong evidence that initiation of methamphetamine use may increase sexual risk behaviour among HIV-negative MSM. Causal links between drug use and CLS may in part be explained by sexual disinhibition, higher libido, altered mental state, and reduced ability to experience pain conferred by drug use (and chemsex-associated drugs in particular); these effects could in turn lead to low condom self-efficacy, and increased risk of physically traumatic sex. Drug use could also lead to increased duration of sexual contact or increased number of partners, factors which may themselves result in greater likelihood of, or amount of, CLS. On the other hand, the association may not be causal, as

recreational drug use could be a marker of 'risky' or sensation-seeking/impulsive personal characteristics, which have been associated with both drug use and CLS.[305] Drug use could be a mediator in the pathway between impulsivity and CLS.

There is a need for longitudinal, episode-level studies comparing times in which drugs have or have not been used during episodes of CLS in the same individual; these could provide more evidence on temporality and causality. Irrespective of causal attributions, this ASTRA analysis demonstrates that polydrug use and CLS are strongly linked among HIV-diagnosed MSM in the UK, and that polydrug users are likely to be a group at possible risk for transmission of HIV and other STIs.

6.5.5 Associations of alcohol misuse, recreational drug use, and sexual risk behaviours

The association between alcohol misuse and sexual risk behaviours has not been well studied among HIV-diagnosed MSM in the UK. A recent systematic review of 27 US studies among HIV-diagnosed men and women found significant associations between three measures of alcohol use (any alcohol consumption, problematic drinking, and alcohol consumption in sexual settings) and higher prevalence of any CLS.[373] The majority of these studies, however, did not differentiate gender/sexual orientation or perform adjusted analyses (e.g. for recreational drug use), thus not accounting for possible mediating factors. As with recreational drug use, any association between alcohol misuse and higher risk sex is complex and not necessarily causative. Alcohol intoxication can have disinhibitory effects which could reduce condom self-efficacy, but other factors (such as drug use, sensation seeking/impulsivity[374]) might predispose individuals to both alcohol misuse and CLS.[116]

In ASTRA, higher alcohol consumption (measured by the WHO-AUDIT-C) was independently associated with CLS-D and higher HIV risk CLS-D, even after adjustment for core factors and recreational drug use. The association with higher HIV risk CLS-D may in part be driven by not being on ART or having detectable VL. There was no significant association of alcohol consumption with other measures of sexual behaviours (including CLS-C). Evidence of alcohol dependency (measured by the CAGE questionnaire) was not associated with any sexual behaviour in unadjusted or adjusted analyses. The discrepancy between the two alcohol measures in associations with CLS may be due to the screening tools themselves. While the CAGE is valid for detection of alcohol dependence in inpatients, the AUDIT is able to screen for less severe forms of drinking.[217] Poorer mental or physical health status may be associated with both lower prevalence of alcohol use and of any sex; hence, inclusion of those with lower alcohol consumption (on the AUDIT) in the comparison could have inflated the effect sizes between alcohol consumption and CLS-D.

6.5.6 Recreational drug use and ART outcomes

In this study, both recreational drug use and alcohol misuse were associated with non-adherence to ART, independently of core socio-demographic and HIV-related factors. This finding is consistent with previous research demonstrating the significant role of alcohol misuse in lower adherence to ART,[116,375]

and adds to the limited published literature[376] linking drug use and non-adherence. No association was observed between drug use, alcohol misuse, and VL non-suppression in ASTRA (although there was some suggestion of a weak association between polydrug use, alcohol misuse, and lower prevalence of suppressed VL in unadjusted analyses, and confidence intervals were relatively wide). Hence, it is important to note that 87% of HIV-diagnosed MSM on ART who used recreational drugs and 83% of those on ART who used five or more drugs had suppressed VL, demonstrating that drug use is not incompatible with good ART adherence.

6.5.7 **Limitations**

The findings from this study must be interpreted in light of limitations. Under-reporting of drug use and specific sexual behaviours is possible and could have led to underestimation of prevalence, or bias in assessing associations. For example, in the 'London Gyms' study, among HIV-positive MSM, the prevalence of drug use was lower among those recruited from HIV outpatient clinics compared to those recruited from social venues (gyms, clubs, saunas).[289]This may mean that the true prevalence of drug use among HIV-diagnosed MSM in the UK is higher than that reported in ASTRA, which is also a clinic sample.

It was not possible to examine chemsex per se, as the questionnaire enquired about use of chemsex-*associated* drugs (GHB/GBL, mephedrone, methamphetamine) in the past three months rather than specifically use before or during sex. Similarly, the questionnaire examined IDU overall rather than injection of specific drugs. The temporality of associations between drugs and sexual behaviours cannot be ascertained due to the cross-sectional study design. At the time of ASTRA recruitment (2011-2012), new psychoactive substances (NPS), such as methoxetamine and mephedrone, were not yet controlled under the UK Misuse of Drugs Act 2016, and some NPS were later reclassified into more serious offenses (e.g. ketamine was moved to class B in 2014). As a result, trends in drug use may have changed since ASTRA was completed, with possible increases in IDU, chemsex, or newer drugs. Analyses on the association of polydrug use and higher HIV risk CLS-D were underpowered, but categories were collapsed to account for this.

Despite its limitations, ASTRA is the largest questionnaire study of HIV-diagnosed MSM in the UK to date, and was the first to provide estimates on the prevalence of recreational drug and polydrug use in the UK since the 2002 'London Gyms' study. A further strength of the study is the comprehensive information collected on self-reported polydrug use (as well as mephedrone and GHB use specifically) and recent sexual behaviour.

6.5.8 **Conclusion & Implications**

In conclusion, among HIV-diagnosed MSM in the UK, recreational drug use and polydrug use are prevalent, and strongly associated with CLS and multiple new sexual partners. These findings have implications for clinical care, HIV/STI prevention, and epidemiological research. There is ongoing need to prioritise harm reduction services that meet the needs of HIV-diagnosed MSM who use recreational

drugs. Cross-agency collaboration between HIV treatment and substance misuse services may be beneficial in providing tailored, judgment-free harm reduction advice and support to HIV-diagnosed MSM who use recreational drugs, particularly given the reported rise in injection drug use linked to chemsex. All HIV-diagnosed MSM, and particularly younger men, may benefit from support and awareness of the side-effects of drug use, particularly when combined with multiple other drugs, alcohol, or with ART regimens. Peer-led interventions may also be productive in outreach among HIV-diagnosed men who are polydrug users and have multiple sexual partners. National STI and HIV prevention strategies should address recreational drug use and alcohol-related issues. Toolkits for effective interventions in various settings are needed.

More research is needed in understanding the drivers of polydrug and chemsex use and the variations in drug use among MSM in local areas, accounting for change over time. Future epidemiological research could benefit from polydrug use profiles (or polysubstance use when accounting for alcohol) that incorporate measures of frequency and severity, rather than focusing on binary measures of drug use. There remains a need for longitudinal, within-subject studies of drug use, comparing episodes of CLS during which drugs were or were not used. Such designs allow for better understanding of the temporality and direction of associations, and may therefore provide further evidence on causality.

The extent and implications of chemsex have yet to be studied, as it is a relatively new phenomenon. The facilitators of chemsex are likely to be both technological and structural. The migration towards NPS could be due to the internet and geosocial networking applications (which display information on the geographic location of a user relative to others) facilitating the development of online drug marketplaces[377] and thus more accessible sex. The impact of smartphone apps in sourcing NPS and facilitating chemsex, however, remains unknown.

Finally, it is important to avoid sensationalising drug use and sexual behaviour in research and the media, as this could lead to stigmatisation and marginalisation of HIV-diagnosed MSM.[378]

7 Non-disclosure of HIV-serostatus and condomless sex

7.1 Chapter aims

This chapter aims to investigate, among HIV-diagnosed MSM from ASTRA, non-disclosure of HIV serostatus to a stable partner and non-disclosure in a sexual context. A review of literature is conducted with a focus on studies from high income countries since the introduction of ART, examining various constructs of non-disclosure, the prevalence of non-disclosure in social settings and to sexual partners, factors associated with non-disclosure to stable or new sex partners, and associations between non-disclosure (to stable or new partners) and sexual behaviours. The aims of the analyses are to examine, among ASTRA MSM: (i) the prevalence of non-disclosure according to confidant, (ii) associations of socio-demographic, psychological, HIV-related factors with non-disclosure to a stable partner, (iii) prevalence of lower HIV-serostatus disclosure to new sexual partners, (iv) socio-demographic, psychological, HIV-related factors associated with lower sexual disclosure, and (v) associations of non-disclosure to a stable partner and lower sexual disclosure with specific sexual behaviours, including condomless sex (CLS). The prevalence of social disclosure overall is included in order to provide context to the results regarding stable and sexual partners.

7.2 Introduction

Disclosure of HIV-serostatus refers to the situation in which an HIV-diagnosed individual tells someone else that they have been diagnosed with HIV. Conversely, non-disclosure refers to not to telling someone else of one's HIV-positive diagnosis. Disclosure itself can be a difficult decision, balancing risks and benefits. In addition, choosing who to disclose to (family, friends, employers and co-workers, stable long-term partners or spouses, casual sexual partners) has different motivations and implications, and depends on the nature of the relationship with each confidant. Disclosure to family and friends may provide closeness in relationships, which in turn could help in overcoming a diagnosis which may be more complex than other chronic conditions.[379] Disclosure to a stable partner or casual sexual partners carries different implications given potential consequences for HIV transmission.

Studies have focused on disclosure as a means of obtaining social and psychological support for the HIV-positive individual and also as a public health prevention tool in reducing HIV transmission to sexual partners. However, a causal link between disclosure and condom use (or conversely non-disclosure and CLS) is difficult to establish from observational studies. In fact, various intervention studies have been efficacious in increasing disclosure to sexual partners, but whether this had any effect on reducing the prevalence of CLS remains uncertain.[380] Disclosing to a sex partner is not necessarily sufficient in promoting HIV risk reduction behaviours, and additional communication about specific sexual behaviours (such as using condoms, positioning during CLS with HIV-serodifferent partners (CLS-D), and ejaculation inside a serodifferent partner among others) may be relevant as well. Since the publication of conclusive evidence on the extremely low risk of HIV transmission when the HIV-positive partner is on

virally suppressive ART,[9] the role of non-disclosure to sexual partners (including casual and stable partners) remains unclear. There is scarce recent information on attitudes to disclosure of HIV-status to new sexual partners among UK MSM, and whether this may be influenced by knowledge of viral load (VL) status. In addition, the relationship between HIV serostatus non-disclosure and sexual risk behaviour remains inconsistent across studies.

7.2.1 Non-disclosure in the social context

This section reviews literature on non-disclosure to family, friends, and other social settings (such as the workplace) with a focus on prevalence estimates among HIV-diagnosed MSM in high income countries (North America, Western Europe including the UK, Australia) since the introduction of widespread ART (1996-2016).

7.2.1.1 Barriers to HIV-serostatus disclosure

Expectations of negative reactions and consequences constitute significant disincentives to disclosure of HIV-serostatus. These barriers include the lack of a social network, fears of stigma, ostracism, and abuse, subsequent disclosure of stigmatised behaviours (sexual orientation, injecting drug use), conflicts with a partner, potential loss of social support, and breach of confidentiality.[236,381–385] The need to not burden family with one's health issues has also been a deterrent of disclosure.[382,386] Additionally, the HIV-positive person may take time to come to terms with their diagnosis, or may feel their health is a private matter.[386,387]

In the UK, the *Equality Act 2010* makes it unlawful to discriminate against people living with HIV in the workplace.[388] Employers must make adjustments to assist HIV-diagnosed people in their work (such as allowing time away from work to attend clinic appointments) and protect personal sensitive information. However, in order to benefit from the *Act*, people living with HIV must disclose their status to their employer. Fears of being discriminated against at work or of losing employment constitute substantial barriers to disclosure in the workplace. Taken together, the host of psychosocial and legal barriers contribute to choosing not to disclose one's HIV serostatus.

7.2.1.2 Prevalence of non-disclosure

Various constructs of non-disclosure have been used across study settings. These include the number or proportion of people disclosed to[389], levels of disclosure[199,390,391] (never, sometimes, always disclose), mean scores on attitudinal questions derived from Likert scales (for example, "I have disclosed to (insert number) of friends/family")[392], and more commonly, as a binary concept of either disclosed to at least one other person, or not disclosed to anyone.[393,394] Research shows that the prevalence of non-disclosure of HIV-serostatus in a social context (family, friends, and work colleagues) varies by socio-demographic and HIV-related factors of individuals surveyed. Overall, evidence from Western Europe and the USA suggests that MSM tend to report lower prevalence of non-disclosure in the social context compared to heterosexual individuals, regardless of confidant.[133,395,396]

While there have been numerous studies examining non-disclosure in the social context (family, friends), many do not differentiate participants' sexual orientations and so prevalence estimates of non-disclosure cannot be disaggregated for MSM.[236,385,393,396–398] As summarised in Table 7.1, few studies from high-income countries have measured non-disclosure in the social context among HIV-outpatient clinic attendees; data are particularly scarce from MSM in the UK. Overall, a minority of HIV-diagnosed MSM report non-disclosure to anyone in these studies, with prevalence higher among ethnic minorities.[386,391,399,400] In two earlier UK studies with similar study populations and recruitment methods as ASTRA (see Table 2.1), prevalence of non-disclosure to anyone in the social context among MSM was 2.4% in the 'East London' study[394] (2004-2005) and 4.9% in the 'Switching Study'[114,133] (2005-2006).

Non-disclosure in the workplace is a not well-studied and the effect it could have on a person's psychological wellbeing remains unclear. In the 'East London' study, the vast majority of MSM in employment did not disclose in the workplace, with non-disclosure being much higher towards employers than colleagues.[394](Table 7.1) In addition, white MSM were more likely to disclose to colleagues compared to ethnic minority MSM in this study.

7.2.1.3 Correlates of non-disclosure

There is some evidence that belonging to a racial/ethnic minority is associated with higher prevalence of non-disclosure in the social context among MSM in UK and US studies.[379,394,395,398,401] The HIV-diagnosed person's age may also play a role in deciding whether or not to disclose; in the 'East London' study, non-disclosure was associated with older age for MSM.[394] No association was found in the US study of 362 young (<24 years) racial minority MSM not in care.[386] Disclosure to friends and family could be a gradual process that evolves over time. Evidence of this gradual effect with time since receiving an HIV diagnosis was shown in the 'East London' study, and also in a US longitudinal clinic study of 135 white MSM, in which disclosure to parents increased over a period of 15 years (from less than 30% to over 65%).[402] Factors not shown to be consistently associated with non-disclosure in the social context include socio-demographic (education, financial status) and HIV-related measures (ART status, adherence to ART, lab-confirmed VL, and perceived VL).[154,382,398]

Table 7.1: Studies from high income settings on prevalence of non-disclosure in the social context among HIV-diagnosed MSM (2004-2012) ‡

Study	Country	Data collection period	Study setting and recruitment	Population	Definition of non-disclosure measure	Prevalence of non-disclosure measure *	
East London[394]	UK	2004-2005	Cross-sectional questionnaire survey of HIV outpatients receiving care in one of 6 NHS clinics in northeast London.	1407 men and women 740 MSM	"Have you told anyone that you have HIV?" If yes, ‘‘Whom have you told?’’	Non-disclosure to anyone	4.9%
						Not disclosed to parents	61.8%
						Not disclosed to friends	21.2%
						Non-disclosure to employer (n=415 employed)	71.6%
						Non-disclosure to colleagues (n=415)	58.6%
Switching study[114,133]	UK	2005-2006	Cross-sectional questionnaire survey of HIV outpatients receiving care in one of 5 NHS clinics in London and South east England.	778 men and women 496 MSM	Participants indicated whether they had friends or family members and whether disclosed to each of those. Proportion of friends and family not disclosed to was calculated (total number of people not disclosed to/ total number identified within each relationship)	Non-disclosure to anyone	2.4%
Atlanta Clinics[399]	USA	2006-2008	Black minority MSM who were on ART recruited from HIV agencies and organizations in inner-city areas. Must have indicated sex with men at last sex encounter.	156 MSM	Participants indicated whether they had family members and whether disclosed to these family members (proportion of family members not disclosed to)	Non-disclosure to any family members	33.0%
'Young MSM of color initiative'[386]	USA	2006-2009	Young ethnic minority HIV-positive MSM (13-24 years) not currently in care (newly diagnosed or out of HIV care for	362 MSM	Report the persons whom participants disclosed to from a list of options (mother, other relatives, friends etc.)	Non-disclosure to anyone at baseline	3.0%
						Non-disclosure to any family member	23.5%

Study	Country	Data collection period	Study setting and recruitment	Population	Definition of non-disclosure measure	Prevalence of non-disclosure measure *	
			≥6 months) recruited from outreach initiative focused on linkage to care. Face-to-face interview at one of 8 study sites at baseline and 6 months later.			Non-disclosure to friends	39.8%
Project CONNECT [403]	USA	2007-2012	Retrospective analysis of routine data and self-administered questionnaire collected from a cohort of HIV-positive people attending to establish care at HIV clinic (data from first visit)	490 men and women 294 MSM	Disclosure status at initial entry into HIV care: (i) non-disclosure (to no one), (ii) selective disclosure (to only one group of confidants that was mutually exclusive), and (iii) broad disclosure (to >1 group).	Non-disclosure at initial entry into HIV care	12.9%
ANRS-VESPA2 [400]	France	2011-2012	National representative probability sample of HIV-clinic attendees from 73 hospitals. Cross-sectional survey via face-to-face interview using a CASI.	3016 men and women 1180 MSM	Whether disclosed to anyone and if yes, to whom (close family, other relatives, friends, colleagues). Three hierarchical clusters created (high, medium, low).	Low disclosure level	31.4%

Prevalence estimates shown are for HIV-diagnosed MSM in each study only; ART: antiretroviral therapy; CASI: computer assisted self-interviewing; NHS: National Health Service; ‡ Studies detailed in systematic review, section **2.5*

7.2.2 **Non-disclosure to a stable partner**

Non-disclosure of HIV status to stable partners differs from non-disclosure to other close family or friends, as such a partnership usually involves a sexual relationship and thus the potential for HIV transmission. Serostatus disclosure allows the HIV-negative partner to make informed decisions about personal acceptability of risk and any further actions to be taken (such as HIV testing, use of PrEP, or other risk reduction behaviours, if deemed appropriate).[404]

7.2.2.1 Barriers to HIV-serostatus disclosure to stable partner

In this context, decisions about non-disclosure are complicated by factors such as; assumptions or inferences about a partner's HIV status, considerations of the responsibility to disclose to sexual partners, use of HIV risk-reduction strategies (such as seropositioning) instead of disclosure, particularly when the HIV-positive person is on effective ART. Fear of rejection, abuse, and stigmatisation are important disincentives of disclosure to a sexual partner. In addition, considerations about disclosure to casual partners are likely to differ from those for stable or longer-term partners; for example disclosure within a close trusting relationship may be more strongly linked to improved social support.

Another important issue is the potential for legal prosecution in the case of non-disclosure before sex with an HIV-serodifferent partner (regardless of whether or not condoms were used). Since 2001, approximately 30 prosecutions for "reckless sexual transmission of HIV" have been brought in the UK.[405] In England and Wales, the offence applies if the HIV-diagnosed person understands how HIV is transmitted, did not disclose their HIV diagnosis before having CLS, and can be proven to be the source of HIV transmission.[406] These prosecutions undermine the efforts to prevent HIV transmission, raise complex ethical questions, and increase HIV-associated stigma. With conclusive evidence on the extremely low risk of HIV transmission when the HIV-positive partner is on virally suppressive ART[9], disclosure of HIV serostatus to a stable (or otherwise sexual) partner may not be the most relevant HIV prevention effort.

7.2.2.2 Prevalence of non-disclosure to stable partner

Evidence on the prevalence of non-disclosure to a long-term/stable partner among MSM from the UK is limited. Table 7.2 shows the distribution of prevalence estimates of non-disclosure to stable partners in studies of HIV-diagnosed MSM from high-income countries since the introduction of effective ART in 1995. In the 'East London' study, almost 14% of MSM in a stable relationship reported not disclosing to their partner[394], while in the French ANRS-VESPA1 probability sample, only 4.5% had not disclosed.[229] Overall, a number of diverse studies have shown that individuals are more likely to disclose to stable partners compared to casual sex partners.[229,386,396,407–410]

Table 7.2: Summary of studies from high income countries on non-disclosure of HIV-serostatus to stable partners among HIV-diagnosed MSM (2000-2012) ‡

Study /Country/ Data collection period			Study setting and recruitment	Population	Definition of non-disclosure measure	Prevalence of non-disclosure	Prevalence of CLS-D among non-disclosed
Healthy Living Project [408]	USA	2000-2002	Baseline assessment of HIV-diagnosed people recruited from clinics and community agencies participating in an RCT of a cognitive behaviour intervention	742 MSM with a main partner	Non-disclosure to main partner	12.3%	3.3%
Guys & St.Thomas' HIV clinic[304]	UK	2002-2004	MSM with PHI recruited from sexual health services and enrolled in an ART intervention study a median of 7 days post-diagnosis. Electronic questionnaire at baseline and at 12 week follow-up.	52 MSM with a regular partner	Non-disclosure to regular partner	11.5%	66.7%
ANRS-VESPA1[229]	France	2003	National cross-sectional survey among a random stratified sample of HIV-diagnosed people attending HIV clinics. Restricted to MSM with a stable partner for ≥12 months.	285 MSM with a regular HIV-serodifferent partner	Non-disclosure to regular partner	4.5%	35.3%
East London[394]	UK	2004-2005	Cross-sectional questionnaire survey of HIV outpatients receiving care in one of 6 NHS clinics in northeast London.	388 MSM with a stable partner	Non-disclosure to current partner	13.9%	*Not shown*
Latino MSM[195]	USA	2005	Cross-sectional questionnaire study on disclosure by Latino HIV-positive MSM to social networks, recruited from clinics and research sites. Restricted to MSM who had sex in past 12 months.	219 MSM	Non-disclosure to main partner ('had an ongoing intimate sexual and emotional relationship')	19.0%	*Not shown*

Study /Country/ Data collection period			Study setting and recruitment	Population	Definition of non-disclosure measure	Prevalence of non-disclosure	Prevalence of CLS-D among non-disclosed
Adolescent Medicine Trials Network (ATN)[411]	USA	2011	Cross-sectional questionnaire survey of young (16-24) HIV-diagnosed MSM receiving care in clinics in 14 US cities. Restricted to those who had sex with a male partner in past 3 months.	991 MSM	Non-disclosure to current sex partner (not a boyfriend) or to current boyfriend ('someone you knew for a while with whom you have an ongoing relationship')	53.2%	*Not shown*
SAFE Talk[404]	USA	2012	Baseline assessment of 'Safe Talk' RCT evaluating efficacy of motivational interviewing-based safer sex intervention of people in HIV care. This analysis restricted to sexually active with only one partner in past 3 months.	69 MSM	Non-disclosure to current sexual partner	18.8%	30.8%

ART: antiretroviral therapy; CLS-D: condomless sex with an HIV-serodifferent partner (HIV-negative or of HIV-unknown status); NHS: National Health Service; Not shown: study did not provide relevant information; PHI: Primary HIV infection; RCT: randomised controlled trial; ‡Studies described in detail in systematic review, section 2.5.

7.2.2.3 Correlates of non-disclosure to stable partner

A partner's HIV serostatus has consistently been shown to be a significant correlate of non-disclosure to stable and casual sexual partners for MSM; highest proportions of non-disclosure have been observed towards partners of unknown HIV-serostatus, followed by lower proportions of non-disclosure towards known HIV-negative partners, and lowest non-disclosure (i.e. highest prevalence of disclosure) towards known HIV-positive partners.[167,236,407,408,412] This finding may reflect the dynamics of mutual disclosure of HIV status in sexual relationships. More recent HIV diagnosis has also been associated with higher proportions of non-disclosure to a stable partner among MSM, suggesting that disclosure of HIV-status may take time, even to a stable partner.[408,413] It remains unclear whether relationship-related factors, such as length of time in the relationship and cohabitation with the stable partner are associated with non-disclosure to this partner. In addition, it is uncertain whether being on ART or having an undetectable VL are linked to non-disclosure to stable partners, given that these factors would be associated with reduced HIV transmission risk.

7.2.3 Non-disclosure to casual sexual partners

The barriers to disclosure to casual sex partners are similar to those discussed in section 7.2.2.1 on non-disclosure to stable partners, namely, the fear of rejection, abuse, stigma, and breach of privacy. When the risk of HIV transmission is extremely low, such as when a condom is used, or when VL is undetectable on ART, some HIV-diagnosed people may also feel there is no need to disclose their HIV-serostatus. On the other hand, disclosing to sex partners could facilitate discussions about sex.[414]

Prevalence of non-disclosure to casual sexual partners has been extensively studied in the USA, but less so in the UK. An earlier systematic review on levels and patterns of HIV disclosure (1997-2008) found 12 US studies among MSM; the prevalence of non-disclosure to any sexual partners ranged from 20% to 46%, while the prevalence of non-disclosure to 'casual' sex partners was higher, ranging from 58% to 62%.[379] Table 7.3 shows the distribution of prevalence estimates for non-disclosure to casual sex partners among HIV-diagnosed MSM from studies in high-income countries (including studies that were published after the aforementioned systematic review and outside the USA). Prevalence of non-disclosure to casual sex partners varies widely (from 9-66%), according to study setting (HIV clinics or community venues), ART coverage (whether on or off ART), ethnicity (racial minority or not), as well as the method of survey administration (interview or self-completed). In addition, various constructs have been used to describe casual partners in studies of non-disclosure, such as "most recent partner"[415,416], "casual sex partner"[195,199], "any sex partner"[408], or new sex partners[389]. Non-disclosure itself can be operationalised in a number of ways; as a proportion of the number of sex partners the participant disclosed to over a period of time[389,390], a binary construct (disclosed or not at last sex[195,415,416]), or as a categorical variable of degree to which disclosed to casual partners (none, some, all).[199,241,390,392]

Another method of studying patterns of disclosure to sexual partners is to ascertain attitudes towards non-disclosure to casual partners. This has been less commonly studied. For example, the UK "What Do

You Need?" needs-assessment survey of HIV-diagnosed people recruited online, at clinics, or through charities (n=1200 MSM, 2007-2008); 32% of HIV-diagnosed MSM felt '"worried about disclosing to a sexual partner" and 38% were "worried about transmitting HIV to sexual partners".[417]

7.2.3.1 Correlates of non-disclosure to casual sex partners

There is some evidence to suggest that non-disclosure of HIV serostatus to casual sex partners is highest among MSM who are recently diagnosed.[408,417,418] However, This finding was not observed in the SUMIT study of 858 HIV-diagnosed MSM (see Table 7.3); time since HIV diagnosis was not associated with non-disclosure to casual sex partners in the past three months.[199]

Evidence on the association between age of the HIV-diagnosed participant and non-disclosure is also somewhat mixed. In the UK "What Do You Need" survey, MSM who worried about disclosing to sexual partners were significantly younger than MSM who did not have this concern.[417] In the Dublin HIV clinic study of 97 HIV-diagnosed MSM (Table 7.3), men who were older had higher odds of non-disclosure to any sexual partner compared to those who were younger.[390] No association was found between age and non-disclosure to casual partners in the past three months in two US studies ('Positive Connections'[418] and SUMIT baseline survey[199]). Other socio-demographic variables (ethnicity, income, education, employment) were also not found to be associated with non-disclosure in the two aforementioned studies.

HIV-related factors have not been consistently found to be associated with non-disclosure to casual partners; there are mixed findings on the role of ART status, self-reported VL, CD4 count, and undetectable VL on prevalence of non-disclosure to sex partners.[408,416–418] In 'Positive Connections' (see Table 7.3), non-disclosure to casual partners was associated with not knowing personal CD4 count and self-reported undetectable VL, after adjustment for ethnicity, number of partners, and time since HIV diagnosis.[418] A mathematical model estimating the efficacy of disclosure in reducing HIV transmission risk using baseline data from a US RCT of 144 HIV-diagnosed MSM (measuring non-disclosure at last sex) showed no association of self-reported VL and non-disclosure in unadjusted analyses.[416] Among over 1800 HIV-diagnosed MSM from the 'Healthy Living Project' (see Table 7.3), having undetectable VL was also not associated with higher non-disclosure to any sex partners in unadjusted analyses.[408] Overall, information on factors associated with non-disclosure to sexual partners among representative samples of HIV-diagnosed MSM in the UK is lacking.

7.2.4 Evidence on associations of non-disclosure and condomless sex

Few studies have examined the association of HIV-serostatus disclosure and condom use among HIV-diagnosed MSM. It has been hypothesized that disclosure to sexual partners could be linked to higher prevalence of 'safer sex' (condom-protected sex or CLS with other HIV-positive men only, CLS-C), however this implies a causal relationship which has not been empirically supported.[408] A review of eight US studies (1991-2003) examining non-disclosure and 'sexual safety' among MSM found mixed results (and none accounted for confounding variables); half of the studies reported no significant

association of non-disclosure to sexual partners with measures of 'unsafe sex' (any CLS) and the remaining found that disclosure to HIV-negative casual partners was associated with 'safer sex' (consistent condom use).[381] All of the studies included in the review were conducted before the introduction of widespread ART (prior to 1996), and therefore may be less relevant in the current HIV epidemic.

Since that review, certain studies have suggested that non-disclosure is associated with higher prevalence of CLS,[199,389,409,418] other studies have not found a significant association[195,201,236,381,404,415], and others yet have shown that, compared to MSM who disclose to all partners, those who do not disclose are more likely to report having condom-protected sex only.[419] For example, two US studies of HIV-diagnosed MSM (Positive Connections[418] and Healthy Living Project[408], see Table 7.3) found that about one in five MSM did not disclose their HIV-serostatus to any casual partners in the past three months. This group had significantly higher odds of reporting CLS-D compared to those who had disclosed to all partners, even after adjustment for other socio-demographic, lifestyle, and sexual behaviour-related factors.[408,409] On the other hand, among young MSM in the US ATN trials, those who disclosed their HIV-serostatus to sex partners were significantly more likely to report any CLS compared to those who did not disclose to any sex partners, after adjustment for socio-demographic and lifestyle factors.[177,411] In addition, disclosure in this study was not associated with CLS-D, which may indicate that many young MSM were having CLS-C, with mutual disclosure of HIV-status. Studies that examine levels of disclosure to sexual partners (disclosed to none, some, most or all partners) have shown that those who disclose to some partners tend to report higher levels of CLS compared to those who disclose to none or most/all partners.[199,241,392,418,419]

Only two studies from the UK ('East London'[394] and Guys' clinic[304], see Table 7.3) have shown prevalence estimates of non-disclosure to sexual partners, but none examined associations between non-disclosure and CLS. The prevalence of, and factors associated, with non-disclosure of HIV serostatus, as well as any link between non-disclosure and CLS among HIV-diagnosed MSM in the UK remains unclear.

Table 7.3: Summary of studies from high income countries on prevalence of non-disclosure to casual sex partners among HIV-diagnosed MSM‡

Study /Country/ Data collection period			Study setting and recruitment	N HIV-diagnosed MSM	Definition of non-disclosure measure	Prevalence of non-disclosure (% of HIV-diagnosed MSM)	Prevalence of CLS or CLS-D among non-disclosed (% of HIV-diagnosed MSM)
SUMIT[164,199]	USA	2000-2001	Baseline assessment from SUMIT RCT restricted to HIV-diagnosed MSM who had sex with a casual or non-primary male partner in past 3 months	N=858	Non-disclosure to casual sex partners with whom had sex in past 3 months	33.0%	23% had insertive CLS-D 32% receptive CLS-D
Healthy Living Project [408]	USA	2000-2002	*Refer to Table 7.2*	N=1828	Non-disclosure to any casual sex partner	21.5%	16.9% had CLS-D
Dutch Hospitals[201]	Netherlands	2002-2003	Self-administered questionnaire survey of HIV-diagnosed MSM attending for HIV care aged 20-65 years.	N=296	Have never/rarely informed casual sex partners about HIV+-positive status	59.8%	*Not shown*
Latino MSM[195]	USA	2005	*Refer to Table 7.2*	N=219	Non-disclosure to most recent casual partner	66.0%	31.3% had CLS-D
Positive Connections[418]	USA	2005-2006	Baseline survey of self-reported HIV-positive MSM recruited from 'AIDS service organisations' in 6 cities. Reported ≥1 occasion of CLS with a man in past year.	N=675	Non-disclosure to any 'secondary' partners in past 3 months	19.6%	*Not shown*
HIV Outpatients Study (HOPS)[241]	USA	2007-2010	Ongoing open prospective cohort of HIV-diagnosed men and women receiving care in 8 HIV clinics in 6 cities. Results here from cross-sectional annual automated telephone survey among MSM who reported any sex in past 6 months.	N=704	Non-disclosure to any sexual partners	9.2%	*Not shown*
LISA[389]	BC, Canada	2007-2010	Interviewer-administered survey of people on ART recruited through HIV clinics and organisations.	N=243	Don't always disclose to new sex partners in the past 6 months (up to 75% of the time versus always disclose, 76-100% of the time)	48.6%	16.4% report not using condoms 100% of the time

Study /Country/ Data collection period			Study setting and recruitment	N HIV-diagnosed MSM	Definition of non-disclosure measure	Prevalence of non-disclosure (% of HIV-diagnosed MSM)	Prevalence of CLS or CLS-D among non-disclosed (% of HIV-diagnosed MSM)
DiSH[410]	USA	2008-2009	Baseline data from behavioural intervention study to reduce sexual risk behaviours among black HIV-positive and HIV-negative MSM in NYC, recruited at street and venue locations, local organisations, gay press, online. Eligible if reported ≥2 partners and CLS with a man in past 3 months. Survey by ACASI + HIV testing (if status not known). Here showing results for MSM HIV-diagnosed for ≥6 months.	N=205	Non-disclosure during last sexual encounter with a male partner	30.2%	*Not shown*
Positive Choices[419]	USA	2009-2011	RCT testing brief risk reduction intervention to newly diagnosed people (≤3 months) at STI clinic. Restricted to MSM reporting CLS in 3 months prior to diagnosis and completed both screening (time 1) and baseline assessments (time 2: 3 months after time 1) by CASI.	N=92	Disclosure to no partners in 3 months post HIV-diagnosis (at time 2)	32.6%	4.4% had any CLS
SafeTalk[407]	USA	2012	*Refer to Table 7.2 :* Data shown here for all MSM who reported any sex in past 6 months	N=138	Did not fully disclose to all sexual partners (disclosure to <100% of partners)	31.2%	*Not shown*
Dublin HIV clinic[390]	Ireland	2013	Cross-sectional questionnaire study of HIV-outpatients attending largest HIV clinic in Dublin. Restricted to MSM with at least one casual sex partner in past 6 months.	N=97	Never disclosed to casual partners in past 6 months	34.0%	*Not shown*
Atlanta clinics[420]	USA	2013-2014	Cross-sectional survey of HIV-diagnosed men from community services and STI clinics who had anal or vaginal sex in past month. Included urine test for recreational drug use, unannounced phone-based ART pill counts, and daily text-diary assessment for sexual behaviour during previous day, for 28 consecutive days.	N=538	Had CLS-D without disclosing to any partners during 28 day prospective	*Not shown*	16.4% had CLS-D

ACASI: audio computer assisted self-interviewing; ART: antiretroviral therapy; CASI: computer assisted self-interviewing; CLS: condomless sex; CLS-D: condomless sex with HIV-serodifferent partners; LISA study: Longitudinal Investigations into Supportive and Ancillary health services; Not shown: study does not provide relevant information; RCT: randomised controlled trial; STI: sexually transmitted infection; SUMIT: Seropositive Urban Men's Intervention Trial; ‡Studies described in section 2.5, unless otherwise specified.

7.3 Methods

Analyses presented in this chapter include MSM diagnosed with HIV for ≥3 months prior to ASTRA completion (N=2189).

7.3.1 Disclosure in the social context

Participants were asked "Apart from health care staff, have you told anyone that you have HIV?" If they answered "Yes", they specified whether they had told family members, friends and, if applicable, work colleagues, or a stable partner (section 7.3.2). If participants had not disclosed to anyone in these categories they were classified as not having disclosed to anyone in a social context.

Among those who indicated having disclosed to at least one person, participants specified whether they told "none", "some", or "most or all" family members or friends. A combined variable ('disclosure to friends and family') was defined with three categories: (i) "none", if participants had not disclosed to any friends or family ("none" in both, or no answer in one and "none" in the other), (ii) "some", if participants indicated disclosed to "some" in at least one of the two variables, or "most or all" in one and either no answer, "none", or "some" in the other, and (iii) "most or all" if participants disclosed to "most or all" of their friends and "most or all" of their family members.

Among participants reporting current full- or part-time employment, non-disclosure in the workplace was defined as having disclosed to "none" of their work colleagues.

7.3.2 Disclosure to a stable partner/spouse

Non-disclosure to a stable partner was defined as a "No" to the question "I have told a partner/wife/husband that I have HIV" and was assessed only among those who indicated being in an ongoing relationship with a partner (defined as "wife/husband or civil partner or girlfriend/boyfriend").

Those with missing values for the overall disclosure variable were excluded. Similarly, those with missing values for any of the disclosure sub-variables (family/friends, stable partner, and workplace) were excluded from that specific variable. The variables disclosure to; family/friends, a stable partner, and the workplace, have a higher proportion of missing values compared to the overall disclosure variable, as a number of participants who indicated disclosure to at least one person did not provide information on type of confidant. A missing answer in type of confidant disclosed to was thus not assumed to indicate non-disclosure. This approach was taken as it was hypothesized that exclusion of missing values would lead to less bias than classification as 'non-disclosure'.

7.3.3 Lower sexual disclosure

Participants stated their level of agreement to the statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex" on a 5-level Likert scale (strongly agree, tend to agree, undecided/no opinion/not relevant to me, tend to disagree, and strongly disagree). A dichotomous 'sexual disclosure'

variable was created, merging 'strongly agree' and 'tend to agree' into one category (higher sexual disclosure) and 'undecided', 'tend to disagree' and 'strongly disagree' into the second category (lower sexual disclosure).

7.3.4 Socio-demographic, lifestyle, mental health, HIV-related factors and sexual behaviours

All factors included in these analyses have been defined in sections 3.8 and 4.3. To increase power in examining associations, some categorical variables were further collapsed (e.g. age, time since HIV diagnosis, time in relationship, money for basic needs, social support), as shown in sections 7.4.2 and 7.4.3.

7.3.5 Statistical analysis

Analyses were restricted to MSM who were diagnosed with HIV for three months or longer (N=2189). Prevalence of disclosure was assessed overall (no one, at least one person), by confidant (family, friends, co-workers, stable partner), and extent (none, some, most or all). The prevalence of lower sexual disclosure (as defined in section 7.3.3) was assessed among MSM who reported any anal or vaginal sex in the past three months only (N=1392), as it was hypothesized that the validity of the question on likely disclosure to new partners was increased by including sexually active MSM only.

7.3.5.1 Factors associated with non-disclosure

In this section the aim was to examine:

1. The association of socio-demographic, psychological, HIV-related, and relationship factors with non-disclosure to a stable partner (versus disclosure to the stable partner) only among HIV-diagnosed MSM who reported currently being in an ongoing relationship with a partner.
2. The association of socio-demographic, psychological, HIV-related, factors with lower sexual disclosure (versus higher sexual disclosure, as defined in section 7.3.3) among HIV-diagnosed MSM who reported any anal or vaginal sex in the previous three months only.

For both objectives, modified Poisson regression models with cluster-robust error variances were used to produce unadjusted and adjusted prevalence ratios (PRs) with 95% confidence intervals. Two adjustment strategies (core and stepwise) were used, as described in section 3.9.5.

The association of lifestyle factors and lower sexual disclosure was examined separately. These included: recreational drug and polydrug use in the past three months (defined in section 6.3.1), evidence of alcohol dependency, and higher alcohol consumption (by CAGE questionnaire and by WHO-AUDIT-C respectively, both defined in section 3.8.2). Unadjusted and adjusted (for core factors only) modified Poisson regression was used.

7.3.5.2 Association of non-disclosure and sexual behaviours

Among MSM in an ongoing relationship with an HIV-serodifferent (HIV-negative or unknown status) stable partner, descriptive statistics were used to examine the association of non-disclosure and CLS-D

with the stable partner in the past three months. Due to limited sample size it was not possible to perform multivariable analyses.

Among MSM who had any anal or vaginal sex in the previous three months, associations were then examined of lower sexual disclosure with sexual behaviours (CLS, CLS-C, CLS-D, higher HIV risk CLS-D, group sex, use of the internet to find sex, STIs in the past three months; and new sexual partners in the past year.) Modified Poisson regression was used to produce unadjusted and adjusted prevalence ratios; for each sexual behaviour, separate models were run with adjustment for the sexual disclosure variable in addition to core factors. In models with higher HIV risk CLS-D as the dependent variable, ART status was excluded from the core set of factors, as this was defined as CLS-D plus not being on ART or VL>50c/mL (so this model was adjusted for age, ethnicity, time since HIV diagnosis, stable partner status, and sexual disclosure only.)

Among MSM who reported any anal or vaginal sex in the past three months, multinomial logistic regression (MNL) was used to examine associations of lower sexual disclosure with reporting different types of sex according to the single three-category variable of sexual behaviour (see section 4.3.6.3). MSM were classified into one of the following mutually exclusive categories based on sex in the past three months:

1. Condomless sex with HIV-serodifferent partners (CLS-D)
2. Condomless sex with HIV-seroconcordant partners only ('CLS-C without CLS-D')
3. Condom-protected sex only

MSM who had CLS-D (group 1), and those who had 'CLS-C without CLS-D' (group 2) were compared to those who had condom-protected sex only (group 3, the reference category). Multivariable MNL included adjustment for core factors (in addition to the sexual disclosure variable).

7.3.6 **Sensitivity analyses**

All sensitivity analyses were conducted on the sample of MSM who reported any anal or vaginal sex in the past three months.

In the first sensitivity analysis, in assessing the adjusted association of lower sexual disclosure with sexual behaviours, the ART variable (on/off ART) was replaced by the ART/self-reported VL variable. This was done as it was hypothesized that MSM who self-reported undetectable VL on ART would be less likely to disclose HIV-serostatus to new sexual partners. It would not be possible to adjust both for ART status (as a core factor) and ART status/self-reported VL due to collinearity. In models with higher HIV risk CLS-D as the dependent variable, the ART variable was replaced with the self-reported VL variable (self-reported undetectable VL/self-reported detectable VL/does not know personal VL).

In the second sensitivity analysis, sexual disclosure was reclassified into a categorical variable, according to levels of agreement to the statement "I would expect to tell a new partner that I'm HIV-positive

before we have sex": (i.) Higher sexual disclosure (strongly or tend to agree), (ii.) Undecided (undecided/no opinion/not relevant to me), and (iii.) lower sexual disclosure (strongly or tend to disagree). This was done to disentangle any differences in the prevalence of sexual behaviours between categories (ii) and (iii), which were grouped into one category in main analyses. Associations were then examined of the three categories of sexual disclosure and sexual behaviours, using modified Poisson regression adjusted for core factors (as in section 7.3.5.1).

The third sensitivity analysis aimed at allowing for comparisons of the magnitude of associations of a single independent variable (lower sexual disclosure) across a number of dependent binary variables of varying prevalence (discussed in section 3.9.4.3). This was done by presenting associations of lower sexual disclosure and sexual behaviours (CLS, CLS-D, CLS-C, higher HIV risk CLS-D, STIs, group sex, and ≥10 new sex partners in past 12 months) as odds ratios rather than prevalence ratios, using logistic regression with adjustment for core factors only.

7.4 Results

7.4.1 Prevalence of non-disclosure

A total of 2181 (97.0% of 2189) MSM diagnosed with HIV for at least three months provided information on HIV serostatus disclosure. Of these, 4.7% (n=103) had not disclosed their status to anyone. (Table 7.4) Prevalence of non-disclosure to family members was higher than to friends. A total of 1318 MSM were currently employed, of whom 1117 provided information on workplace disclosure; 53.9% of these reported not disclosing to any work colleagues. When including recently diagnosed MSM (n=59) the prevalence of non-disclosure among 2189 MSM was slightly higher: overall non-disclosure was 5.0% (95%CI 4.2-6.0%, n=112), to friends/family combined 12.9% (11.5-14.4%, n=261), to work colleagues 54.2% (51.3-57.1%, n=1146).

Among 1080 MSM who were in an ongoing relationship with a partner, 4.5% (n=49) had not disclosed their HIV-serostatus to a stable partner. When including recently diagnosed MSM, prevalence of non-disclosure to a stable partner among 1109 MSM in an ongoing relationship was 4.8% (3.7-6.2%, n=53).

Table 7.4: Prevalence of non-disclosure measures among HIV-diagnosed MSM participating in ASTRA (N=2181 with available disclosure information)

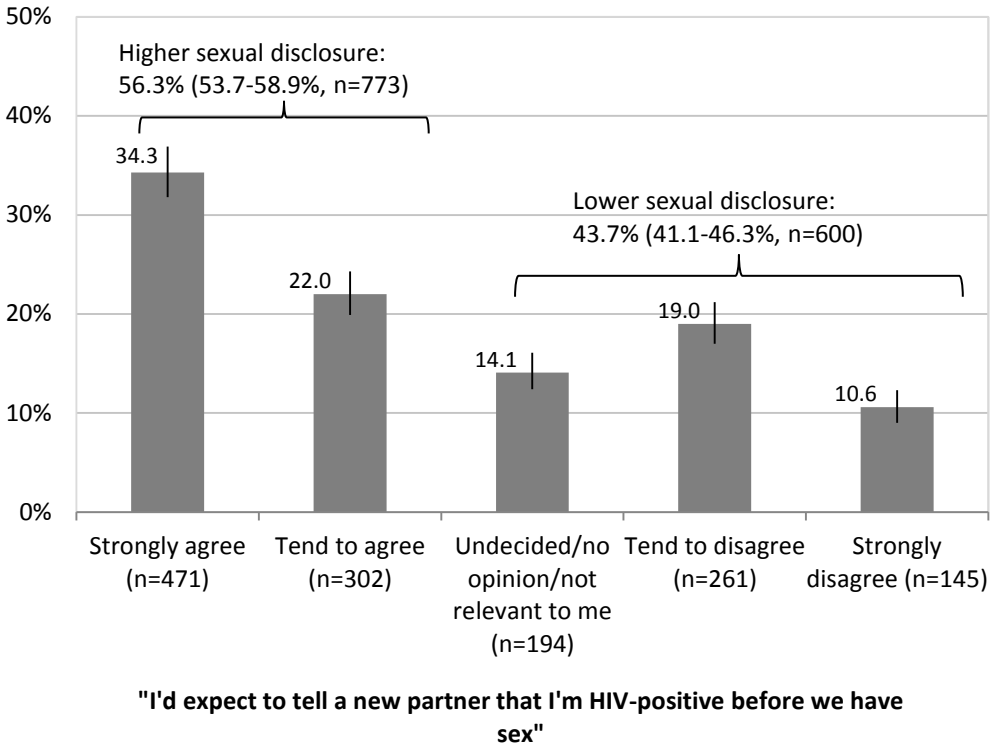
	n	%	[95%CI]
Overall disclosure status (N=2181)			
Disclosed to at least one person	2078	95.3	[94.3,96.1]
Not disclosed to anyone	103	4.7	[3.9,5.7]
Disclosure to family (N=1839)			
None	720	39.2	[36.9,41.4]
Some	608	33.1	[30.9,35.2]
Most or all	511	27.8	[25.8,29.9]
Disclosure to friends (N=1946)			
None	267	13.7	[12.3,15.3]
Some	1081	55.5	[53.3,57.7]
Most or all	598	30.7	[28.7,32.8]
Disclosure to friends/family combined (N=1979)*			
None	245	12.4	[11.0,13.9]
Some	1366	69.0	[66.9,71.0]
Most or all	368	18.6	[16.9,20.4]
Disclosure to work colleagues (N=1117 currently employed)			
None	602	53.9	[51.0,56.8]
Some	443	39.7	[36.8,42.6]
Most or all	72	6.4	[5.1,8.0]
Disclosure to stable partner (N=1080 in ongoing relationship)			
No	49	4.5	[3.4,6.0]
Yes	1031	95.5	[94.0,96.6]
**Combination categories created from disclosure to friends and disclosure to family variables as follows; none: none in both, or no answer in one and none in the other; some: some in at least one of the two variables, or most/all in one and either no answer, none, or some in the other; most/all: both variables most/all. Missing for n=202*			

7.4.1.1 Prevalence of lower sexual disclosure

Among 1392 MSM who had been diagnosed for at least three months and reported any anal or vaginal sex in the previous three months, 1373 (98.7%) provided information on sexual disclosure, as defined by level of agreement to the statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex". (Figure 7.1) Over 34% of MSM strongly agreed with the statement and almost 11% strongly disagreed. The first two categories (strongly and tend to agree) and last three (undecided, tend to and strongly disagree) were combined into two groups of higher and lower sexual disclosure respectively; 43.7% of MSM were thus classified as having lower sexual disclosure.

Among 600 MSM with lower sexual disclosure, over 93% (n=563) had disclosed their HIV serostatus to anyone in their social circle (family, friends, a stable partner, work colleagues) and 6.0% (n=36) had not (p=0.001).

Figure 7.1: Level of agreement to statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex" and derivation of binary grouping of sexual disclosure (N=1392 MSM had any anal or vaginal sex in past three months)



Excluding no answer for n=19. Bars and lines show prevalence and 95%CIs

7.4.2 Factors associated with non-disclosure

7.4.2.1 Socio-demographic, psychological, relationship-, HIV-related factors and associations to non-disclosure to stable partner

Among 1080 MSM diagnosed with HIV for ≥3 months and in an ongoing relationship, prevalence of non-disclosure to a stable partner was higher among MSM: of non-white ethnicity, who were not religious, did not always have money for basic needs, had medium/low social support, had an HIV-negative or unknown status stable partner, and were not on ART (unadjusted analysis, all $p<0.10$).(Table 7.5) A significant negative trend was also observed between more recent HIV diagnosis and higher prevalence of non-disclosure to a stable partner.

After adjustment for core factors, three factors remained significantly associated with non-disclosure to a stable partner ($p<0.05$, models 1: Table 7.5): non-white ethnicity, not always having money for basic needs, and medium/low social support. There was weak evidence of a negative trend between more recent HIV diagnosis and non-disclosure to a stable partner ($p=0.06$). Age, place of birth, education, employment, symptoms of depression or anxiety, years in the current relationship, cohabitation status with the stable partner were not significantly associated with non-disclosure.

In model 2, the following factors were candidates for inclusion in the multivariable model ($p<0.10$ at unadjusted analysis): ethnicity, time since HIV diagnosis, religion, money for basic needs, social support, stable partner's HIV serostatus, ART status, and ART status/self-reported VL. ART status was excluded from the model as it was included in the ART status/self-reported VL variable. Hence, after adjustment for ethnicity, time since HIV-diagnosis, religion, money for basic needs, social support, stable partner status, ART status/self-reported VL, and clinic, there were no significant associations between any factor and non-disclosure to a stable partner (model 2: Table 7.5). It is worth noting that power was lower for this analysis due to the larger number of covariates included. The following factors had weak evidence of associations to non-disclosure to a stable partner: being religious ($p=0.08$), not having money for basic needs ($p=0.07$), and medium/low social support ($p=0.06$).

There was no observed association of non-disclosure in the social circle (to friends, family, co-workers, and a stable partner) and psychological symptoms (as dependent variables); results of this work can be found in the published paper[421] shown in Appendix VII.

Table 7.5: Associations of socio-demographic, psychological, HIV-, and partner-related factors with non-disclosure to a stable partner (N=1080 MSM in an ongoing relationship)

	Unadjusted		Models 1		Model 2	
	PR [95%CI]	p-value	aPR [95%CI]	p-value	aPR [95%CI]	p-value
Age at recruitment, years (N=1073)						
<50	1.0		1.0			
≥50	1.0 [0.6,1.8]	0.948(T)	1.2 [0.6,2.2]	0.636(T)	-	
Ethnicity (N=1071)						
White	1.0		1.0		1.0	
All other (black, Asian, Mixed, other)	2.3 [1.2,4.5]	0.016	2.2 [1.1,4.2]	0.023	1.6 [0.7,3.3]	0.245
Years since HIV diagnosis (N=1074)						
<5	2.1 [1.2, 4.0]		2.0 [0.9,4.3]		2.0 [0.9,4.3]	
5-10	1.1 [0.6,2.3]		1.0 [0.4,2.3]		1.0 [0.4,2.3]	
>10	1.0	0.024(T)	1.0	0.062(T)	1.0	0.097(T)
Place of birth (N=1080)						
UK	1.0		1.0			
Outside the UK	0.7 [0.4,1.2]	0.231	1.0 [0.6,1.8]	0.886	-	
Religious (N=1071)						
Yes	1.0		1.0		1.0	
No	0.5 [0.3,0.9]	0.027	0.6 [0.3,1.1]	0.103	0.6 [0.3,1.1]	0.078
Education (N=1065)						
University degree or above	1.0		1.0		-	
No qualifications or up to A levels	0.9 [0.5,1.6]	0.739	1.0 [0.6,1.8]	0.913		
Employment (N=1065)						
Employed	1.0		1.0			
Unemployed or other (sick, carer, retired, student)	1.1 [0.6,2.1]	0.664	1.2 [0.7,2.3]	0.490	-	
Money for basic needs (N=1068)						
Always	1.0		1.0		1.0	
Mostly/sometimes/never	2.4 [1.3,4.2]	0.004	2.3 [1.2, 4.1]	0.007	1.8 [1.0,3.4]	0.070

	Unadjusted PR [95%CI]	p-value	Models 1 aPR [95%CI]	p-value	Model 2 aPR [95%CI]	p-value
Social support (N=1072) ‡						
High	1.0		1.0		1.0	
Medium/low	2.1 [1.2,3.7]	0.007	2.1 [1.2,3.7]	0.016	1.8 [1.0,3.4]	0.058
Depression symptoms (N=1080) ‡						
No	1.0		1.0		-	
Yes	1.2 [0.6,2.4]	0.514	1.3 [0.7,2.5]	0.443		
Anxiety symptoms (N=1080) ‡						
No	1.0		1.0		-	
Yes	1.2 [0.6,2.5]	0.578	1.3 [0.6,2.5]	0.531		
Stable partner's HIV-serostatus (N=1080)						
HIV-positive	1.0		1.0		1.0	
HIV-negative or unknown status	1.7 [0.9,3.0]	0.097	1.5 [0.8,2.8]	0.179	1.4 [0.8,2.6]	0.254
Years in current relationship (N=1048)						
≤2	1.0		1.0			
2-5	1.4 [0.6,3.4]		1.4 [0.5,3.6]		-	
>5	1.0 [0.5,2.2]	0.822(T)	1.4 [0.6,3.3]	0.437(T)		
Cohabitation with stable partner (N=1080)						
No	1.0		1.0			
Yes	1.2 [0.6,2.2]	0.663	1.3 [0.7,2.5]	0.488	-	
ART status (N=1076)						
On ART	1.0		1.0		-	
Not on ART	2.0 [1.0,3.8]	0.038	1.6 [0.8,3.4]	0.211		
ART status/self-reported VL (N=939)						
On ART, reports undetectable VL	1.0		1.0		1.0	
On ART, does not report undetectable viral load †	1.4 [0.6,3.3]		1.4 [0.6,3.3]		1.3 [0.5,3.2]	
Not on ART	2.2 [1.1,4.2]	0.070	1.8 [0.8,3.9]	0.356	1.7 [0.8,3.8]	0.429

Global p-values by Wald test or test for trend(T); †Self-reported viral load (VL)>50c/mL or "don't know"; PR: prevalence ratio; CI: confidence interval; adjusted PRs (aPR) by modified Poisson regression models; ***Models 1:*** *Each factor adjusted in separate model for 'core' variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, and ART status. Denominators vary due to missing data in each model;* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic. In both cases, model for 'ART status/self-reported VL' omits variable on ART due to collinearity. ‡ For variable definitions refer to section 3.8*

7.4.2.2 Socio-demographic, psychological, HIV-related factors associated with lower sexual disclosure

Associations of various factors with lower sexual disclosure were assessed among 1373 MSM who reported anal or vaginal sex in the past three months and had available disclosure information. (Table 7.6) In unadjusted analysis, lower sexual disclosure was more prevalent among MSM who were older (≥50 years), not born in the UK, had higher educational attainment, always had money for basic needs, had medium/low social support, had an HIV-serodifferent stable partner or no stable partner, and reported undetectable VL on ART.(all $p<0.10$, Table 7.6)

After core adjustment (models 1: Table 7.6) the following factors remained associated with lower sexual disclosure ($p<0.05$), with minor attenuation of estimates: non-white ethnicity, non-UK place of birth, university degree or higher, always having money for basic needs, having an HIV-serodifferent or no stable partner, and reporting undetectable VL on ART.

In model 2, any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in the multivariable model, in addition to clinic. These were: age, ethnicity, place of birth, education, money for basic needs, social support, stable partner status, and knowledge of personal VL. Ethnicity and place of birth were strongly correlated so the latter was excluded from the model; this was done as place of birth may not distinguish between ethnic groups, thus aggregating the underlying diversity in race, culture, and religion, which may be of particular relevance to non-disclosure. Hence, after adjustment for age, ethnicity, education, money for basic needs, social support, stable partner status, ART status/self-reported VL, and clinic, there was no longer a significant trend association with younger age ($p>0.05$). There was some suggestion of weak associations of non-white ethnicity ($p=0.08$), medium/low social support ($p=0.06$), and lower sexual disclosure. (model 2: Table 7.6) Lower sexual disclosure remained significantly more prevalent among MSM with a university degree or higher, who always had money for basic needs, had an HIV-serodifferent partner or no stable partner, and those who reported undetectable VL on ART (all $p<0.05$).

Table 7.6: Associations of socio-demographic, psychological, HIV-related factors with lower sexual disclosure (N=1373 MSM had anal or vaginal sex in past three months)

	n low sexual disclosure/ N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=1358)								
<30	37/87	42.5	1.0		1.0		1.0	
30-39	154/371	41.5	1.0 [0.7,1.3]		1.0 [0.7,1.3]		0.8 [0.6,1.1]	
40-49	236/562	42.0	1.0 [0.8,1.3]		1.0 [0.7,1.3]		0.9 [0.7,1.2]	
≥50	165/338	48.8	1.1 [0.9,1.5]	0.090(T)	1.1 [0.8,1.5]	0.158(T)	1.0 [0.8,1.3]	0.168(T)
Ethnicity (N=1350)								
White	515/1205	42.7	1.0		1.0		1.0	
All other (black, Asian, Mixed, other)	75/145	51.7	1.2 [1.0,1.4]	0.028	1.2 [1.0,1.4]	0.054	1.2 [1.0,1.4]	0.085
Years since HIV diagnosis (N=1369)								
≤2	54/132	40.9	1.0		1.0			
2-5	107/251	42.6	1.0 [0.8,1.3]		1.0 [0.8,1.3]		-	
5-10	161/375	42.9	1.0 [0.8,1.3]		1.0 [0.8,1.3]			
10-15	124/271	45.8	1.1 [0.9,1.4]		1.1 [0.8,1.4]			
>15	153/340	45.0	1.1 [0.9,1.4]	0.306(T)	1.0 [0.8,1.3]	0.944(T)		
Place of birth (N=1373)								
UK	373/920	40.5	1.0		1.0		-	
Outside the UK	227/453	50.1	1.2 [1.1,1.3]	0.001	1.2 [1.1,1.4]	<0.001		
Religious (N=1349)								
Yes	244/555	44.0	1.0		1.0		-	
No	343/794	43.2	1.0 [0.9,1.1]	0.780	0.8 [0.7,0.9]	0.776		
Education (N=1353)								
University degree or above	323/629	51.4	1.0		1.0		1.0	
No qualifications or up to A levels	268/724	37.0	0.7 [0.6,0.8]	<0.001	0.7 [0.6,0.8]	<0.001	0.8 [0.7,0.9]	<0.001

	n low sexual disclosure/ N	row %	unadjusted PR [95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Employment (N=1346)								
Employed	406/917	44.3	1.0		1.0			
Unemployed or other (sick, carer, student,	183/436	42.0	0.9 [0.8,1.1]	0.428	0.9 [0.8,1.0]	0.158	-	
Money for basic needs (N=1352)								
Always	356/733	48.6	1.0		1.0		1.0	
Mostly	142/361	39.3	0.8 [0.7,0.9]		0.8 [0.7,0.9]		0.8 [0.7,1.0]	
Sometimes/never	93/258	36.0	0.7 [0.6,0.9]	<0.001(T)	0.7 [0.6,0.9]	<0.001(T)	0.8 [0.6,0.9]	0.002(T)
Social support (N=1367) ‡								
High	354/844	41.9	1.0		1.0		1.0	
Medium/low	243/523	46.5	1.1 [1.0,1.3]	0.099	1.1 [0.9,1.2]	0.344	1.1 [1.0,1.3]	0.061
Depression symptoms (N=1373) ‡								
No	461/1035	44.5	1.0		1.0		-	
Yes	139/338	41.1	0.9 [0.8,1.1]	0.279	0.9 [0.8,1.0]	0.105		
Anxiety symptoms (N=1373) ‡								
No	491/1110	44.2	1.0		1.0		-	
Yes	109/263	41.4	0.9 [0.8,1.1]	0.420	0.9 [0.8,1.1]	0.235		
Stable partner's HIV-serostatus (N=1373)								
HIV-positive	130/386	33.7	1.0		1.0		1.0	
HIV-negative or unknown status	205/430	47.7	1.4 [1.2,1.7]		1.4 [1.2,1.7]		1.4 [1.2,1.6]	
No stable partner	265/557	47.6	1.4 [1.2,1.7]	<0.001	1.4 [1.2,1.6]	<0.001	1.3 [1.1,1.6]	<0.001
ART status (N=1369)								
On ART	512/1152	44.4	1.0		1.0		-	
Not on ART	87/217	40.1	0.9 [0.8,1.1]	0.249	0.9 [0.7,1.1]	0.312		
ART status/self-reported VL (N=1352)								
On ART, reports undetectable VL	450/966	46.6	1.0		1.0		1.0	
On ART, does not report undetectable VL †	56/169	33.1	0.7 [0.6,0.9]		0.7 [0.6,0.9]		0.8 [0.6,1.0]	
Not on ART	87/217	40.1	0.9 [0.7,1.0]	0.005	0.8 [0.7,1.0]	0.006	0.8 [0.7,1.0]	0.026

Global p-values by Wald test or test for trend(T); PR: prevalence ratio; CI: confidence interval; †Self-reported viral load (VL)>50c/mL or "don't know"; Adjusted PRs (aPR) by modified Poisson regression models: ***Models 1:*** *Each factor adjusted in separate model for core factors. Denominators vary due to missing data in each model.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, in addition to clinic.In both cases, model for 'ART status/self-reported VL' omits variable on ART due to collinearity. ‡ For variable definitions refer to section 3.8*

7.4.2.3 Lifestyle factors associated with lower sexual non-disclosure

There was weak evidence of an association of alcohol dependency (by CAGE) and lower sexual disclosure (Table 7.7). No significant differences were observed between other lifestyle factors (drug and polydrug use in the past three months, higher alcohol consumption) and prevalence of lower sexual disclosure.

Table 7.7: Association of lifestyle factors with lower sexual disclosure (N=1373 MSM reporting anal or vaginal sex in the past three months)

	n lower sexual disclosure/N	row %	unadjusted PR [95%CI]	p-value	aPR [95%CI]	p-value
Recreational drug use (N=1373)						
No	231/516	44.8	1.0		1.0	
Yes	369/857	43.1	1.0 [0.9,1.1]	0.535	1.0 [0.9,1.1]	0.931
Polydrug use (N=857)						
1-3 drugs	241/545	44.2	1.0		1.0	
≥4 drugs	128/312	41.0	0.9 [0.8,1.1]	0.368	1.0 [0.8,1.2]	0.785
Higher alcohol consumption (WHO AUDIT-C‡) (N=1373)						
No	486/1137	42.7	1.0		1.0	
Yes	114/236	48.3	1.1 [1.0,1.3]	0.106	1.1 [1.0,1.3]	0.131
Evidence of alcohol dependency (CAGE◊) (N=1372)						
No	473/1111	42.6	1.0		1.0	
Yes	127/261	48.7	1.1 [1.0,1.3]	0.066	1.1 [1.0,1.3]	0.096

p-values by Wald test; ‡ Modified WHO-AUDIT-C score ≥6; ◊ CAGE score ≥2; PR; prevalence ratios by modified Poisson regression; aPR; adjusted PRs for core factors (age, ethnicity, time since HIV diagnosis, stable partner status, ART status)

7.4.3 Associations of non-disclosure and sexual behaviours

7.4.3.1 Non-disclosure to a stable partner and CLS-D

Among 1080 MSM in an ongoing relationship, 192 (17.8%) had any CLS-D in the past three months, of whom 172 (89.6%) provided information on CLS-D specifically with the stable partner; 71 (41.3%) had CLS-D with their stable partner only, 17 (9.9%) had CLS-D with their stable partner and other casual partners, and 84 (48.9%) only had CLS-D with casual partners but not their stable partner. Due to limited sample size it was not possible to perform significance tests.

7.4.3.2 Association of lower sexual disclosure and sexual behaviours

Among 1373 MSM who reported any anal or vaginal sex in the past three months and provided information on sexual disclosure, the prevalence of lower sexual disclosure was examined according to sexual behaviours in the past three months (or in the past year).(Table 7.8) Any CLS and CLS-C were more prevalent among those with higher sexual disclosure, while CLS-D, group sex, use of the internet to find sex in the past three months, and ≥10 new sexual partners in the past year were more prevalent among those with lower sexual disclosure ($p<0.05$ for all, Table 7.8). There was no significant association of lower sexual disclosure with higher HIV risk CLS-D or other STIs in the past three months.

The pattern of associations remained after adjustment for core factors.(Figure 7.2) The prevalence of any CLS was 20% lower among MSM with lower sexual disclosure compared to those with higher sexual

disclosure (PR=0.8, 95%CI 0.8-0.9), but this differed by type of CLS. Compared to MSM with higher sexual disclosure, MSM with lower sexual disclosure had 30% lower prevalence of CLS-C (PR=0.7, 0.6-0.8), and 30% higher prevalence of CLS-D (PR=1.3, 1.1-1.6) in the past three months. The prevalence of group sex in the past three months and high new partner numbers in the past year was also significantly higher among MSM with lower sexual disclosure ($p<0.05$ for both). There was a weak association of lower sexual disclosure and using the internet to find sex ($p=0.07$). As with univariable analysis, no significant association was observed of lower sexual disclosure with other STIs and higher HIV risk CLS-D (the latter model does not include adjustment for ART status).

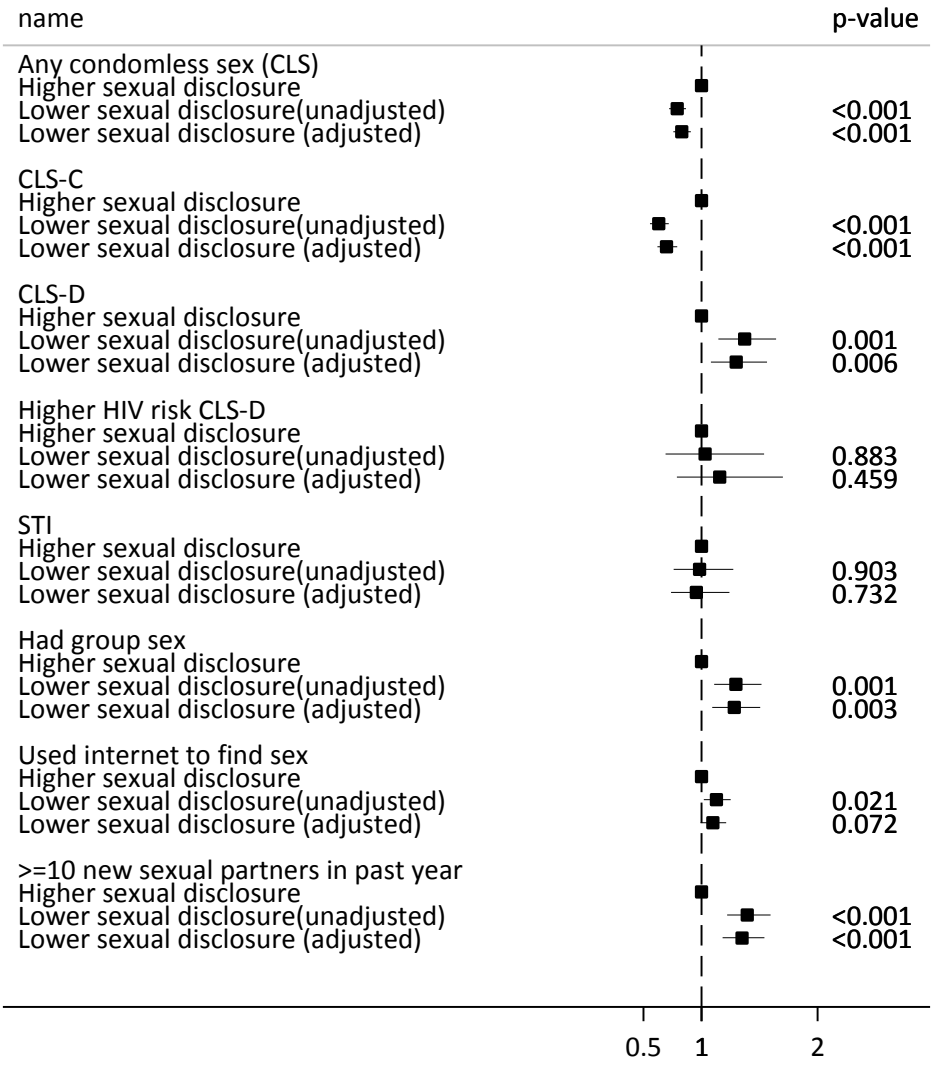
Table 7.8: Prevalence of lower sexual disclosure according to sexual behaviours‡ (N=1373 MSM had anal or vaginal sex in the past three months)

	Any condomless sex (CLS)		CLS-C		CLS-D		Higher HIV risk CLS-D		STI		Group sex		Used the internet to find sex		≥10 new partners in the past year	
	n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)	n/N	(%)
Sexual disclosure																
Higher	511/773	(66.1)	416/773	(53.8)	169/773	(21.9)	50/773	(6.5)	114/766	(14.9)	212/766	(27.7)	371/765	(48.5)	252/773	(32.6)
Lower	313/600	(52.2)	204/600	(34.0)	180/600	(30.0)	40/600	(6.7)	87/594	(14.6)	213/593	(35.9)	326/595	(54.8)	273/600	(45.5)
p-value	<0.001		<0.001		0.001		0.883		0.903		<0.001		0.021		<0.001	

Three month recall of sexual behaviours unless otherwise specified. P-values by chi-squared test; CLS: condomless sex; CLS-C: condomless sex with HIV-seroconcordant partners; CLS-D: condomless sex with HIV-serodifferent partners; Higher HIV risk CLS-D: CLS-D plus not on ART or VL>50c/mL; STI: sexually transmitted infection. CLS-D includes n=31 MSM who reported CLS but did not specify partner's HIV-serostatus

‡ Sexual behaviours defined in section 3.8.4

Figure 7.2: Unadjusted and adjusted associations of lower sexual disclosure and sexual behaviours‡ (N=1373 MSM had any anal or vaginal sex in the past three months)



Prevalence Ratios [95%CI] by modified Poisson regression. Reference group is higher sexual disclosure. Three month recall unless otherwise specified. CLS-C: CLS with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; Higher HIV risk CLS-D: CLS-D plus either not on ART or latest VL>50c/mL; STI: sexually transmitted infection; Multivariable models include (in addition to sexual disclosure variable) adjustment for core factors: age, ethnicity, time since HIV diagnosis, stable partner status, ART status. Model for higher HIV risk CLS-D excludes ART status. ‡All sexual behaviours defined in section 3.8.4

7.4.3.3 Association of lower sexual disclosure and the three-category variable of sexual behaviour

In this analysis, all 1373 MSM who reported any anal or vaginal sex and provided information on sexual disclosure were classified into one of the following mutually exclusive groups of sexual behaviour in the past three months (as described in section 4.3.6.3).

1. CLS-D (n=349)
2. 'CLS-C without CLS-D' (n=476)
3. Condom-protected sex only (n=548)

The prevalence of lower sexual disclosure was 51.6% among MSM in the CLS-D group (n=180), 27.9% in the 'CLS-C without CLS-D' group (n=133), and 52.0% in the condom-protected group (n=285). Unadjusted and adjusted (for core factors) multinomial logistic regression was used to examine the effect of lower sexual disclosure on reporting CLS, using the above three mutually exclusive groups. Relative to MSM who had condom-protected sex, MSM with lower sexual disclosure were significantly less likely to have 'CLS-C without CLS-D' (p<0.001, Table 7.9). Meaning, that disclosure of HIV-serostatus was highest with other HIV-positive partners. There was no significant association between lower sexual disclosure and reporting CLS-D relative to condom-protected sex. This difference in results compared to the previous analysis for CLS-D, is that in that previous analysis, the 'no CLS-D' group included men who had 'CLS-C without CLS-D', resulting in a group with higher levels of disclosure compared to those having CLS-D. Here it can be seen that levels of disclosure were similar in the 'condom-protected sex' and 'CLS-D' groups.

Table 7.9: Associations of lower sexual disclosure and sexual behaviours in past three months (N=1373 MSM who reported any anal or vaginal sex).

	Condom-protected sex (n=548)	'CLS-C without CLS-D' (n=476)		CLS-D (n=349)	
Sexual disclosure		unadjusted OR [95%CI]	adjusted OR [95%CI]	unadjusted OR [95%CI]	adjusted OR [95%CI]
Higher	ref	1.0	1.0	1.0	1.0
Lower		0.4 [0.3,0.5]	0.4 [0.3,0.5]	1.0 [0.8,1.3]	1.0 [0.8,1.3]
p-value		<0.001	<0.001	0.900	0.991

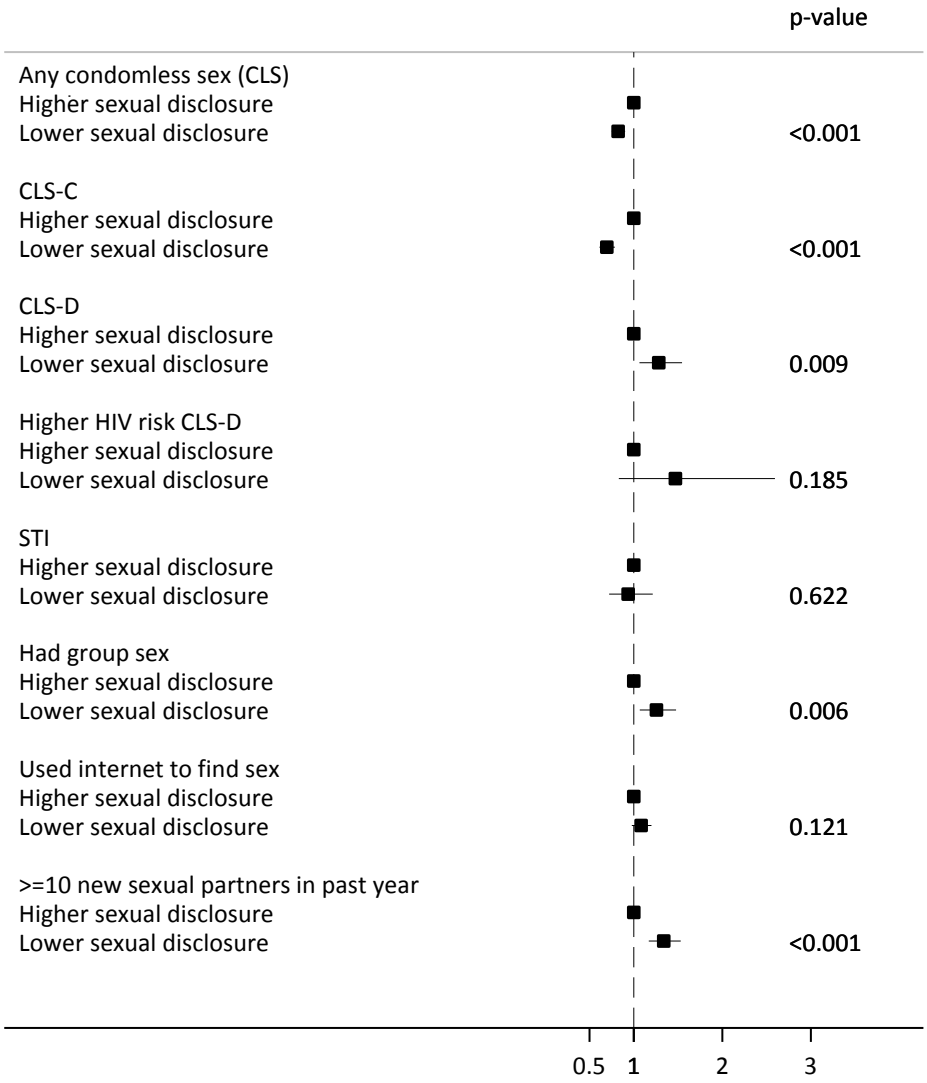
Odds Ratios [95%CIs] by multinomial logistic regression; Mutually exclusive categories of sexual behaviour in the past three months. Ref.: reference(baseline) group. Adjustment for 'core' factors: age, ethnicity, time since HIV diagnosis, stable partner status, ART status.

7.4.4 Sensitivity analyses

In the first sensitivity analysis, associations of lower sexual disclosure and sexual behaviours in the past three months were examined using modified Poisson regression adjusted for age, ethnicity, time since HIV diagnosis, partner status, and ART status/self-reported VL (rather than ART status). This was done as there was a significant association of self-reported undetectable VL on ART and lower sexual disclosure (Table 7.6). The magnitude of associations was similar to those observed in the core-adjusted model;

lower sexual disclosure was significantly associated with lower prevalence of any CLS and CLS-C, and with higher prevalence of CLS-D, group sex, and higher new partner numbers.(Figure 7.3) There was no significant association of lower sexual disclosure with STIs, use of the internet to find sex, or higher HIV risk CLS-D (this model included adjustment for self-reported VL but not ART status, see 7.3.6).

Figure 7.3: Sensitivity analysis 1: Association of lower sexual disclosure and sexual behaviours‡, additionally adjusted for ART status/self-reported viral load (VL) (N=1373 MSM had anal or vaginal sex in past three months)



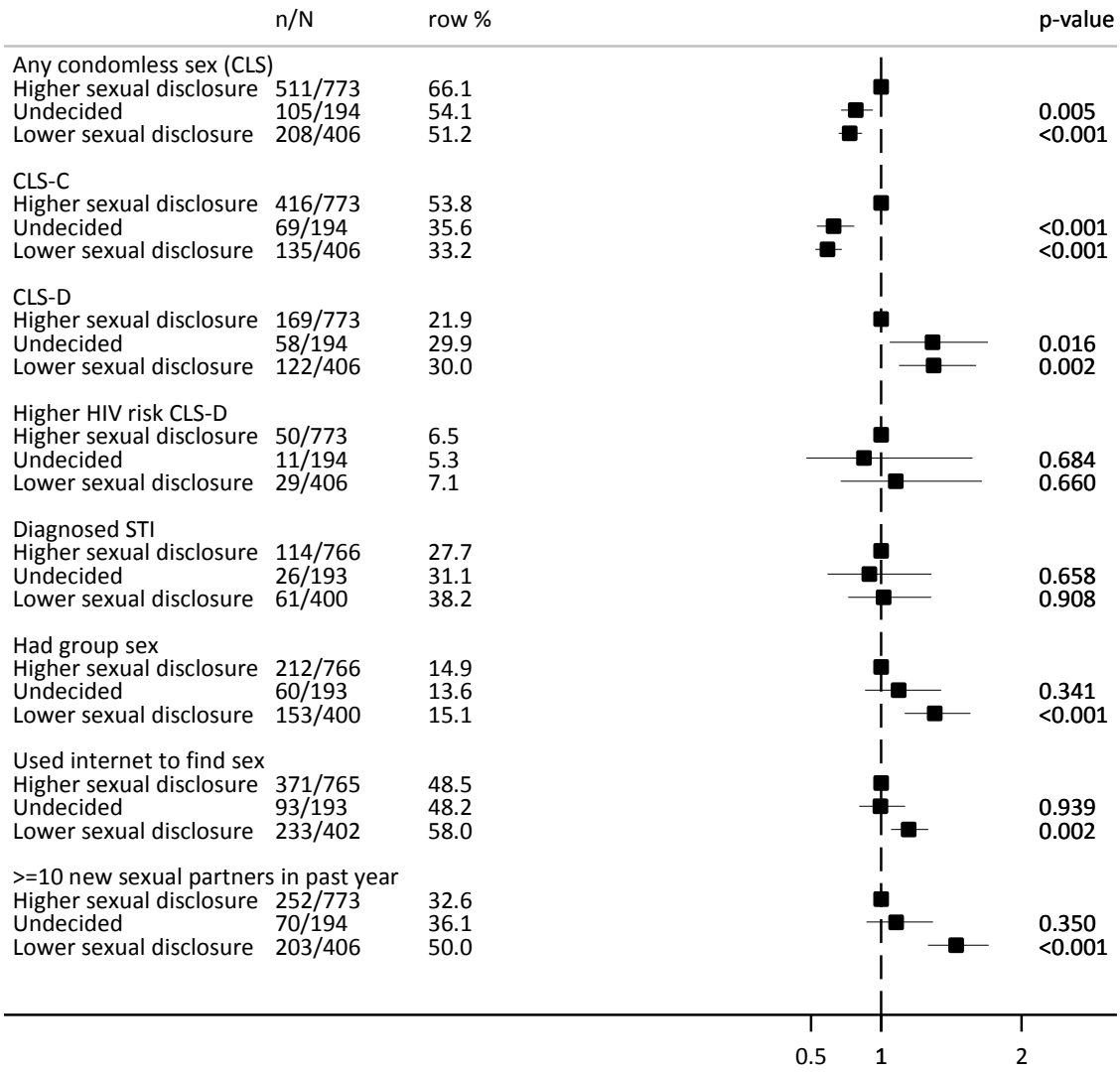
Three month recall unless otherwise specified. Prevalence Ratios [95%CI] by modified Poisson regression adjusted for age, ethnicity, time since HIV diagnosis, stable partner status, ART status/self-reported VL; Model for higher HIV risk CLS-D excludes ART status (adjusted for all other factors and self-reported VL only); CLS-C: CLS with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; STI: sexually transmitted infection; ‡All sexual behaviours defined in section 3.8.4

In the second sensitivity analysis, the sexual disclosure variable was re-categorised to include the middle group ('undecided/no opinion/not relevant to me' in the statement "I'd expect to tell a new partner that I'm HIV-positive"). Associations were examined between the three categories of sexual disclosure (higher, undecided, lower sexual disclosure) and sexual behaviours, among 1373 MSM who had anal or vaginal sex in the past three months.(Figure 7.4) The pattern of associations was similar to analyses

using the binary sexual disclosure categorisation (see Figure 7.2). In terms of CLS variables, the 'undecided' group were similar to the lower disclosure group. MSM who were undecided or had lower sexual disclosure were less likely to report any CLS and CLS-C, and more likely to report CLS-D compared to MSM with higher sexual disclosure ($p<0.05$ for all). MSM with lower sexual disclosure were significantly more likely to have group sex (PR=1.4, 95%CI 1.2-1.6), use the internet to find sex (1.2, 1.1-1.3), and have higher partner numbers (1.5, 1.3-1.8) compared to those with higher sexual disclosure; however, those who were undecided on sexual disclosure did not have significantly higher prevalence of these three behaviours compared to MSM with higher sexual disclosure (group sex: PR=1.1, 0.9-1.4; internet to find sex:1.0, 0.8-1.2; ≥10 new partners: 1.1, 0.9-1.4). There was no significant association of sexual disclosure and higher HIV risk CLS-D or other STIs ($p>0.05$ for both).

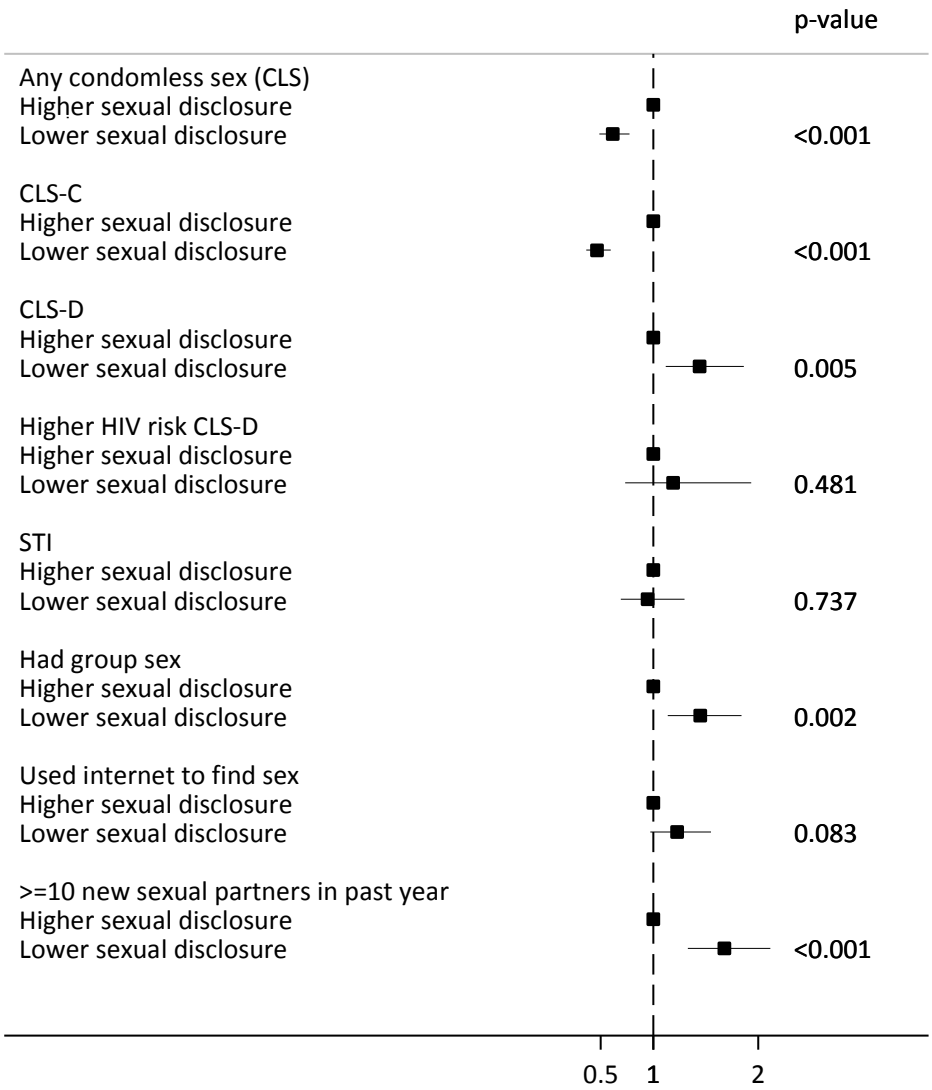
In the final sensitivity analysis, the aim was to examine the magnitude of associations between lower sexual disclosure and sexual behaviours using logistic regression to derive odds ratios (ORs), rather than prevalence ratios.(Figure 7.5) Using this plot, it is possible compare the magnitude of associations between the different sexual behaviour measures. Lower sexual disclosure was most strongly associated with lower prevalence of CLS-C; it was also more strongly associated with higher prevalence of ≥10 new sex partners, than it was with CLS-D and group sex.

Figure 7.4: Sensitivity analysis 2: Adjusted associations of sexual disclosure (three categories) and sexual behaviours‡ (N=1373 MSM had any anal or vaginal sex in past three months)



Three month recall unless otherwise specified. Prevalence ratios [95%CIs] by modified Poisson regression adjusted for core factors. Model for higher HIV risk CLS-D excludes ART status. Showing level of agreement to statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex": higher sexual disclosure ('strongly or tend to agree'), undecided ('no opinion/not relevant to me'), and lower sexual disclosure ('tend to or strongly disagree'); CLS-C: CLS with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; Higher HIV risk CLS-D: CLS-D plus not on ART or latest study-log VL>50c/mL; STI: sexually transmitted infection; ‡ All sexual behaviours defined in section 3.8.4

Figure 7.5: Sensitivity analysis 3: Odds ratios [95%CIs] for the association of lower sexual disclosure and sexual behaviours‡ (N=1373 MSM had anal or vaginal sex)



Three month recall unless otherwise specified. Odds ratios [95%CI] by logistic regression adjusted for core factors; Model for higher HIV risk CLS-D excludes ART status. CLS-C: CLS with HIV-seroconcordant partner; CLS-D: CLS with HIV-serodifferent partner; STI: sexually transmitted infection; ‡ All sexual behaviours defined in section 3.8.4

7.5 Discussion

7.5.1 Summary of findings

Among 2240 HIV-diagnosed MSM participating in the ASTRA study, a small minority of participants (approximately 5%) had not disclosed their HIV-serostatus to anyone. Of MSM in an ongoing relationship, a similar proportion had not disclosed to their stable partner. Among MSM who reported sex in the past three months, a much higher proportion (almost 44%) were classified as having lower sexual disclosure to new sex partners, which included 11% who stated strong disagreement with the statement on HIV-serostatus disclosure to a new sexual partner. There was some indication that more recent diagnosis, non-white ethnicity, higher financial hardship, and lower social support were associated with higher prevalence of non-disclosure to a stable partner. On the other hand, *higher* socio-economic status (university education, no financial hardship) was associated with lower sexual disclosure. Non-UK place of birth and having an HIV-serodifferent or no stable partner were also associated with lower sexual disclosure. In addition, MSM who were on ART with self-reported suppressed VL had lower sexual disclosure than those who were on ART without self-reported suppressed VL and those not on ART. Recreational drug use and alcohol misuse were not associated with lower sexual disclosure. Higher sexual disclosure was also more prevalent among MSM who had CLS compared to those who did not, but this differed by the HIV-serostatus of the sexual partner(s). Compared to MSM with higher sexual disclosure, those with lower sexual disclosure had lower prevalence of CLS-C (compared to no CLS-C), and higher prevalence of CLS-D (compared to no CLS-D), group sex, and high partner numbers. Consideration of the mutually exclusive sexual behaviour variable demonstrated that levels of sexual disclosure were similar among MSM who had condom-protected sex and those who had CLS-D, but sexual disclosure was greater among those who had 'CLS-C without CLS-D'.

7.5.2 Prevalence of non-disclosure of HIV-serostatus among MSM

Prevalence of non-disclosure in ASTRA was comparable to estimates from the earlier 'East London'[394] (2004-2005) and Switching[114,133] (2005-2006) studies of UK HIV-diagnosed clinic attendees, as well as the more recent 'Young MSM of Color Initiative'[386] (2006-2009) from the USA (all ≤5%, see Table 7.1). These studies used similar constructs of non-disclosure as in ASTRA. Non-disclosure was higher towards family than towards friends in ASTRA; this finding was corroborated in the 'East London' study[394], but not in the 'Young MSM of Color Initiative', for whom the prevalence of non-disclosure to friends was higher than to family.[386]

The majority of employed participants had not disclosed to any co-workers (54%). Discrimination against people living with HIV in the workplace is unlawful in the UK.[422] However, the high prevalence of non-disclosure to work colleagues in this sample may be influenced by prevailing fear of harassment and breach of privacy. It may also reflect personal choice regarding disclosure confidants. There is a need for employers to enact clear policies, which demonstrate commitment to confidentiality and non-discrimination of HIV-diagnosed employees.

The prevalence of non-disclosure to a stable partner in ASTRA MSM (4.8%) was overall lower than that found in earlier studies (see Table 7.2), with the exception of the French ANRS-VESPA1; this nationally representative cross-sectional survey found that 4.5% of MSM had not disclosed to their regular HIV-serodifferent partner.[229] In the 'East London' study[394], 14% of MSM had not disclosed to their stable partner, but there have not been other comparable UK studies since on this subject. In addition, prevalence estimates may differ because of diverse definitions used for the concept of a stable partner[423]; this could refer to a partner with whom the participant has regular sex[229], a main partner among other casual partners[408], a monogamous long-term partner[195,394], or a current partner with whom the participant had sex during a specific recall period.[177,404] The way these concepts are explained to survey participants also affects responses.[423] In certain studies, colloquial terms are used (e.g. "boyfriend", "lover")[233,386,411] while in others, as in ASTRA, an explanation is provided to differentiate between partner types.[195,424] Some studies do not provide any description apart from a single term (e.g. "main partner" or "in a relationship").[103,304,408] In ASTRA, it was not possible to ascertain whether disclosure was specifically to a stable partner (phrased as "I have told a partner/wife/husband"), therefore prevalence of non-disclosure to the current stable may have been underestimated. However, restricting answers to MSM who were in an ongoing relationship aimed to increase the sensitivity of this non-disclosure measure.

7.5.3 Factors associated with non-disclosure to a stable partner

There was no evidence of a significant association between participants' age and non-disclosure to a stable partner. In the 'East London' study, older age (>60 years) was significantly associated with higher prevalence of non-disclosure to parents but not to a stable partner.[394] It is possible that older MSM experience or perceive a greater level of stigma surrounding HIV disclosure than younger people, but this may be less relevant in the context of an ongoing relationship with a partner. On the other hand, older people may feel more able to manage HIV without the need to tell others.

Non-disclosure to a stable partner was highest among MSM of black, Asian, Mixed, or other (non-white) ethnicity compared to white MSM. This finding may reflect cultural and structural drivers of non-disclosure among ethnic minority MSM who may experience perceived and actual stigma.[394] Attention should be directed to groups with highest non-disclosure so as to better understand circumstances that encourage or discourage it.

Shorter time since HIV diagnosis tended to be associated with greater non-disclosure to a stable partner, even among MSM in this analysis (who were diagnosed with HIV for at least three months). A comparable finding was observed in the 'Healthy Living Project' of 1828 HIV-diagnosed MSM in the USA (Table 7.2), in which the odds of non-disclosure to all partners (including main and casual) were higher among MSM who were diagnosed for under 5 years.[408] In the 'Young MSM of Color Initiative'[386] there was no evidence of a significant difference in prevalence of disclosure to stable partners among those who were newly diagnosed and those re-engaged in HIV care at baseline; there was weak evidence that disclosure to steady partners increased by 20% at six months follow-up (p=0.06). Disclosure of HIV

status may thus be a gradual process, whereby a newly-diagnosed individual may take time to adjust to their diagnosis and prepare to tell others; this may apply even for close relationships. These findings highlight the need for health facilities to provide a supportive context as soon as possible after diagnosis, and to assist individuals in building communication skills, coping strategies, and in mobilizing support for those who need it.

In terms of socio-economic factors, although education and employment status were not associated with non-disclosure to a stable partner, financial hardship was associated with non-disclosure. MSM who reported not having money for basic needs or who had money only "most" or "some" of the time had significantly higher prevalence of non-disclosure to a stable partner compared to those who always had money ($p=0.002$ for "no/most/sometimes" versus "yes, all of the time"). This was independent of the effect of non-white ethnicity.

While HIV status disclosure has been seen as an important step towards enhancing mental health through increased social support,[425] evidence remains mixed; the majority of results stem from heterosexual HIV-diagnosed populations reporting on overall non-disclosure (to friends and family).[394,395,398,426] Evidence on the association between social support, measures of mental health status, and disclosure to a stable partner is scarce. In ASTRA, there was evidence that medium or low functional social support was associated with higher prevalence of non-disclosure to a stable partner. There was no significant association of depression or anxiety symptoms with non-disclosure to a stable partner. In the 'East London' study, MSM who had suicidal thoughts had higher odds of non-disclosure to their current partner; the effect was significant only for white compared to ethnic minority MSM.[394] Any association between depression, anxiety and non-disclosure may be mediated by low social support[236] and be bidirectional; pre-existing symptoms of poorer mental health and low social support may discourage HIV-serostatus disclosure to a stable partner, or it may be that non-disclosure creates feelings of isolation, decreased peer social support, and more mental health symptoms.

In ASTRA, non-disclosure to a stable partner was independently associated with the current partner's unknown HIV serostatus, consistent with earlier studies of HIV clinic attendees from the UK[412] and the USA.[408] Participants who did not know their stable partner's HIV-serostatus were more likely to have not disclosed their own serostatus, which may reflect the dynamics of mutual disclosure. HIV-diagnosed MSM may be more likely to disclose to a stable partner who is also HIV-positive as the fear of rejection may be lower.[381] Research on the association between relationship-related factors (such as length of time in the relationship, cohabitation) and non-disclosure to a stable partner among MSM is scarce; no association was found in ASTRA or in the 'East London' study.[394]

Although ASTRA MSM not on ART tended to have higher levels of non-disclosure to a stable partner, this association was largely explained by shorter time since HIV diagnosis; results were not significant in multivariable models. There was some evidence that men who reported undetectable VL were more

likely to disclose to a stable partner (compared to those who did not report undetectable VL and those not on ART) after adjustment for ethnicity, time since HIV diagnosis, and partner's HIV serostatus. A detectable or unknown VL level may be an indicator of lack of engagement in medical care, or could possibly suggest denial or avoidance of HIV-status, which may be closely linked to non-disclosure to a partner.

7.5.4 Non-disclosure to a stable partner and sexual behaviours

There were no significant associations of non-disclosure to a stable partner with any sexual behaviour in the past three months or in the past year, although there was low power to examine these associations. Although there was some evidence to suggest that MSM who had not disclosed to their stable partner were more likely to have CLS-C compared to those who disclosed, this association was not significant after adjustment for partner's HIV serostatus. Similarly, MSM who had not disclosed were less likely to have high partner turnover (10 or more new sexual partners) in the past year compared to those who disclosed, however this association did not reach significance.

Disclosure does not necessarily lead to safer sexual behaviour but could inform choice in type of sex within and outside of a stable relationship. Couples' HIV testing and counselling, whereby two people planning to be in a sexual relationship receive HIV testing together, has been shown to facilitate mutual disclosure of serostatus and is associated with a reduction in sex with outside partners and lower prevalence of CLS.[427]

7.5.5 Prevalence of lower sexual disclosure

This study used level of agreement to the statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex" as a proxy for lower sexual disclosure. Overall, almost 44% were classified as having lower sexual disclosure. The prevalence of non-disclosure to casual sex partners ranges widely according to the population sampled and the question posed to participants. For example, in the Dutch hospitals study (see Table 7.3), almost 60% of HIV-diagnosed MSM attending for care reported that they 'never' or 'rarely' disclosed to casual sex partners in the past six months[201], compared to 34% of MSM recruited from the largest HIV clinic in Dublin ('never' disclosed to casual partners in past six months).[390] The lowest prevalence estimate was reported in HOPS, whereby 9.2% of MSM who had any sex in the past six months had not disclosed to 'any sexual partners'.[241] The wide range of prevalence estimates observed is likely due to varying definitions of non-disclosure behaviour and attitudes (number or proportion of partners disclosed to over period of time versus intent to disclose to future partners) as well as classifications of casual partners (any sex partner including stable, new sex partners, or casual but recurring sex partner).

7.5.6 Factors associated with lower sexual disclosure

There was no evidence of an association of age and lower sexual disclosure. Results from previous studies are mixed. In the Dublin HIV clinic study (n=84 MSM) older age was associated with higher odds of not disclosing to casual partners compared to sometimes or always disclosing (adjusted for gay community attachment, HIV-related optimism, and number of partners).[390] On the other hand, there

was no evidence of a significant association between age and non-disclosure to casual partners in the SUMIT baseline survey[199] or in Positive Connections[418] studies from the US. Results similar to those observed in ASTRA were evident in the baseline assessment of a US RCT aiming to assist MSM in disclosing to casual sex partners (2009-2014).[392] This study of 340 HIV-diagnosed MSM recruited via community venues and websites assessed agreement to the statement ''I plan to tell my future sexual partners with whom I have anal sex without a condom about my HIV status'' on a four-point Likert scale. The majority of MSM agreed to the statement and no evidence of an association with age was observed.[392]

Socio-demographic factors emerged as independent correlates of lower sexual disclosure in this study, but the pattern of associations tended to be opposite to that seen for disclosure to a stable partner. MSM who were more educated (university degree versus none or up to A levels) and those who always had money for basic needs (versus not always) were more likely to have lower sexual disclosure. This is in contrast to results from SUMIT and Positive Connections, in which no association was observed between education, income, and non-disclosure to casual sex partners in the past three months.[199,418]

Levels of sexual disclosure were highest among MSM with an HIV-positive stable partner, lower among those with an HIV-negative or HIV-unknown serostatus stable partner, and were lowest for MSM who did not have a stable partner. This association remained significant after adjustment for socio-demographic and HIV-related factors. This may be explained by the fact that MSM with HIV-positive stable partners are more likely to disclose to their stable partner, and therefore consider a higher likelihood of disclosure to a new sexual partner. Possibly, this may also be influenced by a positive experience of mutual disclosure. Although it was not possible to examine attitudes towards non-disclosure to new sex partner by casual partners' HIV-serostatus, these findings are in line with the baseline survey of the US 'SafeTalk' trial (n=138 MSM),[407] which showed that disclosure was highest to other HIV-positive partners, lower towards HIV-negative partners, and was lowest towards HIV-unknown status casual partners.

Additionally, there was an association of self-reported undetectable VL and lower prevalence of disclosure to new sex partners, which was not attenuated by adjustment for core socio-demographic factors. This finding may suggest that HIV-diagnosed MSM with perceived undetectable VL were more likely to consider HIV-serostatus disclosure as not necessary due to their low HIV infectiousness. This also provides further evidence that knowledge of VL status may influence sexual attitudes and behaviour, an effect which may become more apparent with increasing awareness of the impact of ART on infectiousness. To date, no other observational studies have reported on this association. The only other information comes from a US mathematical probability model (based on 164 MSM, see section 7.2.2.3) evaluating effectiveness of disclosure in reducing the risk of HIV transmission, which found no association between self-reported VL and non-disclosure to casual sex partners.[416]

7.5.7 **Lower sexual disclosure and sexual behaviours**

MSM with higher sexual disclosure were significantly more likely to have CLS overall and CLS-C. However, those with *lower* sexual disclosure were *more* likely to have CLS-D, group sex, and high partner numbers compared to those with higher sexual disclosure. These findings reflect the dynamics of mutual disclosure between HIV-positive partners and also indicate that higher disclosure is linked to possible HIV-serosorting. In fact, use of the mutually exclusive categories of sexual behaviour further provided evidence that levels of disclosure to sexual partners were significantly associated with having 'CLS-C without CLS-D', which could indicate HIV-serosorting. In addition, the association of lower sexual disclosure and higher prevalence of CLS-D may reflect the perception that once HIV-positive serostatus is disclosed, HIV-negative partners may not wish to have CLS with an HIV-positive man. Hence, HIV-diagnosed men may be inclined to not disclose to an HIV-serodifferent partner. Further, no association was observed of lower sexual disclosure with higher HIV risk CLS-D. This may also highlight that, to some extent, HIV-diagnosed MSM factor in their personal VL level in the decision to not disclose and have CLS-D, as the risk of HIV transmission when the HIV-positive partner is on effective ART is extremely low.

In earlier US studies of HIV-outpatients (see Table 7.3) prevalence of CLS-D among MSM who did not disclose to casual sex partners (any or new partners) was found to range between 16% and 31%.[199,389,408,420,428] Evidence on the association between non-disclosure to casual sex partners and CLS remains mixed. There was no indication of a significant difference in prevalence of CLS-D among those who did and did not disclose to casual sex partners in four diverse US studies.[177,195,404,410] On the other hand, non-disclosure to casual partners was independently associated with higher odds of having CLS-D in two US studies after adjustment for socio-demographic and lifestyle factors. [409,418]

Lower sexual disclosure was also strongly associated with having high partner numbers in the past year. Similar findings were observed in the US 'Positive Choices'[419] and Canadian LISA studies[389](Table 7.3). In ASTRA, strong associations were also observed of lower sexual disclosure with group sex, which has not been previously studied. There was some suggestion that lower sexual disclosure was associated with using the internet to find sex. Further studies are needed to examine the role of the internet in facilitating or discouraging disclosure of HIV-serostatus, particularly since the widespread availability of geosocial and sexual networking (GSN) mobile apps in the late 2010's.[429,430]

7.5.8 **Limitations**

The direction of associations between socio-demographic, psychological, HIV-related factors and non-disclosure could not be ascertained. It is possible that pre-existing factors (e.g. depression or being on ART) encourage non-disclosure and vice versa.

Prevalence of non-disclosure may be influenced by non-response; if non-disclosure was more prevalent among those who refused study participation, then our study would underestimate non-disclosure. There was a significant proportion of missing data for the disclosure category sub-questions, but not for the overall non-disclosure question on which primary analyses were based. In addition, it was not

possible (from the question wording) to ascertain whether disclosure to a stable partner was to the current stable partner, a previous/concurrent partner, or a casual partner, which could underestimate prevalence of non-disclosure to the current partner. To increase the validity of the partner non-disclosure measure, analysis was restricted to MSM who reported being in an ongoing relationship only. Small sample sizes precluded a more robust examination of associations between non-disclosure to a stable partner and sexual behaviours.

Non-disclosure to new sexual partners was not explicitly ascertained in ASTRA. The statement "I'd expect to tell a new partner that I'm HIV-positive before we have sex" was considered a proxy measure instead. It is encouraging that the prevalence estimates of lower sexual disclosure were comparable to other studies on non-disclosure to new sex partners. Future studies could benefit from employing partner-level analysis of non-disclosure (e.g. number of CLS-D casual partners the participant disclosed to among all partners over a period of time). Finally, it should be emphasised that, while epidemiological studies such as ASTRA provide insight into patterns of non-disclosure among a clinic-based population, they are not able to capture the complex circumstances, motivations, and challenges that may surround the issue of disclosure for an HIV-positive individual.

7.6 Conclusions and Implications

The prevalence of non-disclosure of HIV-serostatus to the social circle, to a stable partner, and new sex partners was overall low among MSM participating in the ASTRA study. A higher proportion of men indicated that they would not always disclose to new sexual partners. These findings provide important insights into non-disclosure among people living with HIV in the UK.

A number of North American studies have examined non-disclosure to stable or casual partners and sexual behaviours among HIV-diagnosed MSM, but evidence from the UK is lacking. Interpretation of findings on associations between non-disclosure and CLS is not straightforward due to methodological differences across studies (diverse populations, non-disclosure measures, and definitions of stable or casual partners). These varying findings, coupled with evidence that HIV disclosure may differ by socioeconomic, HIV-related, and contextual factors, point to the need for additional research in examining patterns of HIV disclosure (type of confidant) and any effects on sexual risk behaviours.[411]

In addition, the role of HIV-serostatus disclosure to sexual partners in the era of effective ART may be changing. Emphasis on HIV-serostatus disclosure to sexual partners places the majority of responsibility of reducing HIV transmission risk on HIV-diagnosed individuals who may already experience perceived or enacted stigma.[408] No association was observed between non-disclosure to a stable partner and any CLS among MSM in an ongoing relationship in ASTRA, but power to examine associations was low.

Lower sexual disclosure was associated with reporting CLS-D, group sex, and high partner numbers; however, over 90% of MSM with lower sexual disclosure who also had CLS-D, were on ART with suppressed VL. With evidence that self-reported undetectable VL is associated with lower sexual

disclosure in our study, it will be important for future studies to continue to assess the impact of self-reported VL on sexual behaviour and attitudes, as ART use expands. The strong association of higher sexual disclosure and CLS-C may further suggest that HIV transmission risk reduction is taking place, in the form of disclosure to HIV-positive partners and HIV-serosorting. Use of the mutually exclusive categorisation of sexual behaviour (condom-protected sex, 'CLS-C without CLS-D', CLS-D) provided further evidence that higher disclosure is linked to possible HIV-serosorting. Future studies could benefit from using this mutually exclusive categorisation of sexual behaviour, in order to disentangle associations of levels of non-disclosure with different types of sex.

Therefore, HIV-diagnosed MSM may not disclose to sex partners but still practice some form of HIV risk reduction, be it having CLS-D while on suppressive ART, or having HIV-seroconcordant partners only. Discussion and agreement on condom use or non-use and acceptable levels of risk for both partners may be more relevant in the context of reducing HIV transmission risk.[381,414] Prevention efforts could benefit from assisting HIV-diagnosed people in effectively communicating and negotiating acceptable sexual behaviours with sex partners, and in providing a supportive context for those who choose not to disclose their status to their social circle, a stable or casual partner.

8 Hepatitis C co-infection, other sexually transmitted infections, and condomless sex

8.1 Chapter aims

The aim of this chapter is to examine the association of socio-demographic, HIV-related, lifestyle factors, and sexual behaviours with prevalent and incident sexually transmitted infections (STIs) among HIV-diagnosed MSM. A background of the aetiology, natural history, treatment, management of relevant bacterial and viral STIs will be provided, along with the impact of each class of STIs on HIV transmission risk and vice versa. A review of the prevalence of any STI, based on self-report, will be undertaken, focussing on studies of HIV-diagnosed MSM clinic attendees in high-income countries between 1995 and 2016. The review will examine firstly, the prevalence and patterns of any self-reported STI, the prevalence of chronic hepatitis C (HCV), and the incidence of HCV; secondly, any socio-demographic, psychological, HIV-related, lifestyle factors, and sexual behaviours that have been identified as correlates of prevalent STIs, HCV, and of incident HCV. The aims of the analyses are to investigate, among ASTRA MSM: (i) the prevalence of any and of specific self-reported STIs, and the cross-sectional association of socio-demographic, psychological, lifestyle, and HIV-related factors with any STI co-infection, (ii) the cumulative prevalence of HCV using linked routine clinical data, and the cross-sectional association of the above factors with chronic HCV, (iii) the incidence of new HCV over follow-up, using linked routine clinical data, and the prospective association of factors associated with incident HCV.

8.2 Introduction

STIs remain a major public health concern. In 2012, the World Health Organisation estimated that, globally, there were almost 184 million new cases of the four most common curable STIs among males (chlamydia, gonorrhoea, syphilis, and trichomonas, see section 8.2.1).[431] STIs can cause morbidity in affected individuals and their sexual partners and present a substantial burden on healthcare services. Increasing resistance and decreased susceptibility to antimicrobials is of particular concern (section 0).[432]

For HIV-positive individuals, concurrent infection with another STI can cause long-term morbidity and may require treatment modifications. STIs are both a marker of condomless sex (CLS) as well as a possible causal factor in HIV transmission and acquisition. HIV-diagnosed MSM in the UK are disproportionally affected by STIs (discussed in section 8.2.8).[433] The high incidence of STIs observed in this population may in part be due to increases in STI testing over the past decade. It could also be due to a genuine increase in incidence, driven by high number of sexual partners, or increased serosorting practices (with lower condom use) among HIV-diagnosed MSM (such as CLS with other HIV-seroconcordant partners, CLS-C). While CLS-C does not pose a risk of HIV transmission when HIV-serostatus is confirmed, it does pose the risk of transmission of other STIs. There is evidence that co-

infection with specific STIs and HIV may increase the risk of onward HIV transmission[22,434–441], but it is unclear whether this is still the case when the HIV-positive partner is on effective ART. Understanding the drivers of the increase in STI/HIV co-infections among HIV-diagnosed MSM thus warrants further study.

8.2.1 Sexually transmitted infections (STIs) included

This chapter focuses on STIs of public health importance among HIV-diagnosed MSM in the UK. They are separated by aetiologic pathogen: STIs caused by infection with bacteria or parasites are summarised in Appendix VI (Table VI.1) and include syphilis, gonorrhoea (NG), chlamydia (CT), lymphogranuloma venereum (LGV), non-specific urethritis/non-gonococcal urethritis (NSU/NGU), and trichomonas (TV).[442–452] STIs caused by infection with a virus are summarised in Appendix Table VI.2 and include genital herpes caused by herpes simplex viruses type 1 and 2 (HSV-1, HSV-2) and genital warts caused by human papilloma virus (HPV).[450,451,453,454] Hepatitis C virus (HCV) infection is discussed separately (section 8.2.6) as a major chronic pathogen among HIV-diagnosed individuals. As the focus of this thesis is on MSM, the clinical presentation of these STIs is discussed among males only (symptoms and natural history vary in females).

CT, NG, NSU/NGU, and TV can be thought of as short-lived curable STIs; they tend to be asymptomatic among males, have high transmission probability and high reinfection rates. While syphilis is a chronic STI that can cause morbidity throughout its natural history if untreated, it is transmissible only during the first one to three years of infection (early stage); it then enters a prolonged latent stage that is not infectious but can be associated with considerable morbidity.[442] LGV, caused by a CT serovar, has a variety of acute and chronic manifestations analogous to syphilis, but the majority of patients recover without sequelae. Viral STIs are longer-lasting, tend to be symptomatic, and have low transmission probability. Once they resolve, viral STIs enter a latent state characterised by recurrence of symptoms and episodes of asymptomatic shedding over a long infectious period (particularly for HSV). HPV infection is normally transient but, in a fraction of cases, can become chronic; some HPV serotypes can progress, among males, to cancer of the penis, anus and oropharynx.[451]

The term ‘co-infected’ in this chapter refers to concurrent infection with HIV and another STI, while ‘mono-infected’ refers to those who are diagnosed with only one STI (for example, HCV-monoinfected refers to those diagnosed with HCV but not another STI or HIV, HIV-monoinfected refers to those diagnosed with HIV only and so on, see section 8.2.7.6).

8.2.2 **Bacterial STIs and HIV co-infection**

Bacterial STIs (bSTIs) have been recognised as important cofactors in the transmission of HIV since the beginning of the HIV epidemic.[455] As discussed in section 1.4.4, cohort studies and RCTs have shown that HIV positive people (both diagnosed and undiagnosed) co-infected with other STIs are more likely to transmit HIV compared to those who are HIV positive but not STI co-infected.[456] Below is a summary of the effect of bSTIs on HIV progression, transmission, and on antimicrobial resistance.

8.2.2.1 Impact of bacterial STI co-infections on HIV

Genital tract bSTIs (including CT, GC, syphilis, TV) increase the detection and concentration of HIV RNA shedding in the genital tract.[456,457] This is particularly the case when infection is associated with recruitment of inflammatory and immune cells to the genital tract. At cellular level, bSTIs can upregulate HIV leading to elevated plasma HIV VL; lesions (as in LGV or syphilis) can also lead to increased HIV RNA genital shedding, but it is unclear if this is still the case when plasma VL is suppressed on ART.[439,458]

8.2.2.2 Antimicrobial resistance

Antimicrobial resistance (AMR) occurs when bacteria develop alterations in their genetic code, which render the antibiotic used to cure infection with that microorganism ineffective.[432] AMR has complicated STI treatment as most available or convenient (e.g. single dose) drugs are no longer effective. The emergence and spread of antimicrobial resistant gonococcal strains is a particular threat to global public health[432,444]; many strains are now resistant to former first and second-line therapies and increasingly more strains are no longer susceptible to third-generation therapies.[451,459] In the UK, a microbial culture of NG is required to detect reduced antimicrobial sensitivity and a test of cure (TOC) is recommended for all cases of NG to monitor treatment failure.[444] Guidelines continue to change rapidly in response to emerging AMR.[448]

8.2.3 **Genital herpes and HIV co-infection**

Genital herpes is an ulcerative STI, caused by infection with herpes simplex virus (HSV) types 1 and 2 (see Appendix VI, Table VI.2). Although antiviral treatment can reduce the duration and severity of herpetic symptoms and control recurrences, HSV infection is lifelong.[460] A substantial body of evidence has documented the epidemiological synergy between HSV and HIV.[461,462] The predominant target cell for HSV is the CD4 lymphocyte[451] and as such, HSV is associated with both increased risk of HIV transmission and acquisition; in turn, HIV infection can increase the severity of clinical HSV disease (among HIV-positive people).[463]

8.2.3.1 Impact of genital herpes on HIV

As discussed in section 1.4.4, among HIV/HSV-2 co-infected individuals, meta-analyses show that HSV-2 shedding increases the concentration of genital HIV RNA, even after accounting for CD4 count and time since HIV diagnosis.[437,456] There is also some indication from the pre-ART era that HSV-2 reactivation may be associated with higher levels of genital HIV RNA, but recent robust results are lacking.[464]

A number of prospective studies and placebo-controlled RCTs (2004-2010) [52,463,465–470] have shown that HSV-2 antiviral treatment with excellent adherence significantly reduced HIV RNA and genital HSV-2 ulcers; however, no reduction was observed in the incidence of HIV transmission to HIV-negative sexual partners. The lack of efficacy of HSV-2 therapy in reducing HIV transmission risk in suggests that a greater reduction in plasma HIV VL would be required to reduce risk of HIV transmission.

8.2.3.2 Impact of HIV on natural history of HSV

There is marked difference in the natural history of HSV between HIV-positive and HIV-negative people. Among ART-naïve HIV/HSV co-infected people, the degree of immunosuppression resulting from HIV is the most important risk factor for HSV recurrence; primary and recurrent genital HSV commonly present with persistent anogenital lesions and serious complications (particularly during advanced HIV infection with low CD4 counts).[450] While ART reduces the frequency of HSV recurrence, it is less efficacious on reducing asymptomatic HSV shedding.[463] In addition, the efficacy of antiviral therapy for HSV is lower in HIV-positive compared to HIV-negative people.

8.2.4 Genital warts and HIV co-infection

Genital warts are benign skin lesions caused by the human papillomavirus (HPV), of which over 100 genotypes have been identified (see Appendix VI, Table VI.2).[453] Over 90% of anogenital warts are caused by HPV types 6 or 11 and usually resolve spontaneously within a year. Although warts are treatable, recurrence is common and accounts for over 40% of all genital wart diagnoses in the UK.[471] Among MSM in the UK, infection with high risk HPV types (16, 18, 31, 45) is the causative agent of invasive anal cancer and of a subset of oral cancers.[460] The impact of HPV/HIV co-infection on the progression of HIV among those on ART has not been well studied.

8.2.4.1 Impact of HIV on genital wart progression

HIV-immunosuppression may hinder spontaneous clearance of genital warts and reactivate latent HPV; this may in turn lead to faster progression of HPV-associated cancerous lesions.[454] A meta-analysis of nine studies among MSM reported that the incidence of HPV-associated anal cancer was higher among HIV-diagnosed men compared to HIV-negative (46 versus 5 per 100,000/year); among HIV-diagnosed men, there was a marked increase observed in the annual incidence of HPV-related anal cancers, from 22 per 100,000 in the pre-ART era (prior to 1996) to 78 per 100,000 after the introduction of ART (1996 onwards).[472] These estimates were not adjusted for age and may be in part explained by improved survival conferred by ART and ageing of the HIV-positive population.[454] The incidence of HPV-related oral malignancies is also increasing among HIV-diagnosed men, with a reported increase of oral warts among those on ART.[436,473,474] It is also hypothesized that ART-related immune restoration may not be enough to clear long-standing HPV or that improved survival allows for longer time to develop anal cancer.[475] It remains unclear to what extent CD4 count contributes to HPV disease progression.

8.2.5 Impact of STIs on acquisition of HIV in HIV-negative individuals

Two biological mechanisms have been identified as contributing to increased susceptibility to HIV acquisition among HIV-negative people who have other (non-HIV) STIs. Firstly, lesions (caused by bSTIs

or HSV-2) and genital warts disrupt genital mucosa allowing a portal of entry for HIV. Secondly, as STIs are reactivated, inflammatory cells (predominantly HIV target cells, CD4) are recruited in the anogenital tract and targeted by HIV, even after lesions or warts have resolved.[463,476–478] Ulcers in both partners can also facilitate blood-to-blood contact and thereby HIV transmission.[439,457]

8.2.5.1 STI control as an HIV prevention strategy

Since 1996, nine RCTs have been conducted worldwide to evaluate whether treatment of STIs can reduce STI prevalence among HIV-serodifferent partners and hence reduce HIV transmission. All were conducted among heterosexual populations in Africa; five focused on control of bSTIs[479–484] and the remaining four on HSV-2.[469,470,485] Only one of these studies showed a significant reduction in HIV incidence as a result of population-level bSTI treatment.[479] This is in part explained by the low prevalence of bSTIs in the populations recruited, additional HIV prevention services introduced in the comparison arm of these trials, low power to evaluate HIV incidence, and different HIV epidemic phases in different populations.[486] Hence there is insufficient evidence to evaluate effects of STI treatment on reducing incidence of HIV and an absence of this sort of research among MSM.[487]

8.2.6 Hepatitis B virus (HBV)

HBV is a DNA virus whose primary target cell is the hepatocyte (liver cell).[488] Transmission is by parenteral exposure to infected blood and body fluids, through sexual contact, injecting drug use, blood to-blood contact, and perinatal transmission.[489] HBV can progress to chronic infection associated with increased risk of chronic liver disease and hepatocellular carcinoma (HCC).[488] HBV can be effectively prevented by immunisation; since 1992, the UK offers vaccination of individuals at high risk of exposure to the virus (incl. HIV-diagnosed people). There are important distinctions in the epidemiology of HIV co-infection with hepatitis B or C; the prevalence of hepatitis C tends to be highest among PWID, followed by MSM, and is lowest in the general population (section 8.2.8). In contrast, prevalence of HBV is overall lower, and similar across exposure groups (MSM, HIV-diagnosed MSM, PWID, and the general population).[490] For these reasons, HCV is of greater focus in this chapter.

8.2.7 Hepatitis C virus (HCV)

HCV is an RNA virus, which, like HBV, primarily targets and replicates within hepatocytes.[451] Genetic variability is high and reflected by different genotypes and subtypes in diverse geographical transmission risk populations; seven main genotypes are recognised (1-7), which are further divided into subtypes (each assigned a letter).

8.2.7.1 HCV transmission

HCV is primarily transmitted via direct blood-to-blood contact. Needle sharing during injection drug use (IDU) is estimated to account for over 50% of HCV infections in high-income countries. For this reason, accounting for prevalence of IDU in studies of HCV is important in interpreting HCV prevalence estimates. While there is evidence that HCV is present in seminal fluid in acute and chronic infection, it is less efficient in sexual transmission (compared to other viral STIs).[491] Sexual transmission of HCV is uncommon among heterosexuals. However, among HIV-diagnosed MSM, sexual transmission has been

high and ongoing in Europe, the USA, and Australia since 2000. Surveillance of HCV outbreaks has revealed large international networks of HCV transmission among HIV-diagnosed MSM, associated with increases in sexual risk behaviours (such as CLS).[492,493] This chapter focuses on sexual transmission of HCV.

8.2.7.2 Life cycle and serology

HCV can cause acute and chronic hepatitis. Acute infection, classed as infection in the first six months since exposure, is asymptomatic in over 60% of patients. (Figure 8.1) Plasma HCV RNA can be detected within 2-14 days of exposure, rising rapidly, and then plateauing. Within two months post-exposure, levels of HCV RNA begin to decline and two patterns are seen: (i) HCV RNA continues to decline leading to spontaneous HCV clearance within six months of initial infection, or (ii) HCV RNA stops declining, may rise to some extent and then stabilise, indicating chronic infection. (Figure 8.1) HCV-specific antibodies (anti-HCV) gradually appear within two months of initial exposure, and persist among those with both acute and chronic HCV.[494] HCV seroconversion can be delayed significantly in HIV positive people.[495]

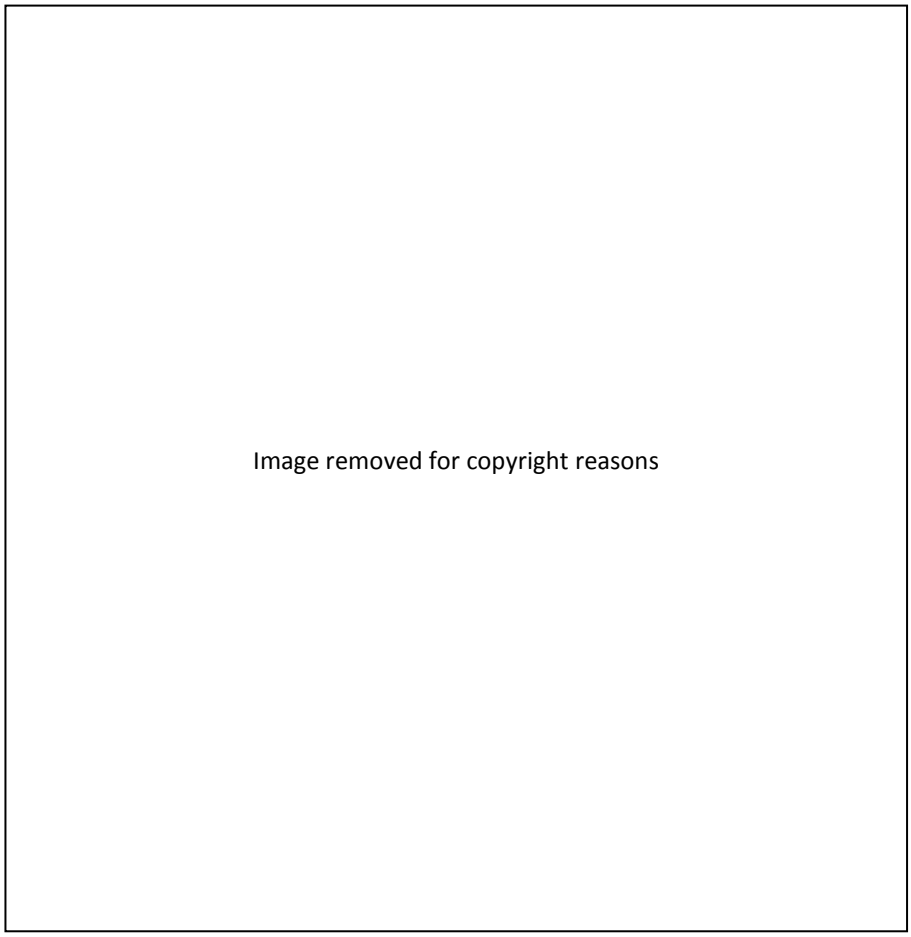
8.2.7.3 Diagnosis

It is estimated that clearance of HCV occurs in a quarter of HCV-infected individuals, while chronic infection remains in the rest (although spontaneous clearance is lower in the HIV positive population).[496] Coupled with the fact that all individuals exposed to HCV develop anti-HCV, screening for anti-HCV (using enzyme linked immunoassays, EIAs) is thus the first-line diagnostic test for HCV infection. Third-generation EIAs for anti-HCV have specificity over 99%.[497] In cases of clinically suspected acute HCV while anti-HCV is negative, HCV-RNA testing is used to confirm infection. In the case of a positive anti-HCV, HCV RNA tests are conducted to establish whether HCV infection is active or cleared.[496] Among HIV-diagnosed individuals, anti-HCV seroconversion may be delayed and HCV RNA may be needed for diagnosis.[495,498]

8.2.7.4 Disease progression

Chronic HCV infection leads to liver fibrosis, the result of liver's wound-healing response to repeated injury.[499] Cirrhosis is a late stage of fibrosis development that results in widespread distortion of liver architecture. A meta-analysis of over 100 prognostic studies showed that advanced liver fibrosis progresses to cirrhosis after a median of 30 years in approximately 35% of those with chronic HCV; this progression is more rapid in those with HIV co-infection and in the presence of hazardous alcohol use.[500] Ultimately, cirrhosis leads to liver failure.[499]

Figure 8.1: Serological course of acute HCV with (A) clearance and (B) progression to chronic infection[501]



8.2.7.5 HCV treatment

The goal of therapy is to cure HCV infection so as to prevent complications including fibrosis, cirrhosis, and HCC.[496] This is measured by sustained virological response (SVR), defined as undetectable HCV RNA (≤15IU/mL) 12 weeks after end of therapy. A discussion of treatment options is beyond the scope of this thesis; briefly, up until 2011, standard treatment for HCV consisted of a combination of pegylated-interferon plus ribavirin (pIFN/Rib), which resulted in SVR in HCV mono-infected patients of 40-45% of those with genotype 1 HCV and 70-80% of those with genotypes 2 or 3 HCV.[502,503] HIV/HCV co-infected patients had lower SVR rates to pIFN/Rib based therapies. Treatment has rapidly evolved with the advent of directly acting agents (DAAs), which became available after 2011 (in the UK, DAAs became more widely available through the NHS after 2015). This represented a major advance in HCV treatment. A number of randomised trials have shown that DAAs can achieve SVR in >95% of individuals with any HCV genotype. This response to DAA is similar in both HCV mono-infected and HIV co-infected patients.[504–506] Latest European treatment guidelines recommend a range of options including new DAAs.[496,498,507]

8.2.7.6 Impact of HCV co-infection on HIV

There is conflicting evidence of the effect of HCV co-infection on progression of HIV to AIDS. A number of cohort studies conducted in the pre-ART era (prior to 1996) found no effect of HCV on CD4 count and HIV VL, or on progression of HIV to a new AIDS event or death (adjusting for HIV-related factors and

IDU).[508,509] A meta-analysis of 27 studies in the ART era (1996-2008) showed that the risk of overall mortality was significantly higher among HCV/HIV co-infected patients on ART compared to HIV-monoinfected individuals (Risk Ratio=1.35, 95%CI 1.11-1.63).[510] More recent results have corroborated these findings adjusting for ART status.[511,512]

Evidence on the effect of HCV co-infection on immunological and virological response to ART is also mixed. A meta-analysis of eight cohort studies (1996-2001) showed that compared to HIV-monoinfected individuals, HCV/HIV co-infected individuals had reduced CD4 counts after 48 weeks on ART.[513] In addition, no significant difference was observed in the virological response to ART between HCV/HIV co-infected and HIV mono-infected individuals.[513,514] Mixed findings may be due the different confounding factors accounted for in various study settings, such as ART adherence, length of time on ART, HCV treatment, prevalence of IDU and co-morbidities in the cohort.

8.2.7.7 Impact of HIV on HCV

Longitudinal studies show that risk of progression to chronic HCV and liver disease is elevated among HCV/HIV co-infected individuals compared to those who have HCV, but not HIV (HCV-monoinfected).[515] Conversely, high CD4 counts and being on ART have been associated with lower risk of liver disease (including HCC) among co-infected compared to HCV-monoinfected individuals.[516,517] Hepatotoxicity (liver damage induced by drugs) can occur in response to ART. Among HCV/HIV co-infected individuals on ART there is an increased risk of developing hepatotoxicity compared to HIV mono-infected individuals.[68,518] This may require consideration of choice of ART regimens and monitoring for liver damage caused by ART, particularly in the period after ART initiation or switch.[519,520] HIV infection may also facilitate HCV transmission by increasing HCV RNA levels and through its negative effects on the lower gastrointestinal immune system.[68]

8.2.8 STI epidemiology in the UK

Recent trends and epidemiology of STIs in England are compiled using data from mandatory reporting of free open-access STI tests and diagnoses made in sexual health clinics and community-based settings. These are then submitted to the PHE-managed Genitourinary Medicine Clinic Activity Dataset (GUMCADv2), which also incorporates reliable data on sexual orientation from sexual health clinics (>90% completion since 2011).[521]

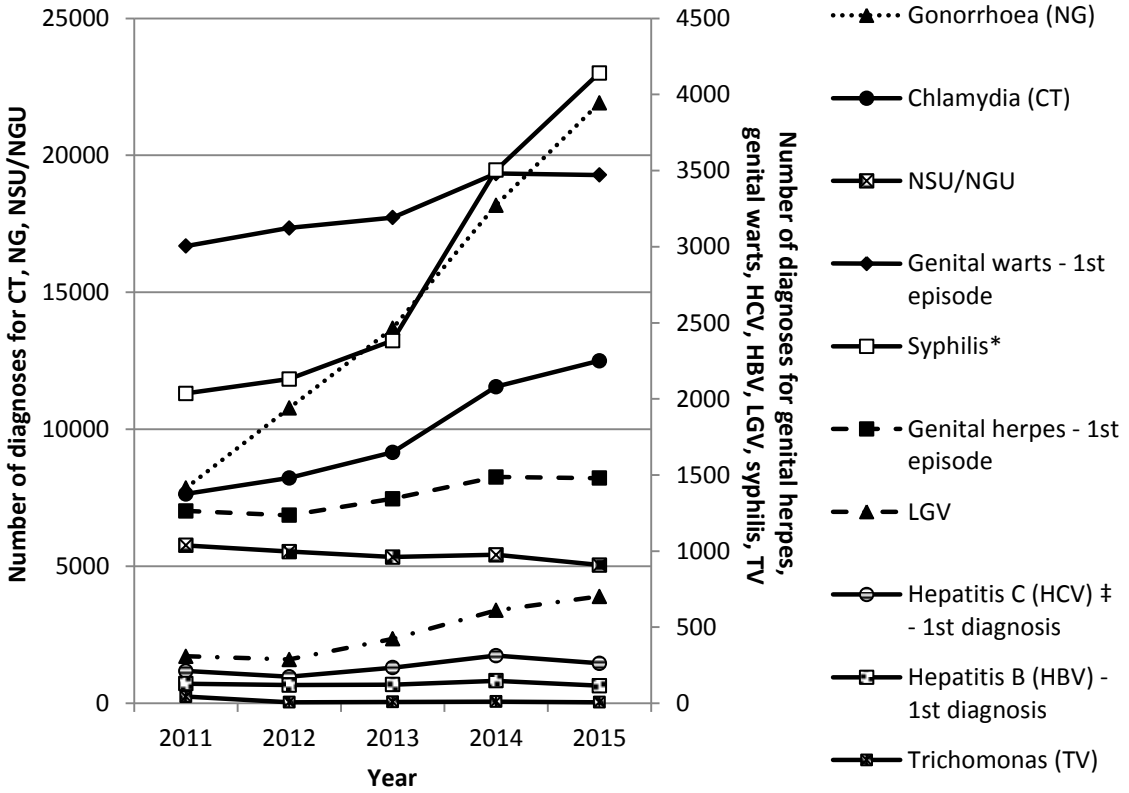
In the case of HCV, data is based on opportunistic testing in England. As HCV can be asymptomatic during seroconversion and for a prolonged period after infection (section 8.2.7.2), estimating the number of individuals with antibodies to HCV is complex. Evidence is synthesised from various data sources including statutory laboratory notifications, unlinked anonymous testing of IDU accessing specialist services (including drug treatment services and prisons), sentinel surveillance of blood-borne virus testing in blood donors, GUM, ante-, and neonatal clinics, as well as community screening surveys in people of South Asian origin.[522,523] Risk factor information (HCV transmission route) is recorded only in laboratory reports, which account for a small minority of prevalent HCV infections.[524,525]

In 2015, over 434,000 new STI diagnoses were made in England; the most prevalent STIs were CT (46%), new genital warts (16%), NSU/NGU (10%), and NG (10%).[471]

8.2.8.1 All MSM

Over the past decade, diagnoses of NG, syphilis, and genital herpes in England have increased considerably among males, compared to females. This is explained mostly by the increase in diagnoses among MSM. (Figure 8.2) In 2015, approximately 224,000 STI diagnoses were made among males attending sexual health clinics, of which over 53,000 were in MSM. This group accounted for the following proportions of diagnoses made among all males; 84% of syphilis diagnoses, 70% of NG, 21% of CT, 12% of genital herpes, and 9% of genital warts diagnoses.[471] NG was the most commonly diagnosed STIs among MSM in 2015. While the majority of MSM presented with genital NG infection, a quarter presented with rectal and a sixth with only pharyngeal NG infection; this may suggest that a considerable number of NG transmissions occurred through CLS. The continuing and rapid rise in syphilis is also of concern and suggests high prevalence of CLS.[526] In 2015, half of acute and probable acute cases of HBV (approx. 500) in the UK had associated exposure information recorded, of which 16% were attributed to sex between men. This proportion was similar to that reported in 2014.[489]

Figure 8.2: Number of new STI diagnoses made among all MSM in sexual health clinics in England (GUMCADv2 data, 2011-2015). *Adapted from*[527]



*NSU: non-specific urethritis; NGU: non-gonoccocal urethritis; LGV: lymphogranuloma venereum; ‡Diagnoses recorded in GUMCADv2 not exclusively transmitted by sexual contact; * Primary, secondary, and early latent syphilis*

8.2.8.2 HIV-diagnosed MSM

Since 2009, STI diagnoses have been steadily increasing among HIV-diagnosed MSM in the UK. Compared to HIV-negative or HIV-unknown status MSM, HIV-diagnosed MSM have four times the population prevalence of acute bSTIs.[471] In 2015, HIV-diagnosed MSM accounted for approximately 40% of syphilis diagnoses among all MSM, 24% of CT, 20% of NG, and 17% of anogenital herpes (first episode).[528] Outbreaks of previously rare STIs, such as LGV, have also been observed since 2003 among HIV-diagnosed MSM.[149,445,529] Between 2004 and 2015, 78% of UK LGV cases were among HIV-diagnosed MSM, of whom 4% were diagnosed with HIV within three months of LGV diagnosis.[446,471] Ongoing outbreaks of sexually transmissible (non-travel related) enteric infections have also been observed among HIV-diagnosed MSM; these include outbreaks of *Shigella flexneri*[147,238,530], toxin-producing *Escherichia coli*[531], and hepatitis A.[532,533] It has been suggested that CLS between HIV-positive men is strongly linked to these outbreaks and is contributing to ongoing STI transmission in this population.[433]

Evidence from systematic reviews shows that the incidence of HCV is significantly higher among HIV-positive compared to HIV-negative men.[66,534–536] In recent years, outbreaks of acute HCV have been recognised among HIV-positive MSM worldwide.[537–542] Enhanced surveillance of newly acquired HCV infection in MSM in England suggests ongoing but levelling off of rates of sexual transmission of HCV among HIV-positive MSM.[520,543] Between 2008 and 2012 a significant decrease in HCV incidence has been observed in HIV-positive MSM, from 0.73 to 0.24 per 100 PY.[544]

8.2.8.3 Prevalence of self-reported STIs among HIV-diagnosed MSM

Table 8.1 reviews evidence from cross-sectional and cohort studies conducted among HIV-diagnosed MSM in high-income countries since 1996, which include information on self-reported STI status. Prevalence of any self-reported STI in the past 12 months was found to range from 13.0% in the French ANRS VESPA2[545] to 41.0% in the UK behavioural surveillance study.[141] Information on the prevalence of specific self-reported STIs is scarce. Only one study reported on multiple STI co-infections, with 22.6% of HIV-diagnosed MSM reporting two or more STIs (in addition to HIV) in the past 12 months.[545] Information presented in Table 8.1 relates to studies based on STI screening (of asymptomatic individuals), which enables undiagnosed STIs to be accounted for as well.

Table 8.1: Prevalence of STIs in studies of HIV-diagnosed MSM in high-income countries between 1996 and 2016, according to method of STI ascertainment (self-reported or laboratory-confirmed)

						Prevalence of specific Sexually Transmitted Infection (%)								
	Study	Observation period	Country	N HIV+ MSM	Recall period (self-reported only)/ Timing of STI screen or diagnostic test* (lab-confirmed only)	Any	CT	NG	Syphilis	NSU/ NGU	Genital warts	Genital herpes	LGV	≥2 STIs
Self-reported STIs	**UK behavioural surveillance**[141]	2003-2004	UK	248	Past 12 months	41.0	-	-	-	-	-	-	-	-
	Sex and Love project[298]	2006	USA	122	Past 12 months	-	-	-	6.5	8.2	9.8	7.5	-	-
	SHCS[546]	2009-2010	Switzerland	112	Past 12 months	19.0	16.1	4.5	14.3	-	-	-	-	-
	ANRS VESPA2[545]	2011-2012	France	1037	Past 12 months	13.0	-	-	-	-	-	-	-	22.6
	Scotland GMSHS[142]	2011	UK	59	Past 12 months	25.4	-	-	-	-	-	-	-	-
	Presse Gays et Lesbiennes[204]	2011	France	1258	Past 12 months	30.8	-	-	-	-	-	-	-	-
	Essen HIV clinic[547]	2012-2014	Germany	233	Past 2 years	17.2	2.3	4.3	9.8	-	8.2	3.0	0.5	-
Laboratory-confirmed STIs	**Amsterdam STI clinic**[548]	2002-2003	Netherlands	222	Screening at single clinic visit	-	-	15.8	4.2 †	-	-	-	-	-
	SHCS[549]	2004-2006	Switzerland	2650	Routine annual syphilis serology: % positive tested during observation period	-	-	-	23.2	-	-	-	-	-
	UCLA Medical Center[550]	2004-2006	USA	212	Screening at first HIV clinic visit	28.0	5.7	8.0	-	-	-	-	-	-
	Positive Health[551]	2005-2006	Australia	295	Screening at enrolment	-	8.0	3.2	18.6	-	-	-	-	-
	Kings College HIV clinic[552]	2006	UK	77	Diagnostic testing of symptomatic patients	49.0	8.0	12.0	13.0 †	15.6	5.2	0.0	1.3	-
	University Hospitals[553]	2007-2008	Netherlands	616	Screening at enrolment	16.0	8.6	5.2	5.0 †	-	-	-	-	-
	SHCS[546]	2009-2010	Switzerland	112	Screening at enrolment	-	10.7	2.7	34.8	-	-	51.8	0.9	-
	Maple Leaf Medical Clinic[554]	2010-2012	Canada	294	Screening at single STI clinic visit	-	1.0	0.3	11.0 †	-	67.6	55.9	-	-
	Ohio sexual health clinic[555]	2012-2013	USA	41	Screening at single STI clinic visit	-	-	-	-	-	-	-	-	-

*CT: chlamydia; NG: gonorrhoea, NSU/NGU: non-specific urethritis/non-gonococcal urethritis; HCV: hepatitis C; LGV: lymphogranuloma venereum; SHCS: Swiss HIV Cohort Study; † Syphilis estimates in these studies are for early (infectious) syphilis only, remaining studies show combined early and latent syphilis estimates. *Screening refers to STI testing of asymptomatic (but potentially at risk) individuals while diagnostic testing aims at establishing the presence/absence of STIs in symptomatic individuals (or asymptomatic individuals with a positive screen).*

8.2.9 **Cumulative prevalence of hepatitis C among HIV-diagnosed MSM**

Table 8.2 summarises estimates of HCV prevalence among HIV-diagnosed MSM observed from studies in clinical settings in high-income countries.[537,556–558] These are presented as cumulative prevalence, meaning the proportion of individuals with positive anti-HCV results or HCV RNA detected out of all individuals under follow-up who had ever tested, or out of all individuals under follow-up in a given year and tested by the end of that year. In the four longitudinal studies shown, the cumulative prevalence of HCV ranged from 3.0% to 7.2%; two studies[537,557] did not exclude HCV infection through IDU, while another study[558] only included those who did not report IDU as a HIV risk factor or following HIV diagnosis. The three cross-sectional studies shown in Table 8.2 reported HCV prevalence among non-IDU HIV-diagnosed MSM, ranging from 3.6% to 8.7%.[554,559,560] Recently, a systematic review of HCV prevalence in 13 studies from North America, Western Europe, and Japan (2000-2015) reported a pooled estimate of 7.1% (5.1-9.0%) among over 9500 HIV-diagnosed MSM with no prior or current IDU.[536]

8.2.10 **Incidence of hepatitis C among HIV-diagnosed MSM**

Four meta-analyses have reported pooled HCV incidence rates among HIV-diagnosed MSM in Europe, Asia, Australia, and North America, from 1984 to 2016.[66,534–536] All presented estimates from studies that do not distinguish between MSM with and without history of IDU. Pooled HCV incidence (per 100 PY) in these meta-analyses was similar: 0.53 (95%CI 0.49-0.58)[66], 0.61 (0.52-0.70)[534], 0.64 (95%CI 0.46-0.81)[536], and 0.78 (0.60-0.96).[535] As CLS has emerged as an important route of HCV transmission among HIV-positive MSM since the early 2000's, more recent studies have considered IDU status in population eligibility criteria. Table 8.3 summarises the incidence rates of HCV per 100 PY observed in cohort studies of HIV-diagnosed MSM in high-income countries, according to whether self-reported IDU (ever, current) was excluded from the calculation. In the five cohort studies of HIV-diagnosed MSM with no history of IDU, HCV incidence ranged from 0.11 to 1.38 per 100 PY.[561,562] Some of these studies might overestimate incidence in HIV-diagnosed MSM overall, as they require participants to be tested during follow-up in order to include them in the denominator; in an observational cohort it may be those at greatest risk who are tested more frequently.

Table 8.2: Prevalence of hepatitis C virus (HCV) in cohort and cross-sectional studies of HIV-diagnosed MSM from high income countries (1996-2016)

Study	Observation period	Country	Study type	N HIV+ MSM	Observation period/HCV prevalence measure	Overall HCV prevalence (95%CI)‡	HCV prevalence among non-IDU (95%CI) ‡
Amsterdam Cohort Study[537]	1984-2003	Netherlands	Cohort	504	Retrospective anti-HCV screening among MSM with ≥2 cohort visits during FU	3.0% (-)	-
SHCS[556]	2000-2004	Switzerland	Cohort	2550	Cumulative anti-HCV prevalence among those with ≥1 serological HCV test result during FU	4.0% (-)	34.0% (-)
UK CHIC[557]	2000-2007	UK	Cohort	12059	Cumulative anti-HCV prevalence over FU	7.2% (-)	-
OCS[558]	2000-2010	Canada	Cohort	1227	Cumulative anti-HCV prevalence over FU (incl. those with anti-HCV positive at first test)	-	7.7% (-)
NHBS[559]	2004 and 2008	USA	Cross-sectional serial survey	207	Anti-HCV point prevalence at each survey round	2004: 15.2% (7.7-22.7%) 2008: 8.3% (1.9-15.5%)	2004: 8.7% (1.9-15.5%) 2008: 4.5% (0.1-8.9%)
GMSS[560]	2008	UK	Cross-sectional serial survey	168	Anti-HCV point prevalence at recruitment	7.7% (4.2-12.9%)	-
Maple Leaf Medical Clinic[554]	2010-2012	Canada	Cross-sectional survey	294	Anti-HCV point prevalence at recruitment	10.4% (7.1-14.5%)	3.6%

‡ 95%CIs where available; anti-HCV: HCV antibody; FU: follow-up; GMSS: Gay Men's Sexual Health Survey; IDU: injection drug use; NHBS: National HIV Behavioural Surveillance System; OCS: Ontario Cohort Study; SHCS: Swiss HIV Cohort Study; UK CHIC: UK Collaborative HIV Cohort Study

Table 8.3: Incidence rate (IR) of hepatitis C virus (HCV) in cohort studies of HIV-diagnosed MSM in high-income countries (1983-2016)

Study	Observation period	Country	N HIV+ MSM	Inclusion criteria	% IDU in sample	N HCV seroconversions	Overall IR/100 PY (95%CI)‡	IR/100 PY among non-IDU (95%CI)
Amsterdam Cohort Study[537]	1983-2003	Netherlands	514	Anti-HCV positive serology before 2003 was re-tested to determine if participant was HCV-positive at entry or, if not, to establish HCV seroconversion date. Followed by confirmatory HCV RNA	-	8	0.18 (0.08-0.36)	-
MACS[67]	1984-2003	USA	2041	Anti-HCV positive test at≥2 FU visits	-	99	0.42 (-)	-
SHCS[561]	1998-2001	Switzerland	3333	Anti-HCV negative at entry and had ≥1 HCV test during FU. Excluding MSM with history of IDU and those with HCV re-infection over FU.	2.1%	101	-	1998: 0.11 (0.03-0.35) 2011: 3.56 (2.19-5.53)
CASCADE[563]	1998-2007	Europe and Canada	3014	Anti-HCV negative with ≥2 FU tests only after routine HCV data collection began in each of 11 cohorts	-	92	2005: 1.68 (1.03-2.74) 2007: 2.34 (0.82-6.69)	-
CASCADE[564]	1990-2014	Europe, Australia, Canada	4326	As above in each of 16 cohorts of MSM only	-	279	1990: 0.30 (0.04-1.80) 2014: 2.10 (1.00-4.20)	-
SHCS[556]	2000-2004	Switzerland	1571	Anti-HCV negative at entry and had ≥1 HCV test during FU. Excluding MSM with history of IDU.	1.8%	14	-	Had CLS: 0.70 (0.30-1.40) No CLS: 0.20 (0.07-0.43)
OCS[558]	2000-2010	Canada	1534	Anti-HCV negative at entry and ≥1 HCV test during FU. Excludes MSM with IDU as HIV risk factor or IDU following HIV diagnosis.	-	41	-	0.51 (0.39-0.67)
London & Brighton GUM/HIV clinics[540]	2002-2006	UK	42985 patient-years	Case-series reports: newly acquired HCV defined as HCV RNA detected or anti-HCV positive test with ≥1 HCV negative test in past 3 years	-	398	0.9 (-)	-

Study	Observation period	Country	N HIV+ MSM	Inclusion criteria	% IDU in sample	N HCV seroconversions	Overall IR/100 PY (95%CI)‡	IR/100 PY among non-IDU (95%CI)
Chase Brexton Health Care[565]	2004-2014	USA	899	≥1 clinic visit between 2011 and 2013, engaged in care for >1 year, and initial anti-HCV negative followed by ≥1 subsequent anti-HCV test. Excluding those with history of IDU	-	31	-	2004-2007: 1.31-1.58 2008-2011: 0.27-0.62 2013-2014: 1.00-1.33
Melbourne Sexual Health Centre[562]	2008-2016	Australia	822	Anti-HCV negative at first test with ≥1 anti-HCV FU test and no history of IDU	-	37	-	1.19 (0.99-1.38)

‡ 95%CIs where available; Anti-HCV: HCV antibody; CASCADE: Concerted Action on SeroConversion to AIDS and Death in Europe; CLS: condomless sex; FU: follow-up; GUM: genito-urinary medicine; IDU: injection drug use; IR: incidence rate; MACS: Multicenter AIDS Cohort Study; OCS: Ontario Cohort Study; PY: person-years at risk; SHCS: Swiss HIV Cohort Study

8.2.11 **Factors associated with STI-HIV co-infections**

This section summarises literature incorporating individual-level factors (socio-demographic and HIV-related, sexual behaviours), which may be associated with higher prevalence of any STI co-infection (including prevalent and incident HCV) among HIV-diagnosed MSM in high-income countries since the introduction of ART (1996 onwards). Of the 39 studies included in this review (and another five meta-analyses discussed), five studies[547,548,556,561,566,567] adjusted for condomless sex (CLS) or other sexual behaviours (number of sexual partners over a period of time) when examining factors associated with prevalent or incident STIs. These five studies aimed to assess factors that are associated with STIs over and above the effect of CLS, which may be indicative of increased risk or vulnerability to STIs even after accounting for levels of sexual behaviour. Level of CLS is likely to be the dominating factor in STI risk; studies that do not adjust for CLS thus explore factors associated with prevalent or incident STI, which may be the same ones as those that are associated with higher prevalence of CLS.

8.2.11.1 Socio-demographic characteristics

Evidence on the association between a participant's age and prevalence of bacterial STI co-infections (bSTIs) is mixed. Of the five studies identified, none adjusted for levels of CLS or other sexual behaviours; two did not find any association between age and co-infection with any (lab-confirmed) prevalent STI,[553,554] one found that older age was associated with higher risk of positive syphilis serology[549], and two studies showed that younger HIV-diagnosed MSM had higher risk of incident STIs (NG, CT, syphilis) over follow-up.[550,562] It is possible that the association of younger and incident STIs in these studies is explained by higher prevalence of CLS or higher partner numbers, which have not been accounted for.

The significance of age as a risk factor for HCV among HIV-diagnosed MSM is also heterogeneous across studies. HCV prevalence among HIV-diagnosed MSM did not differ significantly by participants' age in two UK cross-sectional questionnaire surveys, SHARP (N=308 HIV-positive MSM)[568] and the 2008 GMSS (N=168).[560] Two other studies, which adjusted estimates for socio-demographic, lifestyle factors, and other STIs (but not level of CLS) showed mixed results; in a Canadian cross-sectional survey of almost 300 HIV-diagnosed MSM attending sexual health services, older age was significantly associated with HCV co-infection,[554] while in the French ANRS VESPA2 national probability sample survey (N=1037), HCV co-infection was associated with younger age.[545]

Similar mixed findings have been observed between age and incident HCV. Two sub-studies of the Swiss HIV Cohort Study (SHCS) of HIV-diagnosed MSM with no history of IDU, adjusted for condom use (and other factors) in the association of age and incident HCV; in both sub-studies, while younger MSM were at elevated risk of HCV seroconversion, the association was not significant after adjustment for CLS.[556,561] In the MACS cohort (N=2377 HIV-diagnosed MSM), every 10-year increase in age conferred a 44% higher risk of HCV seroconversion; this estimate was adjusted for socio-demographic factors but

not CLS or number of sex partners.[67] In this case, the authors hypothesise that older age may be indicative of a lower HCV infection threshold, but direct evidence is lacking.

Among HIV-diagnosed MSM, ethnicity and educational attainment have consistently not been found to have any association with prevalence of any (self-reported or lab-confirmed) bSTI[554,558,560], prevalent, or incident HCV.[545,554,558,560,561,565,568] As in the case of participant's age, current employment was not significantly associated with prevalent bSTIs in SHARP or the 2008 GMMS.[560,568] The US Chase Brexton retrospective cohort study (see Table 8.3) used electronic medical records from over 900 HIV-diagnosed MSM attending for HIV care and engaged in care for more than a year (2004-2014).[565] After adjustment for a number of socio-demographic, lifestyle factors, and other STIs, current employment was significantly associated with higher risk of incident HCV only when MSM with no history of IDU were excluded from analyses. No association was observed between employment status and HCV incidence when including MSM with prior IDU. This latter finding was also observed in the ANRS VESPA2 study.[545]

8.2.11.2 HIV-related factors

The role of ART status on prevalent STIs remains unclear. A worldwide systematic review of 37 studies (2000-2009) reported on clinically or lab-diagnosed genital ulcers and bSTIs among HIV-diagnosed men and women; this review showed that the overall STI point prevalence in 14 studies that reported participants receiving ART did not differ significantly from that in studies that did not on report ART use (16.2% vs 16.5% respectively).[569] Within studies reporting on ART use, no significant association was observed between ART use and prevalent STI co-infections, either. One of the studies included in this meta-analysis, a cross-sectional questionnaire study of over 200 HIV-diagnosed MSM attending for free STI testing in Amsterdam (see Table 8.1) found that not being on ART in the past six months was associated with almost three-fold prevalence of rectal NG compared to being on ART (adjusted for CLS).[548] This association could be explained by time since HIV diagnosis, as STIs may have been acquired at a time of higher risk, when HIV was transmitted. In the case of incident HCV, four studies[67,561,568] showed no significant effect of ART at baseline/time updated. In the Ontario HIV Cohort Study[558] and the ANRS VESPA2[545], ART use was associated with HCV seroconversion.

CD4 count is an important marker of immune system function in HIV-diagnosed people, and as such, would be expected to have some association with higher prevalence or incidence of STIs. A repeat cross-sectional survey of over 200 HIV outpatient MSM attendees in California (2004-2006, see Table 8.1) showed that for every 100cell/mm^3 increase in CD4 count, the risk of incident NG and CT increased by 15% (adjusted for repeat measures only).[550] The SHCS did not observe a significant association between CD4 count and positive syphilis serology among over 2600 HIV-diagnosed MSM (2004-2006).[549] In the MACS cohort[67], HCV incidence was inversely proportional to CD4 cell count among HIV-diagnosed MSM with CD4≤500cells/mm^3; in contrast, no association was observed between CD4 count and HCV incidence when CD4 was >500cells/mm^3. In the Melbourne Sexual Health Centre study of over 800 HIV-diagnosed MSM under care (see Table 8.3), nadir CD4 prior to HCV testing was associated with increased risk of HCV seroconversion after adjustment for age and HIV VL; most recent CD4 count,

however, was not associated with HCV incidence.[562] In other studies, no significant effect was reported between CD4 count and HCV prevalence or incidence.[545,558,561,568] In fact, of 101 incident HCV infections in the SHCS (see Table 8.3), 93% occurred among MSM on ART and over 96% among those with CD4 counts>200cells/mm^3.[561]

In two studies that have assessed prevalent bSTIs by self-report rather than laboratory/clinician-confirmation, detectable HIV VL (>50c/mL) was associated with higher prevalence of bSTIs in the past three months, following adjustment for socio-demographic, HIV-related, and lifestyle covariates.[239,547] No other studies were identified as showing any association between HIV plasma VL and bSTIs or HCV (refer to Table 8.1 and Table 8.2).[545,549,550,558,561,565,568]

The role of length of time living with diagnosed HIV has scarcely been examined as a correlate of STI co-infection among HIV-diagnosed MSM. In one sub-analysis of the SHCS, the risk of newly detected syphilis was significantly higher among MSM diagnosed with HIV longer (>3 vs ≤3 years), even after adjustment for age.[549] Two other studies that assessed time since HIV diagnosis did not observe any significant association with incident HCV[558] or re-infection with HCV after SVR (see 8.2.7.5).[570]

8.2.11.3 Prior syphilis and HCV seroincidence

In a recent meta-analysis of 28 studies from Europe, North America, Australia, and Taiwan, syphilis emerged as a risk factor for HCV incidence in eight studies; lifetime prevalence of syphilis as well as acute syphilis (in the past 6,12,18 months or during the study period) were both associated with increased risk of HCV among all MSM (mixed HIV serostatus).[535] Among HIV-diagnosed MSM in the US Chase Brexton cohort who did not report IDU (current, ever), a history of anogenital ulcerative STIs (syphilis and warts) was also associated with increased risk of HCV incidence, independent of other sexual behaviours.[565]

8.2.11.4 Non-injection recreational drug use and condomless sex (CLS)

Sexual transmission of HCV may be mediated by non-injection recreational drug use (NIDU), as drug-induced sexual disinhibition can lead to traumatic and prolonged sex practices that facilitate blood-borne virus transmission (see section 6.5.4). NIDU and more recently, chemsex-associated drug use, has been identified as a key factor in the transmission of enteric bSTIs and HCV among HIV-diagnosed MSM in the UK (see section 8.2.8.2).[148,370,539,568,571,572] However, very few studies have considered NIDU use as a risk factor for HCV transmission. Chemsex drug use in particular is characterised by high prevalence of IDU.[573,574]

An important distinction between studies examining the association of NIDU and incident or prevalent STIs, is whether analyses include adjustment for sexual behaviours (such as CLS and number of partners), as CLS is the main risk factor for STIs. When studies adjust for CLS in the association of NIDU and STIs, they aim to explore the additional risk that NIDU confers to STI acquisition, over and above the existing risk conferred by CLS. Two studies of HIV-diagnosed MSM who did not have history of or current

IDU (SHCS[561] and Chase Brexton[565]) explored the association of NIDU and incident HCV; in the SHCS, current NIDU was not significantly associated with incident HCV after adjustment for CLS and number of sex partners; the authors hypothesised that the lack of association may have been due to underreporting of NIDU in this cohort. However, it may also be that the association was mediated by CLS in the first place, and so it would be expected that NIDU no longer remains significant after adjustment for CLS. In the US Chase Brexton cohort, non-injection polydrug use (≥2 non-injection drugs) was associated with five-fold higher risk of HCV seroconversion (p=0.02), but no adjustment was made for CLS.[565] Therefore, the association of NIDU and incident HCV in Chase Brexton probably parallels the underlying association of CLS and incident HCV in the cohort.

8.2.11.5 Other sexual behaviours

A number of studies have examined other sexual behaviours as potential risk factors for HCV seroconversion among HIV-diagnosed MSM, but the majority have only provided unadjusted estimates[568] or included MSM with current or lifetime IDU in analyses[557,560] (meaning that HCV transmission via needle sharing cannot be ruled out). Four studies[556,561,566,573] reported adjusted estimates among non-IDU HIV-diagnosed MSM, showing that various sexual behaviours were associated with an increased risk of HCV seroconversion. These include "unsafe sex"[556], receptive CLS with ejaculation[67,566], receptive fisting (without gloves or sharing gloves), inconsistent condom use[561], sex while "high" on methamphetamine[566], and use of inhaled drugs.[573] Similarly, prevalent HCV among HIV-diagnosed MSM has been associated with receptive CLS[538,560,575] and fisting.[538,539,573,576,577] High numbers of sexual partners have been associated with prevalent and incident bSTIs and HCV.[282,545,557,567] In the MACS study (section 8.2.11.4), the risk of HCV seroconversion was examined according to CLS status and number of male sex partners in the past six months. Compared to HIV-diagnosed MSM with no or one sex partner, those with multiple sex partners but only one receptive CLS partner were not at higher risk of incident HCV (p=0.33); those who had receptive CLS with multiple partners, however, had three-fold higher risk of incident HCV (p=0.001).[67] These estimates were adjusted for socio-demographic factors but not recreational drug use.

8.3 Methods

Analyses presented in sections 8.4.1-8.4.3 include 2189 ASTRA MSM diagnosed with HIV for ≥3 months, while analyses in sections 8.4.4-8.4.8 include a subgroup of the above, with 1811 MSM who also consented to linkage of ASTRA to routine clinical data.

8.3.1 Sexually transmitted infections

Participants were asked whether they had been diagnosed with an STI (not including HIV) in the past three months, and if so, which ones of the following: syphilis, gonorrhoea, chlamydia, LGV, new hepatitis B, new hepatitis C, genital herpes (new or recurrent), genital warts (new or recurrent), trichomonas, NSU (non-specific urethritis), NGU (non-gonococcal urethritis), and 'other (please specify)'. Free-text responses in the 'other (please specify)' category were examined case-by-case and recoded to the above categories if applicable, or left as 'other' if not classifiable (e.g. reporting STI symptoms such as testicular pain).

8.3.2 Other factors and sexual behaviours

Participants were asked whether they currently had any of the following symptoms: abnormal discharge from penis, anal discharge, pain on passing urine, pain in the genital area or anus, red sores or rash on the genital area or anus. STI screening was assessed by the question "in the past two years, have you had a sexual health screen (tests for sexually transmitted infections, not including HIV)?"

All other socio-demographic, psychological, lifestyle, HIV-related factors, and sexual behaviours examined in this chapter have been defined in sections 3.8 and 4.3. Measures of recreational drug use and alcohol consumption/dependency are defined in section 6.3.

8.3.3 Statistical analysis – prevalence of any STI

The prevalence of any STI and of each specific STI was assessed in the past three months. Prevalence of specific STIs was examined according to number of STIs reported in the past three months.

8.3.3.1 Factors associated with any STI among all MSM

Associations were examined of socio-demographic, psychological, HIV-related, and lifestyle factors, with any self-reported STI in the past three months among all MSM with available STI data. Unadjusted and adjusted modified Poisson regression models were used with robust error variances. In multivariable analyses, two adjustment strategies were used, as described in section 3.9.5. Firstly, each factor was adjusted separately for core factors, and secondly, any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in the multivariable model in addition to clinic. Collinear variables were excluded accordingly (see sections 8.4.2, 8.4.7) In both multivariable strategies, models for the association of study log-recorded viral load (VL) and any self-reported STI excluded the variable ART status as they were correlated.

Associations were then examined of sexual behaviours in the past three months (any anal or vaginal sex, any CLS, any CLS-D, any CLS-C, group sex, use of the internet to find sex, total number of sex partners), number of new sex partners in the past year, with any self-reported STI in the past three months. Modified Poisson regression was used for unadjusted and adjusted models. Slightly different multivariable adjustment strategies were used in these analyses. Firstly, each factor was adjusted separately for core factors (as above), and secondly, each factor was adjusted separately for core factors plus recreational drug use in the past three months (yes/no).

8.3.3.2 Factors associated with any STI among MSM reporting any anal or vaginal sex

MSM who did not report any anal or vaginal sex in the previous three months were excluded, and all remaining MSM were classified into one of the following mutually exclusive categories based on sex in the past three months (see section 4.3.3).

1. Condomless sex with HIV-serodifferent partners (CLS-D)
2. Condomless sex with HIV-seroconcordant partners only ('CLS-C without CLS-D')
3. Condom-protected sex only

Associations of this three-category variable and reporting any STI in the past three months were examined in unadjusted and adjusted modified Poisson regression, with condom-protected sex (group 3) as the reference category. In this analysis, models were first adjusted for core factors only (as in 8.3.3.1), then for core factors plus recreational drug use in the past three months (yes, no), and lastly, for core factors, recreational drug use, and total number of sex partners in the past three months (1, 2-4, 5-9, 10-19, ≥20).

8.3.4 Cumulative prevalence of hepatitis C (HCV)

8.3.4.1 Sample derivation

Analyses in this section include HIV-diagnosed MSM (diagnosed for ≥3 months) who consented to linkage of ASTRA and routine clinical data, and for whom clinic data were available at any point prior to questionnaire completion. (Figure 8.6) Details of consent to routine clinic linkage are discussed in section 3.6. Of the eight clinical centres recruiting ASTRA participants, four provided linked routine hepatitis clinical data; three in London (Homerton, Mortimer Market, Royal Free hospital) and one in Brighton.

Cumulative prevalence of HCV was defined as any positive anti-HCV or HCV-RNA test result at any point prior to questionnaire completion (chronic/prevalent HCV). The prevalence of chronic HCV is also shown: (i). including MSM who also reported lifetime prevalence of HCV on the questionnaire (defined as a positive answer to the question "have you ever been told by a doctor that you have hepatitis C?"), and (ii). excluding MSM who reported any IDU in the past three months on the questionnaire.

8.3.4.2 Statistical analysis

To examine associations of socio-demographic, psychological, lifestyle, and HIV-related factors with chronic/prevalent HCV, unadjusted and adjusted modified Poisson regression was used with robust error variances. In multivariable models, the two adjustment strategies were used (core adjustment and stepwise, as in section 3.9.5).

Adjusted associations of sexual behaviours and any other self-reported diagnosed STIs with cumulative HCV prevalence were examined using slightly different adjustment strategies. First, each sexual behaviour and STI variable was adjusted in separate models for core factors only. Second, each sexual behaviour and STI variable was then adjusted for core factors plus IDU in the past three months. This was done firstly, in order to account for possible IDU as a route of HCV transmission, and secondly as it would not be possible to include all sexual behaviours in a single model due to multicollinearity.

8.3.5 Incident hepatitis C (HCV) over follow-up

8.3.5.1 Cohort derivation

Individuals were included in the analysis of HCV incidence if they were tested for either anti-HCV or HCV-RNA at any point from ASTRA questionnaire completion onwards (start of follow-up, FU). All HCV tests up until the end of one year after the start of follow up (FU) were used to define an individual's

HCV status at the start of FU. For participants with changing results in the first year of FU, only the first results were used to define their HCV status.

MSM with the following criteria were included in the analysis (details in Figure 8.6):

(i.) Negative anti-HCV test and negative or missing HCV-RNA test at the beginning of FU, and

(ii.) ≥1 further test for either anti-HCV or HCV-RNA

MSM with any of the following criteria were excluded from the analysis:

(i.) Self-reported lifetime HCV diagnosis at questionnaire (positive answer to "have you ever been told by a doctor that you have hepatitis C?"), or

(ii.) Positive anti-HCV test or positive HCV-RNA test prior to the date of questionnaire completion, or

(iii.) Positive anti-HCV test or positive HCV-RNA test on the same date as questionnaire completion, or

(iv.) Did not have any HCV test results available after the questionnaire.

New (incident) infection was defined as any positive anti-HCV or HCV-RNA test after the start of FU. Individuals were followed up from the date of ASTRA questionnaire completion until they had a positive anti-HCV or positive HCV-RNA test result or until they were last seen (last FU). The latest date for which clinical hepatitis records were available was 22 July 2014.

8.3.5.2 Statistical analysis

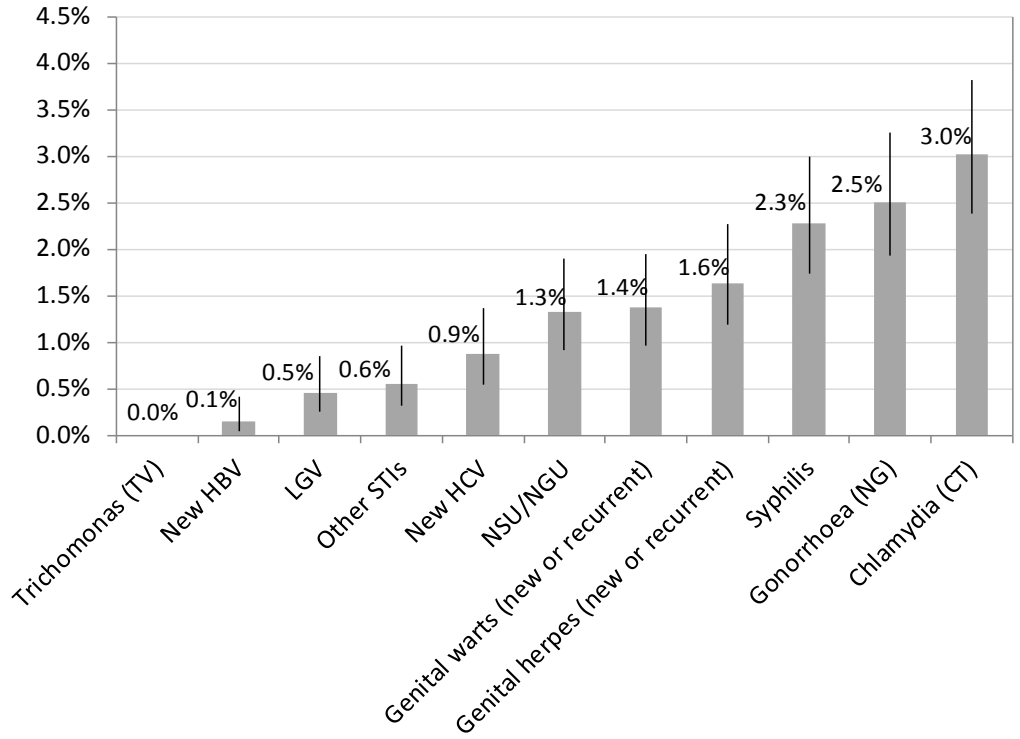
Incidence rate of HCV (95%CIs) was calculated by dividing the total number of incident HCV infections by the total number of person years (PY) of FU. Associations were examined of socio-demographic, HIV-related, lifestyle factors, sexual behaviours and other STIs with new HCV diagnosis. The small number of incident events in this analysis allowed for estimation of unadjusted incidence rate ratios (IRRs) per 100 PY, with p-values derived by exact significance tests. Clinic-recorded VL and CD4 counts were the test results nearest to the HCV diagnosis date.

8.4 Results

8.4.1 Prevalence of self-reported STIs

Among 2189 MSM diagnosed with HIV for ≥3 months prior to ASTRA questionnaire completion, information on self-reported STIs was available for 2160 (98.7%). The prevalence of any self-reported STI in the past three months among all 2189 MSM was 10.9% (95%CI 9.7-12.3%, n=236). Figure 8.3 shows that the most prevalent self-reported STIs (>2% prevalence) were CT (3.0%, 2.4-3.8%), NG (2.5%, 1.9-3.3%), and syphilis (2.3%, 1.7-3.0%). New HCV or HBV, LGV, and any other STIs (not specified), were each reported by under 1% of MSM. There were no participants who reported TV in the past three months.

Figure 8.3: Prevalence (95%CI) of self-reported STIs in the past three months (N=2189)



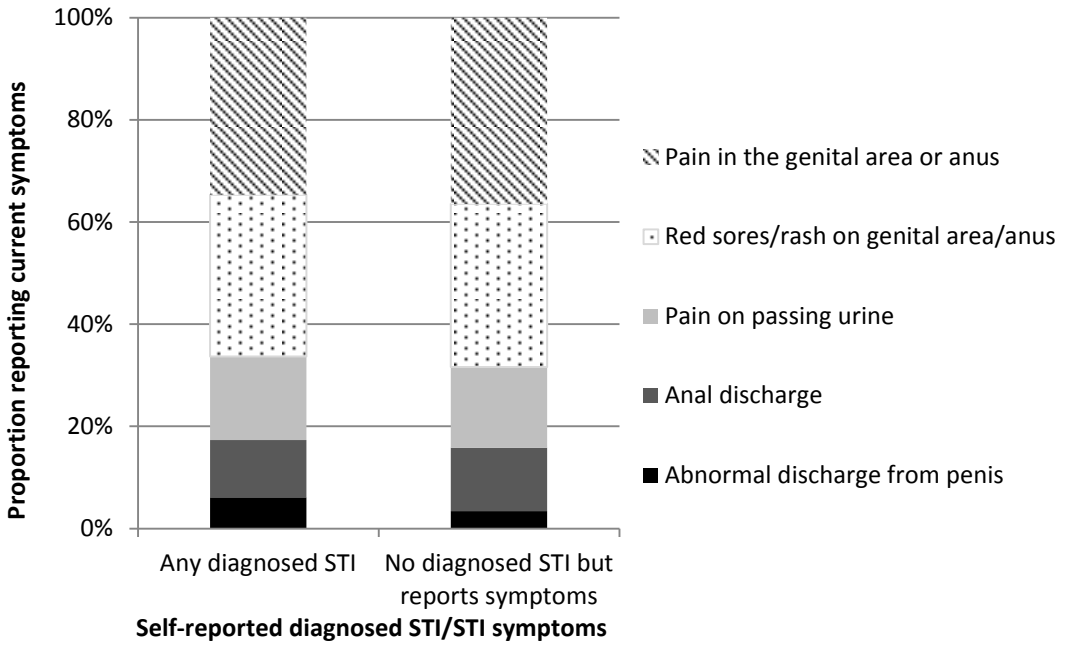
Bars and lines represent prevalence and 95%CI
HBV: hepatitis B virus; HCV: hepatitis C virus; LGV: lymphogranuloma venereum; NSU/NGU: non-specific urethritis/non-gonoccocal urethritis; Other STIs: self-reported shigella, HPV, non-specific STI symptoms, other non-specified STI

Among 236 HIV-diagnosed MSM with a self-reported STI, 172 (72.9%, 95%CI 66.8-78.2%) had one STI, 55 (23.3%, 18.3-29.2%) had two, and 9 (3.8%, 2.0-7.1%) had three or more STIs. Overall, 58.4% of 310 responses were for bSTIs (CT, NG, LGV, syphilis), 28.4% were for viral STIs (new HCV, HBV, genital warts and herpes), and the remaining were for NSU/NGU and other (unspecified) STIs.

Current symptoms of STIs (at questionnaire completion) were reported by 273 MSM (12.5% of 2189). The most prevalent current symptoms (>5%) among 2189 MSM were pain (6.5%) and red sores/rash (5.7%) in the anogenital area. Among 273 MSM who reported any symptoms, 64.8% reported one symptom, 27.1% reported two, and 8.1% reported three or more symptoms. A total of 211 MSM (9.8% of 2160) did not report a diagnosed STI but did report symptoms of STIs. (Figure 8.4) This proportion represents those with potentially undiagnosed symptomatic STIs in the sample.

Over 78% of 2189 MSM reported having a sexual health screen (for any STI other than HIV) in the past two years.

Figure 8.4: Prevalence of specific current STI symptoms according to self-reported diagnosed STIs in the past three months or current self-reported STI symptoms without STI diagnosis (N=447)



8.4.2 Factors associated with prevalence of any self-reported STI in the past three months

8.4.2.1 Socio-demographic, psychological, HIV-related, and lifestyle factors

Table 8.4 shows the associations of socio-demographic, psychological, HIV-related, and lifestyle factors with any self-reported STI co-infection in the past three months (N=2160 MSM with available STI data). In unadjusted analysis, prevalence of STIs was strongly associated with younger age, non-white ethnicity, more recent HIV diagnosis, non-UK place of birth, being employed, financial hardship, having an HIV-positive stable partner, not being on ART, having detectable VL, recreational drug, and polydrug, injection, and chemsex-associated drug use. STI co-infection was not significantly associated with country of birth, education, religion, social support, depression, anxiety, harmful alcohol drinking or dependency, or CD4 count.

After adjustment for core factors (models 1, Table 8.4), the following factors remained associated with self-reported STI co-infection ($p<0.05$) with little or no attenuation in magnitude of associations: younger age (a significant inverse trend was observed with lower STI prevalence at older ages), not being on ART, and having detectable VL; MSM with study log-recorded VL>50c/mL had 30% higher prevalence of any STI in the past three months compared to those with VL≤50c/mL. A significant positive trend was also observed between higher number of recreational drugs used and prevalence of STI co-infections. Strong associations were observed of IDU, chemsex-associated drug use, and STI co-

infections. The associations with shorter time since HIV diagnosis and employment were not significant in the core-adjusted models, primarily due to adjustment for age.

In model 2, any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in the multivariable model, in addition to clinic. (Table 8.4) These were: age, ethnicity, time since HIV diagnosis, place of birth, employment, financial hardship, stable partner status, ART status, and ART status/self-reported VL, recreational drug use, number of drugs used, chemsex-associated, and injection drug use. As these last four (drug use) variables incorporated the same factors, only recreational drug use was retained. ART status was also excluded from the model as it was incorporated in the ART status/self-reported VL variable. Hence, after adjustment for age, ethnicity, time since HIV diagnosis, place of birth, employment, financial hardship, detectable study log-recorded VL, recreational drug use, and clinic, the following factors remained significantly associated with self-reported STI co-infection: younger age, higher financial hardship, detectable VL, and recreational drug use. There was also a weak association of non-UK place of birth and prevalence of self-reported STIs ($p=0.05$).

Table 8.4: Association of socio-demographic, psychological, HIV-related, lifestyle factors with any self-reported STI in the past three months (n/N=236/2160)

	n reporting STI/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=2138)								
<30	20/95	21.1	2.6 [1.6,4.2]		2.2 [1.3,3.8]		1.4 [0.8,2.5]	
30-39	84/482	17.4	2.2 [1.6,3.0]		2.0 [1.4,2.9]		1.3 [0.9,1.9]	
40-49	78/915	8.5	1.1 [0.8,1.5]		1.0 [0.7,1.4]		0.7 [0.5,1.0]	
≥50	52/646	8.0	1.0	<0.001(T)	1.0	<0.001(T)	1.0	0.021(T)
Ethnicity (N=2127)								
White	197/1908	10.3	1.0		1.0		1.0	
All other (black, Asian, Mixed, other)	34/219	15.5	1.5 [1.1,2.1]	0.017	1.4 [1.0,1.9]	0.082	1.0 [0.7,1.5]	0.818
Years since HIV diagnosis (N=2149)								
≤2	27/182	14.8	1.0		1.0		1.0	
2-5	39/335	11.6	0.8 [0.5,1.2]		0.9 [0.5,1.4]		1.0 [0.6,1.6]	
5-10	65/542	12.0	0.8 [0.5,1.2]		1.1 [0.7,1.7]		1.3 [0.8,2.0]	
10-15	47/455	10.3	0.7 [0.4,1.1]		1.1 [0.7,1.8]		1.3 [0.8,2.0]	
>15	57/635	9.0	0.6 [0.4,0.9]	0.017(T)	1.1 [0.7,1.7]	0.656(T)	1.1 [0.7,1.8]	0.870(T)
Place of birth (N=2160)								
UK	140/1487	9.4	1.0		1.0		1.0	
Outside the UK	96/673	14.3	1.5 [1.2,1.9]	<0.001	1.3 [1.0,1.6]	0.059	1.3 [1.0,1.7]	0.050
Religious (N=2126)								
Yes	104/904	11.5	1.0		1.0		-	
No	128/1222	10.5	0.9 [0.7,1.2]	0.452	0.9 [0.7,1.2]	0.454		
Education (N=2123)								
University degree or above	109/943	11.6	1.0		1.0		-	
No qualifications or up to A levels	123/1180	10.4	0.9 [0.7,1.2]	0.405	0.9 [0.7,1.2]	0.584		
Employment (N=2116)								
Employed	154/1305	11.8	1.0		1.0		1.0	
Unemployed or other(carer, student, retired)	76/811	9.4	0.8 [0.6,1.0]	0.083	0.9 [0.7,1.2]	0.418	0.8 [0.6,1.1]	0.097
Money for basic needs (N=2132)								
Always	112/1103	10.2	1.0		1.0		1.0	
Mostly	58/590	9.8	1.0 [0.7,1.3]		0.9 [0.7,1.2]		1.0 [0.7,1.3]	
Sometimes	40/269	14.9	1.5 [1.0,2.0]		1.3 [0.9,1.9]		1.7 [1.2,2.4]	
Never	22/170	12.9	1.3 [0.8,2.0]	0.060 (T)	1.2 [0.8,1.9]	0.194(T)	1.5 [0.9,2.5]	0.031(T)

	n reporting STI/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Social support (N=2152) ‡								
High	123/1276	9.6	1.0		1.0			
Medium	89/661	13.5	1.4 [1.1,1.8]		1.3 [1.0,1.7]		-	
Low	22/215	10.2	1.1 [0.7,1.6]	0.118(T)	0.9 [0.5,1.4]	0.613(T)		
Depression symptoms (N=2160) ‡								
No	161/1568	10.3	1.0		1.0		-	
Yes	75/592	12.7	1.2 [1.0,1.6]	0.109	1.2 [0.9,1.5]	0.281		
Anxiety symptoms (N=2160) ‡								
No	179/1702	10.5	1.0		1.0		-	
Yes	57/458	12.4	1.2 [0.9,1.6]	0.238	1.1 [0.8,1.5]	0.458		
Stable partner's HIV-serostatus (N=2160)								
HIV-positive	61/505	12.1	1.0		1.0		1.0	
HIV-negative or unknown status	56/680	8.2	0.7 [0.5,1.0]		0.7 [0.5,1.0]		0.8 [0.5,1.1]	
No stable partner	119/975	12.2	1.0 [0.8,1.3]	0.028	1.0 [0.7,1.3]	0.061	1.0 [0.8,1.4]	0.194
ART status (N=2152)								
On ART	186/1867	10.0	1.0		1.0		-	
Not on ART	49/285	17.2	1.7 [1.3,2.3]	<0.001	1.5 [1.1,2.0]	0.029		
ART status/self-reported VL (N=2119)* ‡								
On ART, reports undetectable VL	158/1556	10.2	1.0		1.0			
On ART, does not report undetectable VL	26/278	9.4	0.9 [0.6,1.4]		0.8 [0.5,1.2]		-	
Not on ART	49/285	17.2	1.7 [1.3,2.3]	0.001	1.4 [1.0,2.0]	0.043		
Study log-recorded VL (N=2159)*								
≤50c/mL	157/1658	9.5	1.0		1.0		1.0	
>50c/mL	71/472	15.0	1.6 [1.2,2.0]	0.001	1.3 [1.0,1.8]	0.027	1.4 [1.1,1.9]	0.019
Study log-recorded CD4 count (N=2159)								
>350cells/mm^3	199/1808	11.0	1.0		1.0		-	
≤350cells/mm^3	29/323	9.0	0.8 [0.5,1.2]	0.282	0.8 [0.5,1.1]	0.210		
Higher alcohol consumption(N=2159) ‡								
No	189/1742	10.9	1.0		1.0		-	
Yes	46/417	11.0	1.0 [0.8,1.4]	0.915	1.0 [0.7,1.3]	0.839		

	n reporting STI/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Evidence of alcohol dependency (N=2160) ‡								
No	199/1798	11.1	1.0		1.0		-	
Yes	37/362	10.2	0.9 [0.7,1.3]	0.639	1.0 [0.7,1.3]	0.801		
Recreational drug use (N=2160)								
No	74/1063	7.0	1.0		1.0		1.0	
Yes	162/1097	14.8	2.1 [1.6,2.8]	<0.001	1.9 [1.5,2.5]	<0.001	2.0 [1.5,2.6]	<0.001
Number of recreational drugs used (N=2160)								
None	74/1063	7.0	1.0		1.0			
1	32/355	9.0	1.3 [0.9,1.9]		1.3 [0.8,1.9]		-	
2-4	76/509	14.9	2.1 [1.6,2.9]		2.0 [1.4,2.7]			
≥5	54/233	23.2	3.3 [2.4,4.6]	<0.001(T)	2.8 [2.0,4.0]	<0.001(T)		
Injection drug use (IDU) (N=2160)								
No	215/2095	10.3	1.0		1.0			
Yes	21/65	32.3	3.1 [2.2,4.6]	<0.001	2.6 [1.8,3.9]	<0.001	-	
Type of recreational drug used (N=2160) ‡								
None	74/1063	7.0	1.0		1.0			
Chemsex-associated drugs	80/326	24.5	3.5 [2.6,4.7]		2.9 [2.1,4.1]		-	
All other (not chemsex-associated)	82/771	10.6	1.5 [1.1,2.1]	<0.001	1.5 [1.1,2.0]	<0.001		

Global p-values by Wald test or test for trend (T); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1:*** *Each factor adjusted in separate model for core variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, and ART status. Denominators vary due to missing data in each model.* ***Model 2:*** *Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic. (Only recreational drug use retained in model 2 due to collinearity with number of drugs, IDU, type of drugs used). *In both cases, models for study log-recorded VL and for 'ART status/self-reported VL' omit variable on ART due to collinearity. Alcohol consumption by WHO-AUDIT-C, alcohol dependency by CAGE questionnaire. Chemsex-associated drugs: mephedrone, crystal methamphetamine, GHB/GBL.*

‡ *Variables defined in sections 3.8 and 6.3*

8.4.2.2 Sexual behaviours associated with any self-reported STI

Table 8.5 shows the association of various sexual behaviours and any self-reported STI in the past three months (N=2160 MSM with available STI data). Of 782 MSM who reported not having any anal or vaginal sex in the past three months, 4.1% (n=32) also reported having one or more STIs in the same period. Among these 32 men, there were 38 STIs specified; the most prevalent STIs (>10% of 38 responses) were genital warts (23.7%), genital herpes (18.4%), syphilis (18.4%), CT (13.2%), and new HCV (10.5%).

All sexual behaviours shown in Table 8.5 were associated with self-reported STI co-infection in unadjusted analysis. There was a striking association of higher partner numbers (measured by total number of partners in the past three months, or number of new partners in the past year), with greater prevalence of STIs.

In core-adjusted models (models 1A, Table 8.5), all sexual behaviours remained significantly associated with prevalent STIs, with some attenuation ($p<0.001$ for all). In models adjusted for core factors and recreational drug use in the past three months (models 1B, Table 8.5), estimates for all sexual behaviours were attenuated slightly, but remained strong; the prevalence of any STI was 2.5-fold higher among MSM who had any CLS compared to those who did not. Compared to MSM with only one sex partner in the past three months, MSM with 20 or more partners had over four-fold prevalence of STIs (aPR=4.5, 95%CI 2.9-7.1, p-trend<0.001); compared to MSM with only one new sex partner in the past year, MSM with 30 or more new sex partners had over two-fold prevalence of STIs (aPR=2.4, 1.8-3.2, p-trend<0.001).

Table 8.5: Association of sexual behaviours and any self-reported STI in the previous three months (n/N=236/2160)

	n reporting STI/N	row %	unadjusted PR[95%CI]	p-value	Models 1A: Core only aPR [95%CI]	p-value	Models 1B: Core + drugs aPR [95%CI]	p-value
Any anal and/or vaginal sex (N=2160)								
No	32/782	4.1	1.0		1.0		1.0	
Yes	204/1378	14.8	3.6 [2.5,5.2]	<0.001	3.4 [2.3,4.9]	<0.001	2.9 [2.0,4.3]	<0.001
Condomless sex (CLS) (N=2160)								
No	83/1335	6.2	1.0		1.0		1.0	
Yes	153/825	18.5	3.0 [2.3,3.8]	<0.001	2.8 [2.1,3.6]	<0.001	2.5 [1.9,3.3]	<0.001
CLS with HIV-seroconcordant partners (CLS-C) (N=2160)								
No	113/1541	7.3	1.0		1.0		1.0	
Yes	123/619	19.9	2.7 [2.1,3.4]	<0.001	2.6 [2.0,3.4]	<0.001	2.3 [1.7,3.0]	<0.001
CLS with HIV-serodifferent partners (CLS-D) (N=2160)								
No	160/1809	8.8	1.0		1.0		1.0	
Yes	76/351	21.7	2.4 [1.9,3.1]	<0.001	2.5 [1.9,3.2]	<0.001	2.2 [1.7,2.9]	<0.001
Participated in group sex (N=2118)								
No	127/1669	7.6	1.0		1.0		1.0	
Yes	105/449	23.4	3.1 [2.4,3.9]	<0.001	2.8 [2.2,3.6]	<0.001	2.5 [1.9,3.2]	<0.001
Used the internet to find sex (N=2122)								
No	85/1335	6.4	1.0		1.0		1.0	
Yes	147/787	18.7	2.9 [2.3,3.8]	<0.001	2.6 [2.0,3.4]	<0.001	2.3 [1.8,3.1]	<0.001
Total number of partners (N=2160)								
None	40/817	4.9	1.0		1.0		1.0	
1	41/589	7.0	1.4 [0.9,2.2]		1.3 [0.9,2.1]		1.3 [0.8,2.0]	
2-4	59/373	15.8	3.2 [2.2,4.7]		3.0 [2.0,4.4]		2.7 [1.8,4.1]	
5-9	38/199	19.1	3.9 [2.6,5.9]		3.6 [2.3,5.4]		3.2 [2.1,4.9]	
10-19	28/103	27.2	5.6 [3.6,8.6]		4.6 [2.9,7.2]		4.0 [2.5,6.4]	
≥20	30/79	38.0	7.8 [5.1,11.7]	<0.001(T)	6.1 [3.9,9.6]	<0.001(T)	5.3 [3.3,8.6]	<0.001(T)

	n reporting STI/N	row %	unadjusted PR[95%CI]	p-value	Models 1A: Core only aPR [95%CI]	p-value	Models 1B: Core + drugs aPR [95%CI]	p-value
Number of new sexual partners in past year (N=2039)								
No new partners	26/873	3.0	1.0		1.0		1.0	
1-9	79/638	12.4	4.2 [2.7,6.4]		4.4 [2.8,6.9]		4.2 [2.6,6.6]	
10-19	33/218	15.1	5.1 [3.1,8.3]		5.0 [2.9,8.4]		4.5 [2.6,7.7]	
20-29	23/127	18.1	6.1 [3.6,10.3]		6.1 [3.5,10.5]		5.5 [3.1,9.6]	
≥30	63/183	34.4	11.6 [7.5,17.7]	<0.001(T)	10.6 [6.7,16.7]	<0.001(T)	9.6 [6.0,15.4]	<0.001(T)

Three month recall unless otherwise specified; Global p-values by Wald test, test for trend (T), or Fisher's exact (F); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1A****: Each factor adjusted in separate model for core factors: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, ART status. Denominators vary due to missing data in each model.* ***Models 1B****: Each factor adjusted in separate model for core factors plus recreational drug use in the past three months (yes/no)*

8.4.3 **STIs and the mutually exclusive categorical variable of sexual behaviour**

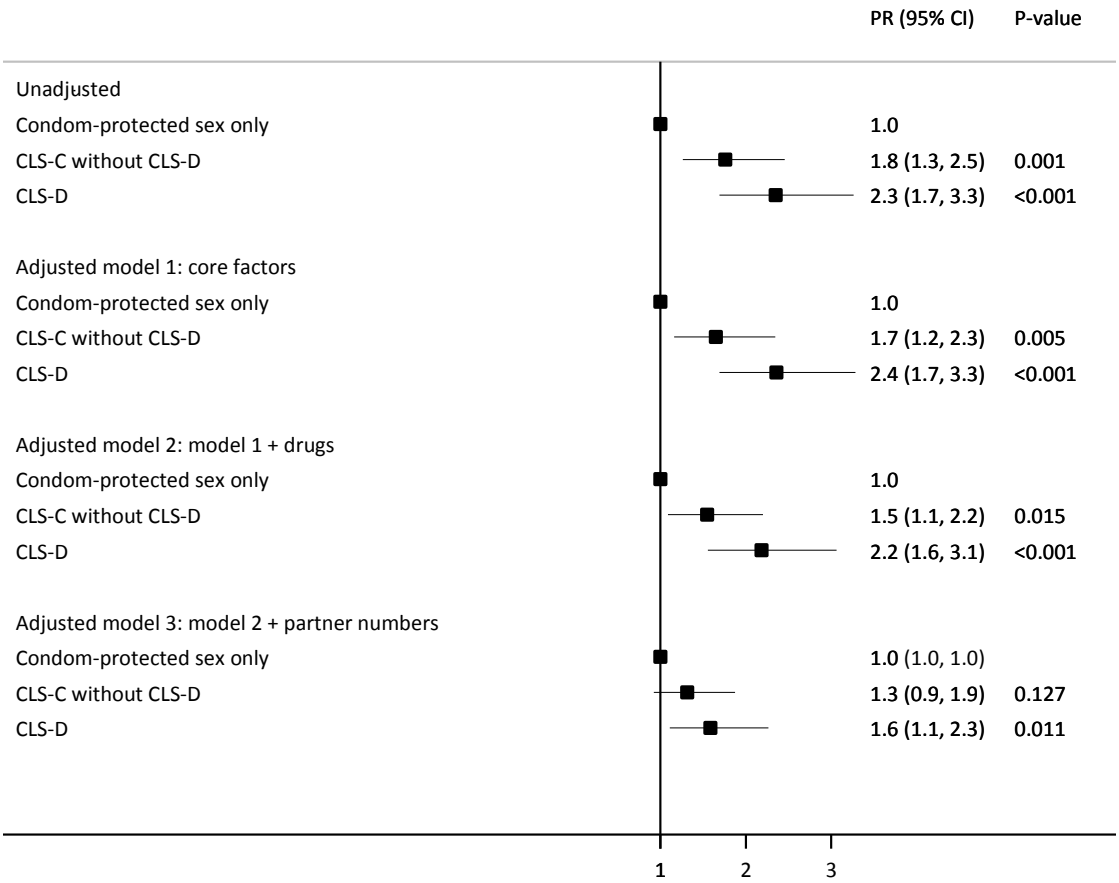
All 2160 MSM with available STI data were classified into one of the following mutually exclusive groups of sexual behaviour in the past three months (as described in section 4.3.3):

1. CLS-D (n=351)
2. 'CLS-C without CLS-D' (n=474)
3. Condom-protected sex only (n=553)
4. No anal or vaginal sex (n=782)

MSM who did not have sex in the past three months (group 4) were then excluded. Among 1378 remaining MSM, the prevalence (95%CI) of self-reported STIs in the past three months was highest for MSM who had CLS-D (group 1: 21.6%, 17.6-26.3%), followed by those who had 'CLS-C without CLS-D' (group 2: 16.2%, 13.2-19.9%), and lowest for those who had condom-protected sex only (group 3: 9.2%, 7.1-11.9%).

Figure 8.5 shows the prevalence of any self-reported STIs in the past three months (as defined in section 8.3.3.1) according to the three mutually exclusive categories of sexual behaviour (N=1378 reported anal or vaginal sex in past three months). In unadjusted analysis, MSM who had CLS-D had 2.3 times higher prevalence of STIs compared to MSM who had condom-protected sex. After adjustment for core factors, the magnitude of associations attenuated but remained strong. Additional adjustment for recreational drug use in the past three months (in addition to core factors) resulted in slight attenuation of magnitude of associations. After additional adjustment for total number of sexual partners in the past three months, the association of the sexual behaviour variable with STIs was considerably attenuated: prevalence of STIs was no longer significantly associated with reporting 'CLS-C without CLS-D', but remained significantly elevated among MSM who had CLS-D compared to those who had condom-protected sex.

Figure 8.5: Unadjusted and adjusted associations of mutually exclusive categories of sexual behaviour and any self-reported STI diagnosis in past three months (N=1378 MSM had anal or vaginal sex in past three months)



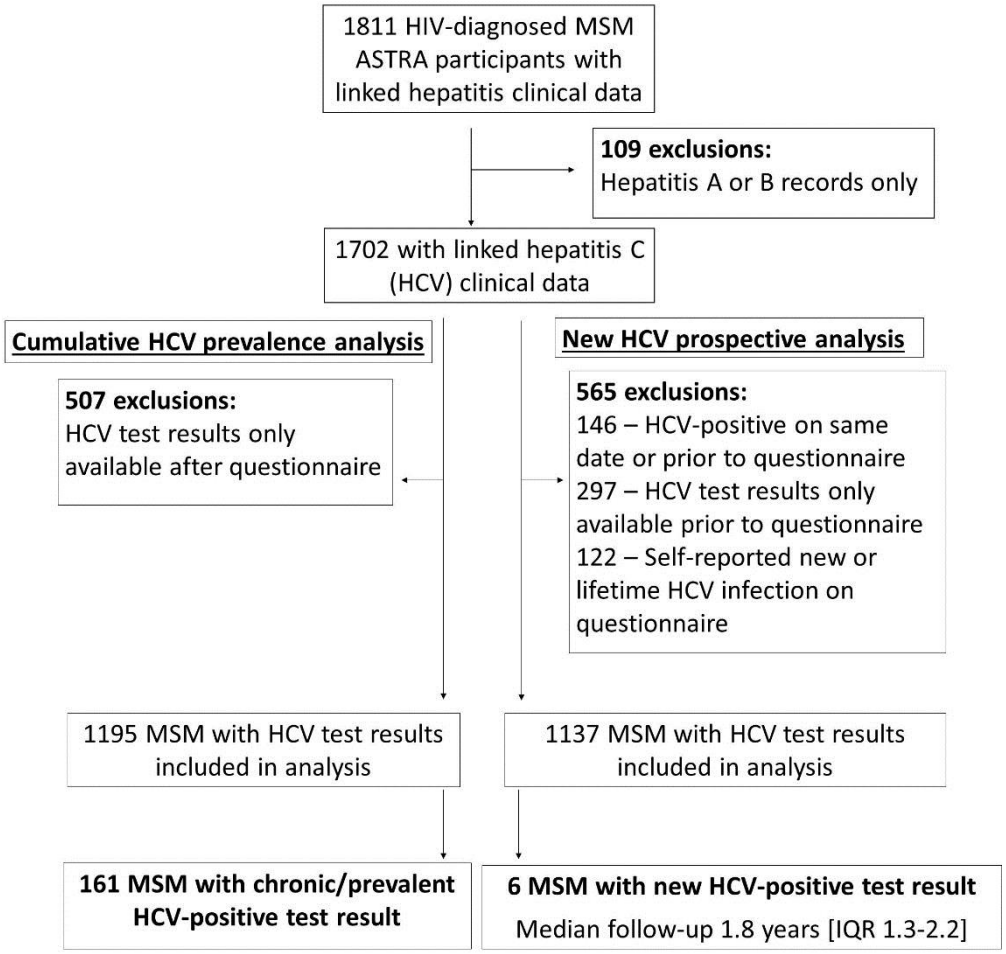
PR: prevalence ratios; Condom-protected sex is the reference group; Model 1: core factors only; Model 2: core factors and recreational drug use in past three months; Model 3: core factors, recreational drug use, and total number of sex partners in the past three months.

8.4.4 Linked clinical hepatitis C analysis

8.4.5 Hepatitis C cohort

Analyses presented in this section are based on data from HIV-diagnosed MSM participating in ASTRA who consented to linkage of the questionnaire with routine clinical data; 1811 HIV-diagnosed MSM had hepatitis clinical data linked to questionnaire data, of whom 1702 had hepatitis C data (Figure 8.6).

Figure 8.6: Cohort flow diagram



8.4.6 Cumulative prevalence of HCV

MSM were excluded from this analysis if HCV test results were available only after ASTRA completion (Figure 8.6, left panel). Hence, among 1195 MSM ASTRA participants with HCV test results, 161 had a chronic/prevalent HCV-positive record, resulting in cumulative HCV prevalence of 13.5% (95%CI 11.6-15.5%). When excluding 18 MSM who reported IDU in the past three months, cumulative HCV prevalence was 12.4% (10.6-14.3%).

A total of 188 MSM reported lifetime diagnosis of HCV on the questionnaire (see section 3.8.4); of these, 138 (73.4%) were identified as having chronic/prevalent HCV in clinical records as well, while 50 (26.6%) were not. When including the 50 MSM who said they had lifetime HCV diagnosis on the questionnaire, the cumulative prevalence of HCV among 1195 MSM was 17.7% (15.6-19.9%, n=211). A small minority

(2.2%) of 161 MSM with prevalent/chronic HCV in clinical records did not report having lifetime diagnosis of HCV on the questionnaire.

8.4.7 Factors associated with cumulative HCV prevalence

8.4.7.1 Socio-demographic, psychological, HIV-related, and lifestyle factors

In unadjusted analysis (Table 8.6), cumulative prevalence of HCV was higher for MSM who were of white ethnicity, had symptoms of depression, an HIV-positive stable partner, did not have evidence of alcohol dependency (by CAGE questionnaire), used recreational drugs, injected drugs, and used chemsex-associated drugs; positive trends were also observed with increasing financial hardship and higher HCV prevalence, as well as increasing number of drugs used ($p<0.10$ for all factors). Of note, 30.9% of MSM who used chemsex-associated drugs had prevalent HCV, compared to 14.4% who used any other drug (but not chemsex-associated). Age, ethnicity, time since HIV diagnosis, place of birth, religion, employment, social support, anxiety, ART status, and higher alcohol consumption (by modified WHO-AUDIT-C) were not associated with cumulative HCV prevalence.

After adjustment for core factors, the following remained significantly associated with higher cumulative HCV prevalence, with little attenuation: symptoms of depression, having an HIV-positive stable partner, no evidence of alcohol dependency, and all recreational drug use factors ($p<0.05$ for all, models 1, Table 8.6). The strong positive trends with increasing financial hardship and increasing number of drugs used in the past three months also remained robust.

Any factor with $p<0.10$ at unadjusted analysis was a candidate for inclusion in a single multivariable model.(Model 2, Table 8.6) These were: ethnicity, financial hardship, depression symptoms, stable partner status, evidence of alcohol dependency, recreational drug use, number of drugs used, injection drug use (IDU), and type of recreational drugs used. Ethnicity was not retained in the model due to low prevalence of non-white ethnicity in this analysis. As all recreational variables could not be included in a single model, only IDU was retained. Hence, after adjustment for financial hardship, depression, stable partner status, alcohol dependency, and IDU, all factors, except for financial hardship, remained strongly associated with cumulative HCV prevalence. The prevalence of HCV was 80% higher among MSM with symptoms of depression compared to those without, and three-fold higher in relative terms among MSM who injected drugs compared to those who did not (both factors $p<0.001$). MSM who did not have evidence of alcohol dependency were more likely to have prevalent HCV compared to those with evidence. ($p<0.001$)

Table 8.6: Associations of socio-demographic, psychological, HIV-related, and lifestyle factors with cumulative prevalence of hepatitis C (HCV) (n/N=161/1195)

	n prevalent HCV/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Age at recruitment, years (N=1175)								
<40	34/270	12.6	1.2 [0.8,1.8]		1.3 [0.9,2.1]			
40-49	83/513	16.2	1.5 [1.1,2.1]		1.5 [1.1,2.1]		-	
≥50	42/392	10.7	1.0	0.297(T)	1.0	0.104(T)		
Ethnicity (N=1171)								
White	152/1082	14.0	1.0		1.0		-	
All other (black, Asian, Mixed, other)	6/89	6.7	0.5 [0.2,1.1]	0.068	0.5 [0.2,1.1]	0.098		
Years since HIV diagnosis (N=1195)								
≤10	74/565	13.1	1.0		1.0		-	
>10	87/630	13.8	1.1 [0.8,1.4]	0.719(T)	1.1 [0.8,1.5]	0.399(T)		
Place of birth (N=1195)								
UK	115/846	13.6	1.0		1.0		-	
Outside the UK	46/349	13.2	0.9 [0.7,1.3]	0.850	1.1 [0.8,1.5]	0.605		
Religious (N=1174)								
Yes	65/471	13.8	1.0		1.0			
No	95/703	13.5	1.0 [0.7,1.3]	0.888	0.9 [0.7,1.2]	0.499	-	
Education (N=1177)								
University degree or above	74/517	14.3	1.0		1.0		-	
No qualifications or up to A levels	86/660	13.0	1.0 [0.8,1.4]	0.524	0.9 [0.7,1.2]	0.333		
Employment (N=1177)								
Employed	91/704	12.9	1.0		1.0		-	
Unemployed or other(carer, student, retired)	69/473	14.6	1.1 [0.8,1.5]	0.415	1.2 [0.9,1.6]	0.224		
Money for basic needs (N=1178)								
Always	73/618	11.8	1.0		1.0		1.0	
Mostly	48/332	14.5	1.2 [0.9,1.7]		1.2 [0.9,1.7]		1.2 [0.8,1.6]	
Sometimes/never	38/228	16.7	1.4 [1.0,2.0]	0.052(T)	1.4 [1.0,2.1]	0.043(T)	1.2 [0.8,1.7]	0.348(T)
Social support (N=1188) ‡								
High	91/713	12.8	1.0		1.0		-	
Medium/low	70/475	14.7	1.2 [0.9,1.5]	0.330(T)	1.2 [0.9,1.6]	0.240(T)		

	n prevalent HCV/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Depression symptoms (N=1195) ‡								
No	99/881	11.2	1.0		1.0		1.0	
Yes	62/314	19.7	1.8 [1.3,2.3]	<0.001	1.8 [1.4,2.4]	<0.001	1.8 [1.3,2.4]	<0.001
Anxiety symptoms (N=1195) ‡								
No	121/946	12.8	1.0		1.0		-	
Yes	40/249	16.1	1.3 [0.9,1.7]	0.175	1.3 [0.9,1.8]	0.119		
Stable partner's HIV-serostatus (N=1195)								
HIV-positive	63/272	23.2	1.0		1.0		1.0	
HIV-negative or unknown status	31/393	7.9	0.3 [0.2,0.5]		0.4 [0.2,0.5]		0.4 [0.2,0.6]	
No stable partner	67/530	12.6	0.5 [0.4,0.7]	<0.001	0.5 [0.4,0.7]	<0.001	0.5 [0.4,0.7]	<0.001
ART status (N=1190)								
On ART	143/1034	13.8	1.0		1.0		-	
Not on ART	17/156	10.9	0.8 [0.5,1.3]	0.325	0.7 [0.5,1.2]	0.259		
ART status/self-reported VL (N=1170)* ‡								
On ART, reports undetectable VL	116/850	13.6	1.0		1.0		-	
On ART, does not report undetectable VL	22/164	13.4	1.0 [0.6,1.5]		1.1 [0.7,1.6]			
Not on ART	17/156	10.9	0.8 [0.5,1.3]	0.655	0.8 [0.5,1.2]	0.508		
Study log-recorded VL (N=1188)*								
≤50c/mL	119/912	13.1	1.0		1.0		-	
>50c/mL	42/276	15.2	1.1 [0.8,1.6]	0.354	1.1 [0.8,1.6]	0.353		
Study log-recorded CD4 count (N=1188)								
≤350cells/mm^3	13/144	9.0	1.0		1.0		-	
>350cells/mm^3	148/1044	14.2	1.5 [0.9-2.6]	0.111	1.4 [0.8,2.4]	0.209		
Higher alcohol consumption(N=1194) ‡								
No	136/956	14.2	1.0		1.0		-	
Yes	25/238	10.5	0.7 [0.5,1.1]	0.140	0.7 [0.5,1.1]	0.122		
Evidence of alcohol dependency (N=1195) ‡								
No	148/983	15.1	1.0		1.0		1.0	
Yes	13/212	6.1	0.4 [0.2,0.7]	0.001	0.4 [0.2,0.7]	0.002	0.4 [0.2,0.7]	0.001
Recreational drug use (N=1195) ‡								
No	43/576	7.5	1.0		1.0		-	
Yes	118/619	19.1	2.6 [1.8,3.6]	<0.001	2.2 [1.6,3.1]	<0.001		

	n prevalent HCV/N	row %	unadjusted PR[95%CI]	p-value	Models 1: aPR [95%CI]	p-value	Model 2: aPR [95%CI]	p-value
Number of recreational drugs used (N=1195)‡								
None	43/576	7.5	1.0		1.0		-	
1	21/208	10.1	1.4 [0.8,2.2]		1.3 [0.8,2.1]			
2-4	62/284	21.8	2.9 [2.0,4.2]		2.5 [1.7,3.6]			
≥5	91/713	27.6	3.7 [2.5,5.5]	<0.001	3.0 [2.0,4.6]	<0.001		
Injection drug use (IDU) (N=1195) ‡								
No	143/1157	12.4	1.0		1.0		1.0	
Yes	18/38	47.4	3.8 [2.7,5.5]	<0.001	3.4 [2.4,4.9]	<0.001	3.0 [2.1,4.2]	<0.001
Type of recreational drug used (N=1195) ‡								
None	43/576	7.5	1.0		1.0			
Chemsex-associated drugs	54/175	30.9	4.1 [2.9,5.9]		3.4 [2.3,5.0]		-	
All other (not chemsex-associated)	64/444	14.4	1.9 [1.3,2.8]	<0.001	1.7 [1.2,2.5]	<0.001		

Global p-values by Wald test or test for trend (T); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1:*** *Each factor adjusted in separate model for core variables: age, ethnicity, time since HIV diagnosis, stable partner's HIV serostatus, and ART status. Denominators vary due to missing data in each model.* ***Model 2****: Any factor with p<0.10 in unadjusted analysis included in a single model, plus clinic. (Only IDU retained in model 2 due to collinearity with recreational drug use, number of drugs, type of drugs used). *In both cases, model for 'ART status/self-reported VL' and model for study log-recorded VL omit variable on ART due to collinearity. Alcohol consumption by WHO-AUDIT-C, alcohol dependency by CAGE questionnaire.*

‡ *All factors defined in section 3.8.*

8.4.7.2 Sexual behaviours, other STIs and cumulative HCV prevalence

In unadjusted analysis (Table 8.7), all sexual behaviours and any self-reported diagnosed STIs were associated with cumulative HCV prevalence. After adjustment for core factors, all sexual behaviours and self-reported STIs in the past three months remained significantly associated with higher HCV prevalence ($p<0.05$ for all, models 1A: Table 8.7). Significant positive trends were also observed with increasing number of partners in the past three months, as well as with increasing number of new sex partners in the past year (p-trend<0.001 for both).

Additional adjustment for injection drug use (IDU) in the past three months (and core factors) resulted in attenuated, but still robust associations with cumulative HCV prevalence (models 1B: Table 8.7). MSM who had CLS-C had over two-fold higher prevalence of HCV compared to those who did not; similarly, those who had any other self-reported diagnosed STI in the past three months had 40% higher prevalence of HCV in relative terms compared to those without another STI.

8.4.8 Incident HCV over follow-up

Of the initial 1702 MSM with available HCV data, participants were excluded if they had clinically-verified or self-reported HCV infection prior to ASTRA completion; 1137 MSM remained.(Figure 8.6, right panel) Over a median of 1.8 years [IQR 1.3-2.2] and 1935 person-years (PY) at risk, 6 new HCV cases were recorded. Incidence of HCV was 0.31 per 100 PY (95% 0.13-0.69). Conclusions drawn on the basis of these six incident cases are limited, but the framework of analysis demonstrates the approach that will be taken once greater follow-up (FU) is accrued.

8.4.8.1 Factors associated with incident HCV

Table 8.8 shows the associations of factors with new HCV over FU. The median time elapsed between clinic-recorded VL and incident HCV diagnosis date was 1.5 years (IQR 0.2-4.2) and of clinic-recorded CD4 count was 1.1 years (0.3-2.7). All six MSM with incident HCV had high clinic-recorded CD4 counts prior to HCV diagnosis (median 500, IQR 410-840 cells/mm^3). There was an indication, despite the very small number of incident HCV cases, that IDU and chemsex-associated drug use in the three months prior to questionnaire completion conferred higher risk of incident HCV. There was some suggestion of elevated risk of incident HCV among MSM who had CLS, CLS-C, CLS-D, or a self-reported diagnosis of syphilis in the past three months, as well as among those with 10 or more new sex partners in the past year. However, conclusions based on the small number of incident cases are limited.

Table 8.7: Associations of sexual behaviours, other STIs in the past three months and cumulative prevalence of hepatitis C (HCV) (n/N=161/1195)

	n with chronic/ prevalent HCV/N	row %	unadjusted PR[95%CI]	p-value	Models 1A: Core only aPR [95%CI]	p-value	Models 1B: Core + IDU aPR [95%CI]	p-value
Any anal and/or vaginal sex (N=1195)								
No	36/430	8.4	1.0		1.0		1.0	
Yes	125/765	16.3	2.0 [1.4,2.8]	<0.001	1.8 [1.3,2.6]	0.001	1.7 [1.2,2.4]	0.005
Condomless sex (CLS) (N=1195)								
No	64/736	8.7	1.0		1.0		1.0	
Yes	97/459	21.1	2.4 [1.8,3.3]	<0.001	2.2 [1.6,2.9]	<0.001	1.9 [1.4,2.7]	<0.001
CLS with HIV-seroconcordant partners (CLS-C) (N=1195)								
No	74/844	8.8	1.0		1.0		1.0	
Yes	87/351	24.8	2.8 [2.1,3.8]	<0.001	2.4 [1.7,3.3]	<0.001	2.1 [1.5,2.9]	<0.001
CLS with HIV-serodifferent partners (CLS-D) (N=1195)								
No	130/1009	12.9	1.0		1.0		1.0	
Yes	31/186	16.7	1.3 [0.9,1.9]	0.160	1.6 [1.1,2.2]	0.011	1.6 [1.1,2.2]	0.013
Participated in group sex (N=1167)								
No	99/927	10.7	1.0		1.0		1.0	
Yes	58/240	24.2	2.3 [1.7,3.0]	<0.001	2.2 [1.7,3.0]	<0.001	2.1 [1.5,2.8]	<0.001
Used the internet to find sex (N=1171)								
No	79/735	10.7	1.0		1.0		1.0	
Yes	78/436	17.9	1.7 [1.2,2.2]	<0.001	1.7 [1.3,2.3]	<0.001	1.6 [1.2,2.1]	0.002
Total number of partners (N=1195)								
None	38/451	8.4	1.0		1.0		1.0	
1	43/336	12.8	1.5 [1.0,2.3]		1.3 [0.9,2.0]		1.3 [0.8,1.9]	
2-4	63/319	19.7	2.3 [1.6,3.4]		2.2 [1.5,3.2]		2.0 [1.4,3.0]	
≥5	17/89	19.1	2.3 [1.3,3.8]	<0.001(T)	2.3 [1.4,3.8]	<0.001(T)	2.0 [1.2,3.4]	<0.001(T)
Number of <u>new</u> sexual partners in past year (N=1130)								
No new partners	42/480	8.8	1.0		1.0		1.0	
1-9	57/357	16.0	1.8 [1.3,2.7]		1.7 [1.1,2.4]		1.6 [1.1,2.3]	
10-19	25/133	18.8	2.1 [1.4,3.4]		2.4 [1.5,3.7]		2.0 [1.3,3.2]	
≥20	31/160	19.4	2.2 [1.4,3.4]	<0.001(T)	2.2 [1.5,3.4]	<0.001(T)	1.9 [1.3,3.0]	<0.001(T)

	n with chronic/ prevalent HCV/N	row %	unadjusted PR[95%CI]	p-value	Models 1A: Core only aPR [95%CI]	p-value	Models 1B: Core + IDU aPR [95%CI]	p-value
Any self-reported STI (N=1180)								
No	136/1065	12.8	1.0		1.0		1.0	
Yes	24/115	20.9	1.6 [1.1,2.4]	0.013	1.7 [1.1,2.5]	0.011	1.4 [1.0,2.2]	0.074
Number of self-reported STIs (N=1195)								
None	137/1080	12.7	1.0		-		-	
1	21/90	23.3	1.8 [1.2,2.8]					
≥2	3/25	12.0	0.9 [0.3,2.8]	0.014(F)				
Self-reported syphilis (N=1195)								
No	157/1170	13.4	1.0		-		-	
Yes	4/25	16.0	1.2 [0.5,3.0]	0.765(F)				

Three month recall of sexual behaviours unless otherwise specified; Global p-values by Wald test, test for trend (T), or Fisher's exact (F); PR: prevalence ratio; CI: confidence interval; Adjusted PRs (aPR) by modified Poisson regression; ***Models 1A:*** *Each factor adjusted in separate model for core factors.* ***Models 1B:*** *Each factor adjusted in separate model for core factors and injection drug use (IDU) in the past three months. Denominators vary due to missing data in each model.*

Table 8.8: Associations of socio-demographic, HIV-related, lifestyle characteristics, sexual behaviours and incident hepatitis C diagnosis (n/N=6/1137)

	n/PY	IR/100PY [95%CI]	unadjusted IRR/100 PY [95%CI]	p-value (exact)
Age at recruitment, years (N=1118)				
<40	3/608	0.49 [0.16-1.53]	2.5 [0.3,23.7]	
40-49	2/808	0.25 [0.06-0.99]	1.2 [0.1,13.4]	
≥50	1/485	0.21 [0.03-1.46]	1.0	0.638
Years since HIV diagnosis (N=1137)				
≤10	3/1023	0.29 [0.09-0.91]	1.0	
>10	3/913	0.33 [0.11-1.02]	1.1 [0.2,5.7]	0.870
Stable partner's HIV-serostatus (N=1137)				
HIV-positive	2/435	0.46 [0.12-1.84]	1.0	
HIV-negative or unknown status	2/653	0.31 [0.08-1.23]	0.6 [0.1,4.6]	
No stable partner	2/848	0.24 [0.06-0.94]	0.5 [0.1,3.5]	0.777
ART status (N=1132)				
On ART	4/1598	0.25 [0.09-0.67]	1.0	
Not on ART	2/329	0.61 [0.15-2.43]	2.2 [0.4,12.1]	0.361
Clinic-recorded VL (N=1130)*				
≤50c/mL	2/1219	0.16 [0.04-0.66]	1.0	
>50c/mL	4/707	0.57 [0.21-1.51]	3.5 [0.6, 18.6]	0.156
Clinic-recorded CD4 count (N=1133)*				
<350cells/mm3	0/349	-	-	-
≥350cells/mm3	6/1581	0.38 [0.17-0.84]		
Higher alcohol consumption(N=1137) ‡				
No	5/1576	0.32 [0.13-0.76]	1.0	
Yes	1/359	0.28 [0.04-1.98]	0.9 [0.1,7.6]	0.918
Recreational drug use (N=1137) ‡				
No	0/933	-		
Yes	6/1002	0.6 [0.27-1.33]	-	-
Number of recreational drugs used (N=1137)‡				
1-3	4/682	0.59 [0.22-1.56]	1.0	
≥4	2/320	0.63 [0.16-2.5]	1.1 [0.2,6.1]	0.901
Injection drug use (IDU) (N=1137) ‡				
No	5/1892	0.26 [0.11-0.63]	1.0	
Yes	1/43	2.31 [0.33-16.39]	10.4 [1.2,89.4]	0.033
Chemsex-associated drug use (N=1137) ‡				
No	3/1633	0.18 [0.06-0.57]	1.0	
Yes	3/303	0.99 [0.32-3.07]	4.8 [1.0,24.0]	0.054
Any anal and/or vaginal sex (N=1137)				
No	1/659	0.15 [0.02-1.08]	1.0	
Yes	5/1276	0.39 [0.16-0.94]	2.6 [0.3,22.4]	0.380
Condomless sex (CLS) (N=1137)				
No	1/1168	0.09 [0.01-0.61]	1.0	
Yes	5/767	0.65 [0.27-1.57]	7.5 [0.9,63.9]	0.067
CLS with HIV-seroconcordant partners (CLS-C) (N=1137)				
No	2/1351	0.15 [0.04-0.59]	1.0	
Yes	4/584	0.68 [0.26-1.82]	4.6 [0.8,25.0]	0.080

	n/PY	IR/100PY [95%CI]	unadjusted IRR/100 PY [95%CI]	p-value (exact)
CLS with HIV-serodifferent partners (CLS-D) (N=1137)				
No	3/1624	0.18 [0.06-0.57]	1.0	
Yes	3/311	0.96 [0.31-2.99]	5.3 [1.1,26.0]	0.042
Participated in group sex (N=1111)				
No	4/1460	0.27 [0.1-0.73]	1.0	
Yes	2/431	0.46 [0.12-1.86]	1.6 [0.3,8.8]	0.586
Used the internet to find sex (N=1112)				
No	2/1172	0.17 [0.04-0.68]	1.0	
Yes	4/719	0.56 [0.21-1.48]	3.6 [0.7,19.5]	0.143
Total number of partners (N=1137)				
0-4	4/1738	0.23 [0.09-0.61]	1.0	
≥5	2/198	1.01 [0.25-4.04]	4.2 [0.8,23.1]	0.097
Number of new sexual partners in past year (N=1137)				
0-9	1/1353	0.07 [0.01-0.52]	1.0	
≥10	5/583	0.86 [0.36-2.06]	10.8 [1.3,92.5]	0.030
Any other STI (N=1121)				
No	4/1669	0.24 [0.09-0.64]	1.0	
Yes	2/237	0.84 [0.21-3.37]	3.3 [0.6,17.8]	0.173
Syphilis (N=1121)				
No	5/1887	0.26 [0.11-0.64]	1.0	
Yes	1/49	2.06 [0.29-14.61]	7.3 [0.8,62.1]	0.071

*Three month recall unless otherwise specified. p-values by exact significance test; IR: incidence rate; IRR: incidence rate ratio; PY: person-years; STI: sexually transmitted infection. *Clinic-recorded VL and CD4 closest to HCV test date.*

***ǂ** All factors defined in sections 3.8 and 6.3*

8.5 Discussion

8.5.1 Summary of findings

In this large study of HIV-diagnosed MSM attending for HIV care, one in 10 had a self-reported diagnosis of STIs (other than HIV) in the past three months. The majority of STI co-infections were bacterial, with chlamydia (CT), gonorrhoea (NG), and syphilis being most prevalent. STI co-infections were more prevalent among MSM who were younger, had an HIV-positive stable partner, were not on ART, and used recreational drugs in the past three months (including IDU and chemsex-associated drugs). Prevalence of STI co-infections was also associated with reporting any anal or vaginal sex, any CLS, CLS-C, CLS-D, group sex, and high partner numbers, even after adjustment for socio-demographic, HIV-related factors, and recreational drug use (including IDU). Among those who had sex in the past three months, those who had CLS-D had significantly higher prevalence of STI co-infections compared to those who had condom-protected sex. In longitudinal analysis using linked routine clinical data, the cumulative prevalence of any hepatitis C (HCV) diagnosis prior to ASTRA completion was 13.3%. Symptoms of depression, recreational drug use (and IDU), sexual behaviours (any sex, CLS, CLS-C, CLS-D, group sex, high partner numbers), and any other STI co-infection were strongly associated with prevalent HCV. Incident HCV diagnosis over almost two years of follow-up was recorded for six MSM ASTRA participants, yielding an incidence rate of 0.31 per 100 person years (PY). Despite the low

number of incident HCV infections, there was suggestion that incidence was higher among MSM who reported IDU, chemsex-associated drug use, and CLS-D in the past three months.

8.5.2 Prevalence of STIs in ASTRA

The prevalence of any STI among HIV-diagnosed MSM in this study was assessed by self-reported diagnosis with a three month recall period. Previous studies which recruited HIV-diagnosed MSM from outpatient clinics in high income countries and also used self-reported measures found prevalence estimates of any STI in the past 12 months ranging from 13% to 41% (see Table 8.1). The most commonly reported STIs in ASTRA were CT, NG, and syphilis, in line with estimates of STI surveillance among MSM in the UK.[471] This pattern of STI prevalence was also observed in the Swiss HIV cohort study (SHCS)[546] among 112 HIV-diagnosed MSM who reported having sex in the past year. In other studies that provided prevalence estimates for specific STIs (see Table 8.1), genital warts were the most prevalent STI in two US studies[239,298] while syphilis was most prevalent in a German study.[316,547] These differences reflect the prevalence of different STIs in different populations of HIV-diagnosed MSM worldwide.

8.5.3 Factors associated with prevalent self-reported diagnosed STIs

The factors found to be associated with self-reported diagnosis of STIs in this chapter mostly mirror factors that found to be associated with any CLS in the past three months in Chapter 4. As shown in Table 4.4, CLS was more prevalent among younger MSM. In this chapter (Table 8.4), there was also evidence of a consistent association of younger age and higher prevalence of any self-reported STI in the past three months. An earlier US study of over 200 HIV-diagnosed MSM also showed that younger age was predictive of incident bSTIs at follow-up; this estimate was adjusted only for repeated measures (but not any other factors, such as CLS).

In Chapter 4, it was also shown that MSM with an HIV-positive stable partner were more likely to report CLS in the past three months, compared to those who had an HIV-serodifferent or no stable partner. (Table 4.4) Similarly, in this chapter, MSM with an HIV-positive stable partner tended to be more likely to have any STI in the past three months. This finding is in line with recent evidence of enteric STI outbreaks in the UK, in which the majority of cases were HIV-positive MSM who reported CLS with other HIV-positive men only.[521]

In line with earlier studies[554,558,560,568], socio-economic factors such as ethnicity, education, employment status, place of birth were not associated with any STI co-infection in ASTRA. Similarly, none of these socio-economic factors were associated with reporting CLS in the past three months in Chapter 4, either. In this chapter, there was some evidence that MSM who reported financial hardship (no money for basic needs) were more likely to have higher prevalence of STI co-infections; financial hardship was not associated with reporting any CLS in Chapter 4 (Table 4.4).

In this analysis, MSM who were not on ART and those who had detectable VL had significantly higher prevalence of self-reported STIs, even after adjustment for time with HIV diagnosis. The pattern of higher STI prevalence among those not on ART is similar to that seen in Chapter 4, with higher prevalence of CLS among those not on ART. As in our study, three earlier studies also reported significant associations of not being on ART[548] or having detectable HIV VL and self-reported bacterial STIs in the past three months.[239,547] In contrast, a systematic review of 37 studies showed no difference in the prevalence of STI co-infections according to ART status in HIV-diagnosed men and women.[116] It may be that previous STI co-infections may activate HIV replication leading to increased viremia. In this case, elevated HIV VL may be a proxy for having an STI.

Recreational drug use, including IDU, has been identified as a key factor in the transmission of bSTIs and HCV among HIV-diagnosed MSM in the UK.[148,370,539,568,571,572] In this study, all measures of recreational drug use were strongly associated with self-reported prevalent STIs; chemsex-associated drug use was strongly associated with higher prevalence of any STI. Drug-induced sexual disinhibition may facilitate CLS with multiple partners, as well as traumatic and prolonged sex practices that in turn lead to STI transmission.

CLS and high partner numbers were, as expected, strongly associated with any self-reported STI. A small minority of studies reviewed in this chapter explore the factors associated with higher risk of (prevalent or incident) STIs, over and above the risk conferred by CLS (see section 8.2.11). In this ASTRA analysis (and the majority of other studies reviewed) associations with self-reported STIs paralleled associations with reporting CLS and high partner numbers. Specifically, when compared to MSM who had condom-protected sex, MSM who had CLS-D were more likely to report any STI. Maintaining consistent condom use is likely to be challenging in the context of high partner numbers. It is also likely that accurate ascertainment of all partners' HIV status is more uncertain with high partner numbers. Therefore, the number of sex partners reported in the past three months (or number of new partners in the past year) can be used as a predictor of STI risk in epidemiological studies. CLS remains the most useful marker of STI transmission (other than HIV) for epidemiological surveillance and STI prevention among HIV-diagnosed MSM.

8.5.4 **Hepatitis C co-infection**

Over the past two decades, there has been increasing evidence of HCV transmission among MSM who do not report IDU, and of the emergence of acute HCV among HIV-diagnosed MSM in Europe and North America. This evidence has highlighted the importance of the sexual route in changing the pattern of HCV transmission among HIV-diagnosed MSM.

8.5.4.1 Cumulative prevalence of HCV

In ASTRA, the cumulative HCV prevalence (the proportion of MSM ever tested for anti-HCV or HCV RNA who had received a positive HCV test result) was 13.3% overall, 12.4% when excluding men who reported IDU, and 17.7% when including men with self-reported lifetime diagnosis of HCV only. A

systematic review (2000-2015) of 13 studies including over 9500 HIV-diagnosed MSM in high-income countries reported cumulative prevalence of 8.3% (95%CI 6.7-9.9%) overall and 7.1% (5.1-9.0%) when excluding MSM who reported IDU.[536] Our estimates are in line with those from earlier cross-sectional surveys with linked clinical data (HCV prevalence ranging from 7.7% to 15.2%).

8.5.4.2 Factors associated with prevalent HCV

A number of socio-demographic factors were not associated with prevalent HCV in ASTRA. As observed in two earlier UK cross-sectional questionnaire surveys (SHARP[568] and GMSS[560]), HCV prevalence did not differ significantly by participants' age, ethnicity, educational attainment, or employment status in our study.

In ASTRA, a strong association was observed between evidence of depressive symptoms and higher prevalence of chronic HCV; depression was associated with 80% higher prevalence of HCV in relative terms, even after adjustment for markers of lower socio-economic status, IDU, and stable partner status. Prevalence of depression has been shown to be significantly higher among HCV-diagnosed individuals compared to those without HCV.[578] It is possible that this is still the case in HIV/HCV co-infected individuals, but research is scarce in this area. Temporality in the association of depression and HCV cannot be established from ASTRA due to its cross-sectional design. However, it could be hypothesized that depression is a result of living with a diagnosis for a second chronic condition in addition to HIV, as well as of coping with treatment, complications, and morbidity related to HCV. On the other hand, it could also be that HIV-diagnosed people with pre-existing depression may have higher susceptibility to HCV infection; this could be mediated through the strong association of recreational drug use with CLS, as shown in Chapter 6 (see Figure 6.3). With the advent of DAAs, HCV cure rates have improved dramatically[579]; it will remain important to continue screening for and managing depression among HCV/HIV co-infected individuals.

The cumulative prevalence of HCV was over two-fold higher among MSM who did not have evidence of alcohol dependency compared to those who did in ASTRA (based on the CAGE questionnaire[353], a screening tool for alcohol abuse and dependence). Among individuals with chronic HCV, progression of HCV-related liver disease is increased by heavy alcohol use.[580] Our findings could be due to MSM minimising consumption of alcohol as a result of HCV infection.

A quarter of HIV-diagnosed MSM in ASTRA with a stable partner who was also HIV-positive had prevalent HCV; the association remained strong after adjustment for socio-demographic, HIV-related, and lifestyle factors. It could be that this finding is due to lower condom use with HIV-positive stable partners. All types of sex, CLS, and group sex were also strongly associated with prevalent HCV, after accounting for IDU and core factors. Strong positive trends were also observed of the total number of partners and number of new sex partners in the past year. Recreational drug use, IDU, polydrug use, and, specifically, use of chemsex-associated drugs in the past three months were strongly associated with prevalent HCV. In particular, CLS-C was associated with two-fold higher prevalence of HCV,

independent of IDU and other core factors. While it is encouraging that a sizeable proportion of HIV-diagnosed MSM in ASTRA restrict CLS to HIV-positive partners only, this clearly does not eliminate the risk of other STIs, including HCV. Increased diagnoses of HCV, syphilis, NG, and CT among HIV-diagnosed MSM in the UK in the past few years have coincided with the emergence of sexually transmissible enteric infections (see section 8.2.8.2). These overlapping epidemics suggest that sexual networks of HIV-diagnosed MSM engaging in serosorting may contribute to transmission of HCV and other STIs in the UK. Chemsex (and associated sexual behaviours) may play a key role in the development of these sexual networks and in maintaining a pool of prevalent HCV infections resulting in ongoing transmission of HCV among HIV-diagnosed men. In addition, the practice of chemsex and 'slamming' (injecting drugs used in chemsex, particularly methamphetamine and mephedrone) should be distinguished from IDU involving heroin as the drugs, characteristics of users, and risks for STIs, HIV, and other blood-borne viruses may be different.

MSM who used the internet to find sex also had 60% higher prevalence of HCV compared to those who did not. In recent years, the internet has facilitated finding sex partners based on HIV-serostatus and specific sexual interests (such as CLS-C and chemsex); geosocial networking smartphone apps may thus play an important role in the ongoing increase in incidence of HCV and other bSTIs among MSM in the UK.

8.5.4.3 Incident HCV over follow-up

Among HIV-diagnosed MSM in ASTRA, the incidence of HCV diagnosis was 0.31 per 100 PY based on six seroconversions. This estimate is in line with those from enhanced surveillance of newly acquired HCV among HIV-diagnosed MSM in England (0.24 per 100 PY in 2012).[544] There is evidence of ongoing but declining sexual transmission of HCV among HIV-diagnosed MSM in England. On the other hand, results from the CASCADE collaboration showed a significant increase in the incidence of HCV among HIV-diagnosed MSM in northern and Western Europe between 1990 and 2014 (from 0.07 to 1.8 per 100PY).[564]

8.5.4.4 Factors associated with incident HCV

Conclusions drawn from this analysis are limited due to the low number of incident HCV cases. In unadjusted analyses there was no evidence to suggest higher incidence of HCV according to participants' age or time since HIV diagnosis. In the CASCADE collaboration, HCV incidence was elevated among younger HIV-diagnosed MSM compared to older (incidence remained highest and stable until age 35 and declined thereafter) and those who were recently HIV-diagnosed.[564] The discrepancy in findings may be due to regional differences in local HCV epidemics among HIV-diagnosed MSM, as CASCADE includes 16 cohorts across Europe, Australia, and North America.

The incidence of HCV was somewhat elevated among MSM with detectable HIV VL in ASTRA, although there was insufficient power to detect a statistical difference. Few studies have examined the association of HIV VL and HCV incidence: three cohort studies of HIV-diagnosed MSM did not find any

association of HIV plasma VL and incident HCV[492,561,563], although one of these[561] included ART status in multivariable adjustment thus masking the true effect of VL. A more recent CASCADE collaboration analysis showed that higher VL (especially when $\log_{10}$VL≥5c/mL) was significantly associated with HCV incidence, while CD4 count was not.[564] The association of higher HIV VL and incident HCV may be due to HIV-related activation of HCV target cells which facilitate transmission of HCV.[451,494]

As expected, IDU was associated with higher HCV incidence in our study. However, as only one of six MSM with incident HCV reported any IDU in the three months prior to ASTRA, it was not possible to examine the effect of IDU in multivariable models. Chemsex-associated drug use conferred almost five-fold higher risk of incident HCV compared to no drug use/any other drug use. CLS-D and having 10 or more new sex partners in the past year was associated with elevated risk of incident HCV; evidence was weak for the association of CLS and CLS-C with incident HCV.

Prior syphilis (lifetime or acute) has been shown to be a risk factor for HCV incidence among all MSM (regardless of HIV serostatus).[535] In our study, there was some suggestion of elevated risk of HCV seroconversion with self-reported syphilis in the three months prior to ASTRA completion. Syphilis co-infection may increase the risk of sexual transmission of HCV among HIV-diagnosed MSM, as syphilitic lesions may damage genital mucosa and facilitate HCV transmission[561]; syphilis co-infection may also be a proxy for CLS in dense sexual networks of HIV-positive men.[535]

8.5.5 **Limitations**

A number of important limitations must be considered in interpreting the results of analyses presented in this chapter. Firstly, with the exception of prevalent and incident HCV, all other STI diagnoses were measured by self-report with a three month recall. Underreporting of prevalent STIs may have resulted in recall bias and thus underestimation of prevalence of self-reported STIs. It was not possible to obtain clinically/lab-verified STI diagnoses at questionnaire completion due to the way GUM and HIV clinical services are separated, making data integration of routine HIV and GUMCAD data difficult. In addition, as the study was conducted in 2011-2012, prior to the emergence of outbreaks of sexually transmissible enteric infections (e.g. *Shigella*, E.coli, hepatitis A, and *Giardia*) in the UK, these STIs were not included as one of the options for self-reported STIs in the past three months. However, the incidence and prevalence of these infections remains low in the UK (for instance, 26 new cases of any *Shighella* serovar were recorded among MSM in 2015 in England); partly because they are self-limiting and affected people may not seek treatment. Sexual behaviours which may lead to mucosal trauma and thus transmission of STIs, such as fisting with/without gloves and sharing of sex toys, were not collected in ASTRA.

The nature of this cross-sectional study does not allow for establishing temporality of self-reported STIs; it is not possible to know whether other STIs were acquired before or after HIV infection, or to infer causality in the direction of the co-infection. MSM who were recently diagnosed (≤3 months prior to

questionnaire completion) were excluded from analyses; this was done in order to refine temporality, so that the HIV diagnosis predated the other STIs.

Prospective analysis of HCV incidence is currently limited by the small number of incident cases (only 6). For this reason, only unadjusted analyses were presented and results examined in terms of associations with less focus on p-values. The aim is to repeat the analysis with longer follow-up. Although this analysis was underpowered, with additional accrual of follow-up (and more incident cases), ASTRA is unique in providing linked behavioural data from the questionnaire to new HCV diagnoses.

Routine clinical data was collected prior to the first two oral DAAs becoming available for treatment of HCV among HIV-diagnosed individuals in 2011; by end of follow-up, in 2014, three new DAAs were licensed for use in Europe. Although European treatment guidelines now recommend use of DAAs for HIV/HCV co-infected individuals, access to these treatments is still limited due to prohibitive costs.[581]

8.6 Conclusions and Implications

One in 10 HIV-diagnosed MSM in this study reported having a recent diagnosed STI. Self-reported STIs were most prevalent among MSM who were younger, not on ART, had detectable VL, and used recreational drugs (including injection and chemsex-associated drugs). These associations mirror those observed for CLS in Chapter 4. They also emphasize the importance of STI prevention strategies that particularly focus on HIV-diagnosed MSM. All types of CLS and higher partner numbers were strongly associated with reporting any diagnosed STI. In terms of assessing and monitoring risk of transmission of STIs among HIV-diagnosed MSM, 'any condomless sex' is likely to remain the most relevant measure. The number of partners reported is also a useful marker of STI transmission risk, particularly for MSM reporting chemsex and IDU. While condomless sex with other HIV-positive partners (CLS-C) does not confer risk of HIV transmission to HIV-negative partners, it does confer risk of transmission of other STIs. Given the increasing incidence of bacterial and viral STIs among HIV-diagnosed MSM in the UK, testing, control, and prevention of STIs remains a cornerstone of HIV control.

While evidence on the effect of treating STIs in HIV-diagnosed people on directly reducing HIV infectiousness is insufficient, detection and control of STIs remains critical in this population for a number of reasons.[582] First, STI co-infections may increase genital HIV VL and thus facilitate HIV transmission to HIV-negative partners; it is still unclear, however, whether this is still the case in the presence of effective ART and suppressed plasma VL. Second, co-infections may affect the natural history of HIV via a number of biological mechanisms thus increasing the risk of morbidity and mortality. Conversely, HIV-induced immunosuppression may lead to reactivation of STI-coinfections that are otherwise undetectable.[451] Third, transmission of STIs is perpetuated by higher rates of partner change and complex sexual networks, which can lead to localised outbreaks.[583,584] Fourth, reversing the trend of increasing NG diagnoses is a priority given the spread of resistance to frontline antimicrobials used in the treatment of NG and the depletion of effective treatment options.[432]

BHIVA recommendations emphasize the routine sexual health assessment of all HIV-diagnosed MSM (at least six-monthly after initial HIV diagnosis and syphilis serology 2-4 times yearly).[585] Extra-genital screening (rectal, pharyngeal) for CT and NG can detect up to 80% more asymptomatic infections compared to urine testing.[567] There is a need for scaling up extra-genital screening approaches in HIV clinics, particularly for asymptomatic MSM who report receptive or insertive condomless anal or oral sex and those who engage in chemsex. Although HIV-diagnosed MSM are at increased risk of anal cancer (associated with genital warts and HIV co-infection), anal cytology is not routinely recommended in the UK. Self-collected specimens have recently been shown to be a convenient and acceptable way of testing, and may address some of the barriers to screening in this population.[586]

DAAs are highly effective, have favourable tolerability, short treatment duration, and are expected to increase treatment uptake and SVR rates at population level.[535] The effect of DAAs will be modest without expansion of access to testing and treatment. Prevention in this case is imperative in limiting the possibility of HCV reinfection after SVR. Regular routine HCV screening among HIV-diagnosed MSM with cleared HCV or SVR and in HIV negative MSM on PrEP would be beneficial in preventing incident HCV infections in HIV positive MSM. The risk of hepatotoxicity and other liver-related complications (see section 8.2.7.4) is still relevant in the era of DAAs and highlights the need for comprehensive management of other risk factors beyond HIV and HCV control, particularly in populations with high alcohol consumption and chemsex use.[587]

9 Summary and conclusions

The aim of this thesis was to describe the sexual behaviours of HIV-diagnosed MSM in the UK in the era of effective ART. The ASTRA study, due to its representative and substantive sample size, comprehensive data collection, and linkage to clinical data, offered enhanced understanding of sexual behaviours of HIV-diagnosed MSM in the UK, and of the co-factors (socio-demographic, psychological, health, lifestyle, HIV-related) that these may be associated with. The study's results have important implications for improved care of HIV-diagnosed people and for national HIV prevention efforts.

9.1 Rationale and background to the ASTRA study

The introduction of antiretroviral therapy (ART) in 1996 was accompanied by reported increases in prevalence of 'high-risk sexual behaviours' (mainly condomless sex, CLS) among all MSM (HIV-negative and HIV-diagnosed/HIV-positive) in Europe and North America.[93–97] This raised concern about a possible causal effect, whereby HIV optimism may prompt complacency around 'safe sex' practices, and thus lead to increases in 'risky' sexual behaviours. A number of studies carried out over the next five to ten years provided evidence that ART use was not associated with sexual behaviours perceived to confer risk of HIV transmission (specifically, condomless sex with HIV-discordant status partners, CLS-D).[100,103,108,110–112,114,115] However, the late 2000's saw fundamental changes in the awareness and understanding of HIV transmission risk.[118] Evidence from observational studies of heterosexual HIV-serodifferent couples accumulated, showing the profound protective effect of virological suppression on ART on reducing an HIV-positive individual's infectiousness to an HIV-negative sexual partner.[7,242] Following the "Swiss statement" in 2008, it was hypothesized that the prevalence and patterns of 'risky' sexual behaviours among HIV-positive people could change as a result of raised awareness of the Swiss Statement.[124] In this context, a programme of work including the ASTRA study was designed as a comprehensive assessment of the preventive role of ART on HIV transmission. There was concern that increased awareness of the protective effect of suppressed viral load (VL) on HIV infectiousness may adversely impact on levels of CLS among MSM with HIV, which may in turn undermine the full potential impact of early treatment in reducing transmission. The ASTRA study aimed to understand the association between use of ART, perceived (self-reported) VL suppression, and sexual behaviours, in order to inform assessment of the public health impact of a possible strategy of early ART initiation.[89] The secondary aims of ASTRA were to investigate sexual behaviours and attitudes among key demographic subgroups, and to examine the association of a range of co-factors (socio-demographic, psychological, HIV-, ART-, health-related, and lifestyle) with specific sexual behaviour measures, in order to inform HIV clinical care and prevention.[205] This thesis made a contribution to these secondary aims and considered HIV-diagnosed MSM only.

Since ASTRA was conducted, further evidence accumulated on the impact of ART on reducing infectiousness of people living with HIV, particularly from PARTNER[9], a study carried out as part of the

same programme of work as ASTRA. Moreover, the START trial demonstrated individual clinical benefit of earlier treatment of HIV.[16] On this basis, treatment policy in the UK and elsewhere changed to recommend immediate ART initiation for all people diagnosed with HIV.[588]

9.2 Thesis summary and implications of main findings

9.2.1 Chapter 2: Literature review of sexual behaviour among HIV-diagnosed men who have sex with men

Chapter 2 provided a historical context to the evolving concept of sex with 'high risk' for HIV transmission among MSM living with HIV since the introduction of ART. A summary of evidence on factors associated with different types of CLS was provided. Evidence from a number of studies did not support the hypothesis that receiving ART or having undetectable viral load (VL) leads to 'risky' sexual behaviours (in particular CLS with HIV-serodifferent partners, CLS-D).[108–111] A literature review was also conducted, focussing on studies of HIV-diagnosed MSM recruited from clinical settings in high-income countries, and examining the prevalence and correlates of various types of CLS. The review found that CLS is overall prevalent among HIV-diagnosed MSM recruited from clinical settings, with estimates for any CLS in the past three months ranging from 31% to 51%. Prevalence estimates of CLS were higher in samples recruiting men from community settings and online. The prevalence of CLS-D ranged from 15% to 27% and of CLS with perceived HIV-seroconcordant partners (CLS-C) overall from 14% to 24%.[103,113,114,131,150–152,156,157,159] While evidence from earlier UK studies of HIV-diagnosed MSM suggested an overall observed increase in the prevalence of CLS between 2000 and 2008, this may have been explained by the concurrent reduction in prevalence of CLS-D and the increase in prevalence of CLS-C during that period.[94,99,115,126,140]

Studies which examined associations of individual-level factors with prevalence of various types of CLS among HIV-diagnosed MSM were also reviewed. Certain co-factors were identified as related to higher prevalence of any CLS, including younger age and having HIV-positive partners, but results varied according to study type, recruitment location, covariates included, measurement of different types of 'risky sex', varying recall periods, adjustment for confounders, and sample sizes. There remain gaps in evidence on patterns of sexual behaviours according to: time living with diagnosed HIV, personal perceptions of virological status, measures of psychological wellbeing (symptoms of depression and anxiety, perceived social support), and type of relationship with a partner (casual or main/stable). Since 2008, there have been very few studies examining sexual behaviour of HIV-diagnosed people in the UK. As a result, evidence on the prevalence of CLS, CLS-D, CLS-C, and other sexual behaviours among HIV-diagnosed MSM in the UK has been lacking.

9.2.2 Chapter 3: Data and methodology

Chapter 3 described the methodology of the thesis. The thesis aims were addressed using data from ASTRA, an observational, cross-sectional, self-administered questionnaire study of HIV outpatients attending one of eight UK NHS clinics from February 2011 to December 2012, with an additional

longitudinal component based on routine linked clinic data. Details of recruitment and confidentiality procedures were provided, along with a description of the ASTRA questionnaire. My involvement in the study started after ASTRA was designed and data was collated; I performed extensive data cleaning, management, and derivation of variables. The rationale and derivation of all variables used in the thesis were explained in detail. A discussion of statistical methods used was also provided, with emphasis on the reasoning behind the use of modified Poisson regression over logistic regression throughout the thesis.

The strengths of the ASTRA study in addressing the aims of the thesis include the large sample size, the confidential, self-reported detailed information on recent sexual behaviour, attitudes, and potential co-factors (such as recreational drug use), and the collection of both subject-reported and clinic-recorded VL level. The overall ASTRA response rate (64% of eligible patients approached) was reasonably high and comparable to earlier UK studies of people attending for HIV care.[131,133,153,589] To assess the generalisability of the ASTRA sample in relation to the population of HIV-diagnosed men and women living in the UK as of the end of recruitment (2012), ASTRA respondents were compared to individuals included in the Survey of Prevalent HIV Infections Diagnosed (SOPHID) during the same period. A lower proportion of younger men (<25 years) and a lower proportion of women and black African individuals were represented in ASTRA, but prevalence of ART use was similar in ASTRA and SOPHID. The patients approached to participate in ASTRA (eligible) accounted for approximately 7% of the national HIV-diagnosed population; the 2248 MSM included in analyses in this thesis comprised approximately 6.5% of all MSM in SOPHID.

9.2.3 Chapter 4: Condomless sex among HIV-diagnosed MSM: prevalence and co-factors

Chapter 4 examined, among HIV-diagnosed MSM participating in ASTRA, the prevalence of and factors associated with recent CLS, including CLS overall, CLS-D, and CLS-C. The co-factors examined included socio-demographic, psychological, HIV and ART-related. The chapter also examined the association of different types of CLS with other sexual behaviours.

The majority of men reported having anal or vaginal sex in the previous three months (64%). Prevalence of any CLS in the previous three months was relatively high (38%): 29% reported CLS-C overall and 15% reported CLS-D. Among those who had CLS-D, there was some evidence of potential HIV risk reduction practices taking place, such as only being the receptive partner (40%), or only being the insertive partner without ejaculation (29%). Among MSM who reported having anal or vaginal sex, the majority of men had less than five sex partners in the past three months and over a quarter had 10 or more *new* sex partners in the past year. When classifying all MSM into mutually exclusive categories of recent sexual behaviour, over a third of men did not report any anal or vaginal sex, a quarter reported condom-protected sex only, a fifth reported 'CLS-C without CLS-D' (which could indicate HIV-serosorting), and a sixth reported CLS-D.

Prevalence of CLS was higher among younger MSM (<30 years); it was lower soon after HIV diagnosis (up to 2 years), then increased (at 2-5 years), and steadily decreased thereafter to lowest levels (at >15 years post-diagnosis), but not independently of participant's age. MSM were more likely to report CLS with an HIV-positive stable partner than with an HIV-serodifferent stable partner. In addition, prevalence of CLS was higher among MSM who were on ART with self-reported undetectable VL (compared to on ART without undetectable VL or not on ART). No association was observed of socioeconomic factors, psychological symptoms, ART adherence, or clinic-recorded VL, with reporting CLS (versus not reporting CLS, which also included those who did not have any sex or those who had condom-protected sex in the past three months).

The pattern of associations was broadly similar for CLS-D. Younger age and having an HIV-serodifferent stable partner were associated with CLS-D. There was some suggestion that prevalence of CLS-D was lower among MSM on ART (compared to those not on ART); among MSM on ART CLS-D prevalence was higher among those with self-reported undetectable VL (compared to self-reported not undetectable VL).

The four mutually exclusive categories of sexual behaviour in the past three months revealed more complex underlying patterns. Compared to the three sexually active groups (CLS-D, 'CLS-C without CLS-D', and condom-protected sex), MSM who did not have sex in the previous three months were significantly different on almost all factors. This group tended to be older, diagnosed with HIV for longer, have lower socio-economic status, low social support, and symptoms of depression and anxiety. In terms of HIV-related factors, men who did not have sex were more likely to be on ART, adherent, and virally suppressed. There were few significant differences in socio-demographic factors between the three sexually active groups, except for age; MSM who had 'CLS-C without CLS-D' were slightly younger than MSM who had CLS-D or condom-protected sex. In addition, MSM who had CLS-D were significantly more likely to report higher financial hardship after adjustment for core socio-demographic and HIV-related variables, compared to those who had 'CLS-C without CLS-D' or condom-protected sex.. Although men who had 'CLS-C without CLS-D' had the highest prevalence of detectable study log VL (27%) followed by those who had CLS-D (25%), and condom-protected sex (17%), there were no significant differences in the distribution of ART use, ART adherence, or VL non-suppression between the three sexually active groups. In fact, MSM on ART with self-reported detectable VL were *more* likely to report having condom-protected sex compared to any CLS, even after adjustment for socio-demographic and other factors. Low social support, symptoms of depression and anxiety followed a similar pattern, with prevalence being higher in the CLS-D group, followed by 'CLS-C without CLS-D', and lowest for the condom-protected group.

When examining factors associated with having 'CLS-C without CLS-D' or CLS-D relative to condom-protected sex, it was shown that MSM who had any CLS (CLS-D or 'CLS-C without CLS-D') were more likely to have symptoms of depression. Additionally, relative to those who had condom-protected sex,

MSM who knew their personal VL were *less likely* to have CLS-D (versus those who did not know their personal VL).

Among MSM who had anal or vaginal sex, those who had CLS-D tended to be more likely than those who had 'CLS-C without CLS-D' to report high partner numbers, recent STI diagnoses, group sex, and low condom self-efficacy; both groups had much higher prevalence of these factors than men reporting condom-protected sex. There was a striking association of the number of *new* sex partners in the past year and prevalence of any CLS in the past three months, particularly for CLS-D. MSM who had 'CLS-C without CLS-D' had the highest prevalence of self-reported lifetime diagnosis of hepatitis C (HCV).

Results presented in this chapter show prevalence estimates of CLS and CLS-D consistent to those shown in earlier UK clinic-based studies (2000-2010). This finding lends support to our ability to reliably and repeatedly measure such sexual behaviours and capture trends. Based on these findings, the prevalence of CLS-D among HIV-diagnosed MSM in the UK attending for care has remained fairly stable since 2008. Use of the mutually exclusive categories of sexual behaviour added specific strengths to this thesis, as it allowed for: (i) examination of the prevalence of 'CLS-C without CLS-D' (as a measure which may indicate active HIV-serosorting), (ii) separation of the condom-protected sex group from the no sex group, (iii) investigation of the differing associations of various co-factors with different types of sexual behaviours. This was particularly important in examining differing effects of psychological factors and knowledge of personal VL, which were not apparent using a binary classification for CLS or CLS-D. Future epidemiological studies examining factors associated with CLS and CLS-D could thus benefit from using such mutually exclusive categorisations of sexual behaviour. The high prevalence of CLS-C overall may suggest actual or perceived serosorting taking place. In order to capture actual serosorting, however, future studies should ascertain intentional CLS with partners of the same HIV-serostatus, as well as the motivations behind it.

9.2.4 **Chapter 5: Characterising CLS-D with higher HIV transmission risk**

For HIV-diagnosed individuals, CLS-D was the main marker of 'risky' sex for HIV transmission before studies demonstrated the profound positive impact of ART use on HIV transmission. There is no consensus yet on a definition of CLS-D with risk of HIV transmission in epidemiological research. Very few studies have examined prevalence of CLS-D with higher risk of HIV transmission among HIV-diagnosed MSM, and none have done so in the UK. This chapter presented a literature review of studies that incorporate clinic-recorded VL level into the definition of higher HIV transmission risk CLS-D, which emerged two years after ASTRA concluded recruitment (2014). These studies used various definitions for 'high HIV transmission risk' sexual behaviour, incorporating factors in addition to CLS-D, such as: VL level, seropositioning, ART status, proportion of CLS acts, and other STI co-infections. As a result, the prevalence of higher HIV risk CLS-D among HIV-diagnosed MSM ranged from 4% to 45%, reflecting differing definitions and variation in study design and methodology, timing of VL measurements, VL cut-offs, method of survey administration, recall period, and potential genuine differences across populations and demographic groups.

This chapter aimed to assess the prevalence of sex with an appreciable risk of HIV transmission among people with diagnosed HIV, by better reflecting the reduction in HIV transmission risk when the HIV-diagnosed person is on virally suppressive ART.[24,242] The main definition of CLS-D with higher HIV transmission risk required reporting CLS-D in the previous three months and not being on ART at the time of the questionnaire or having latest study log-recorded VL>50c/mL. For over 60% of MSM, the VL value was from a test done during the three month period prior to questionnaire completion, which coincided with the recall period for sexual behaviours (including CLS-D). Various supplementary definitions for CLS-D with an appreciable risk of HIV transmission were examined among all ASTRA MSM. In addition to the main definition, the following criteria (which may indicate increased risk of infectiousness even in the presence of a single suppressed VL on ART) were included: having started ART <9 months ago, reporting recent and substantial non-adherence to ART, or having a self-reported recent diagnosis of another STI. The prevalence of higher HIV risk CLS-D in the previous three months ranged from 4.2% to 7.5%, depending on criteria included. Compared to prevalence of CLS-D in the past three months, prevalence of higher HIV risk CLS-D was lower by 50-70% in relative terms. Participants reporting higher HIV risk CLS-D were similar to those reporting other CLS-D in terms of socio-demographic, psychological, lifestyle characteristics and sexual behaviours. Use of the linked routine clinical data allowed assessment of the effect on prevalence if fulfilment of the detectable VL criteria was widened to include any detectable VL within six months prior to questionnaire completion. Such definitions had a small effect on prevalence of higher HIV risk CLS-D. The main definition of higher HIV risk CLS-D developed in this chapter was subsequently used in Chapters 6 and 7.

There remain challenges in defining CLS-D with higher HIV transmission risk, both in epidemiological studies and clinical settings. In order for behavioural studies on HIV transmission to be representative of developments in HIV prevention, there is a need to move away from the concept of 'unsafe' and 'risky' sex defined as CLS-D only. Instead, there is a need to examine other measures of CLS-D which have a greater potential for HIV transmission. Accounting for VL level and ART status concurrent to CLS-D is one of the ways forward in adapting research to contemporary evidence and in standardising definitions for use in epidemiological surveillance. Additional longer-term follow-up from the PARTNER study[9] will also be crucial in providing more precise estimates of HIV transmission risk among MSM in the context of effective ART. Such information is important in refining current guidelines and in helping HIV-diagnosed individuals and their partners make informed decisions on having CLS-D safely. There is a major difference in implications relating to the prevalence of any CLS and of CLS-D with higher HIV transmission risk (38% vs 4% respectively); among HIV-diagnosed people, measures of CLS overall remain most relevant measure for transmission of other (non-HIV) STIs, but measures of CLS-D that account for VL will be the most relevant measures of HIV transmission risk sex.

In future research, the main definition of higher HIV risk CLS-D used in this thesis could also be incorporated as a fifth category into the mutually exclusive sexual behaviour classification (so that the

groupings are: higher HIV risk CLS-D, other CLS-D, 'CLS-C without CLS-D', condom-protected sex, no anal or vaginal sex). This was done in the published paper based on this Chapter (see Appendix VII), in which I separated the two categories of CLS-D and further examined differences in socio-demographic, lifestyle, HIV-related factors, and other sexual behaviours.[590]

9.2.5 Chapter 6: Recreational drug use and condomless sex

Research conducted over the past twenty years has demonstrated that a higher proportion of MSM in the UK and abroad use recreational drugs compared to age-comparable non-MSM populations,[278–282] and that drug use is more prevalent among HIV-positive compared to HIV-negative MSM.[282,287,294–299] Few studies have been conducted on drug use among large representative samples of HIV-diagnosed MSM in the UK. Since 2013, health care services and community organisations in the UK have been reporting shifting trends in popularity and use of specific drugs among MSM,[345,346] suggesting, firstly, an increase in prevalence of 'club drug' use overall, and secondly, the emergence of 'chemsex'. In this context, Chapter 6 aimed to examine the prevalence, patterns, and factors associated with recreational drug use, as well as the association of recreational drug use with CLS and other sexual behaviours among HIV-diagnosed MSM. A secondary aim was to examine the association of drug use and problematic alcohol consumption with ART outcomes (non-adherence and VL non-suppression).

The prevalence of any recreational drug use in ASTRA was high (51% in the past three months); almost 25% used at least three types of drugs during that time period (polydrug use) and 15% reported chemsex-associated drug use. Injection drug use (IDU) was reported by a minority of MSM (3%). There were extremely strong and consistent associations between increasing numbers of drugs used and increasing prevalence of all types of CLS (including CLS-C, CLS-D, and higher HIV transmission risk CLS-D), group sex, higher number of sexual partners, and low condom self-efficacy. Use of the mutually exclusive sexual behaviour categorisation demonstrated differing patterns of drug use according to type of CLS. Compared to condom-protected sex, polydrug use was prevalent both among men who had CLS-D and those who had 'CLS-C without CLS-D'. However, polydrug use and chemsex-associated drug use were most prevalent in the 'CLS-C without CLS-D' group. Use of nitrites was most prevalent among those who had CLS-D.

Higher alcohol consumption was associated with higher prevalence of CLS-D and of higher HIV risk CLS-D, independently of recreational drug use. While drug and polydrug use, higher alcohol consumption, and evidence of alcohol dependency were significantly associated with non-adherence to ART, there was no significant association with VL non-suppression. This may reflect, to some extent, the ability of current ART regimens to achieve and sustain viral suppression, despite suboptimal adherence ('forgiveness').

Ours was the first study since the 2003 'London Gyms' study[289,312] to describe the prevalence and patters of drug use among HIV-diagnosed MSM in the UK, and the first study to report on prevalence of mephedrone use in this population. At the time results from this chapter were published[591](see

Appendix VI), the phenomenon of chemsex was beginning to emerge. There are still no published quantitative studies describing the motivations, prevalence, patterns, and harms of chemsex use among MSM in the UK (regardless of HIV-serostatus). As a result, a number of important questions remain unanswered. Future studies of chemsex will benefit from explicitly defining the concept, enquiring about use of specific drugs before and during sex , further specifying whether chemsex was condomless or condom-protected, the HIV-serostatus of sexual partners. There is also need for research in the determinants as well as the psychological and physical effects of chemsex in a way that aims to minimise harm.

Since ASTRA concluded recruitment (2012), a small number of 'club drug' clinics have been established in London, bridging the gap between HIV treatment and substance misuse services.[592,593] This is a welcome advancement in provision of judgment-free harm reduction advice and support, which must nevertheless continue to expand within and outside of London. The confluence of drugs, condomless anal sex, HIV, and gay men is one that can easily be sensationalised in research and the media. This would be detrimental to efforts to reduce stigma and marginalisation of MSM living with HIV, and may also prevent individuals from seeking advice and support on safer chemsex use. All HIV-diagnosed MSM, and particularly younger men, may benefit from support and awareness of the side-effects of drug use, particularly when combined with multiple other drugs, alcohol, or with ART regimens. National STI/HIV prevention strategies, in collaboration with community organisations, will need to develop and incorporate evidence-based toolkits for the clinical management of recreational drug and chemsex users on ART.

9.2.6 **Chapter 7: Non-disclosure of HIV serostatus and condomless sex**

In the era of suppressive ART, the role of HIV-serostatus disclosure to sexual partners remains unclear. Studies of HIV-diagnosed MSM in high income countries have reported varying prevalence estimates of non-disclosure, due to the different populations sampled and diverse definitions of non-disclosure used; non-disclosure to anyone in the social circle ranged from 2% to 33%, to a stable partner from 4% to 53%, and to new/casual sex partners from 9% to 66%. Evidence on the association of non-disclosure to casual sex partners with CLS is also mixed. This chapter investigated, among HIV-diagnosed MSM from ASTRA, the prevalence of non-disclosure of HIV serostatus to the social network (friends, family, co-workers) and to a stable partner, and attitudes to non-disclosure to new sexual partners. The chapter also examined factors associated with non-disclosure to a stable partner and to new sexual partners, and the association of non-disclosure measures and sexual behaviours.

A small minority of ASTRA MSM had not disclosed their HIV-serostatus to anyone (<5%), including to a stable partner. These estimates were comparable to those observed in earlier UK studies using similar constructs of non-disclosure.[114,133,394] One of the strongest associations with non-disclosure to a stable partner was ethnicity, with non-disclosure being higher among MSM of black, Asian, mixed, or other (non-white) ethnicities, which may reflect cultural barriers. Non-disclosure was highest among MSM recently diagnosed with HIV and declined steadily with longer time since diagnosis, suggesting that

disclosure may be a gradual process. Non-disclosure to a stable partner was independently associated with the current partner's unknown HIV serostatus, consistent with earlier studies of HIV clinic attendees. No associations were observed of socio-economic factors (age, religion, education, and employment), psychological symptoms, relationship-related factors, and non-disclosure to a stable partner.

Among MSM who reported having sex in the past three months, lower sexual disclosure (lower intent to disclose to new sex partners) was prevalent (44%) and associated with markers of *higher* socio-economic status and having an HIV-serodifferent or no stable partner. MSM who were on ART with self-reported suppressed VL had lower sexual disclosure than those who were on ART without self-reported suppressed VL and those not on ART. This finding may suggest that HIV-diagnosed MSM with perceived undetectable VL were more likely to think of HIV-serostatus disclosure as not necessary due to their low HIV infectiousness. This may also provide some evidence that knowledge of personal VL status may influence sexual attitudes and behaviours; this effect may become more widespread with increasing awareness of the positive impact of ART on HIV infectiousness. Recreational drug and alcohol use were not associated with lower sexual disclosure. Lower sexual disclosure was independently associated with CLS, CLS-D, CLS-C, group sex, using the internet to have sex, and high partner numbers in the past year. Use of the mutually exclusive categories of sexual behaviour demonstrated that levels of non-disclosure were similar among MSM who had condom-protected sex and those who had CLS-D; however, sexual disclosure was higher among those who had 'CLS-C without CLS-D', compared to condom-protected sex. This finding may suggest that HIV transmission risk reduction may be in place, in the form of mutual disclosure with HIV-positive partners and HIV-serosorting. Of note, over 90% those who had CLS-D and lower sexual disclosure were on ART with undetectable VL.

HIV status disclosure has been seen as an important step towards enhancing mental health through increased social support. In this chapter there was no evidence that low functional social support, depression, or anxiety symptoms were associated with higher prevalence of non-disclosure to a stable partner. A detailed analysis based on this chapter has been published[594] (see Appendix VI), examining the effect of non-disclosure to anyone in the social circle with prevalence of low social support, psychological symptoms, non-adherence to ART, and VL non-suppression on ART.

Groups with highest non-disclosure may need a supportive context as soon as possible after HIV diagnosis; health facilities must assist individuals in building communication skills, coping strategies, and in mobilizing support for those who need it. Disclosure does not necessarily lead to 'safer' sexual behaviour but could inform choice in type of sex within and outside of a stable relationship. Couples' HIV testing and counselling can facilitate mutual serostatus disclosure and is associated with lower prevalence of condomless sex overall and with reduction in the number of concurrent casual sex partners.[427] Emphasis on HIV-serostatus disclosure to sexual partners places the majority of responsibility of reducing HIV transmission risk on HIV-diagnosed individuals, who may already

experience perceived or enacted stigma.[408] HIV-diagnosed MSM may not disclose to sex partners but still practice some form of HIV risk reduction, be it having CLS-D while being on suppressive ART, or having HIV-seroconcordant partners only. Discussion and agreement on condom use or non-use and acceptable levels of risk for both partners may be more relevant in the context of reducing HIV transmission risk.[381,414] Prevention efforts could benefit from assisting HIV-diagnosed people in effectively communicating and negotiating acceptable sexual behaviours with sex partners, and in providing a supportive context for those who choose not to disclose their HIV-serostatus.

9.2.7 Chapter 8: Hepatitis C co-infection, other sexually transmitted infections, and condomless sex

HIV and other sexually transmitted infections (STIs) have epidemiological synergy, sharing transmission routes, biological interactions, and common risk factors. HIV-diagnosed MSM in the UK remain disproportionally affected by STI co-infections, characterised by: continuing and rapid rise of diagnoses of gonorrhoea, syphilis, and genital herpes; ongoing outbreaks of sexually transmissible enteric infections; and outbreaks of sexually transmitted hepatitis C virus (HCV), not associated with injection drug use (IDU). This chapter examined, among HIV-diagnosed MSM, the prevalence and factors associated with bacterial and viral STI co-infections, the prevalence and incidence of HCV over follow-up, and factors associated with both prevalent and incident HCV.

One in 10 HIV-diagnosed MSM in ASTRA reported having any diagnosed STI (other than HIV) in the previous three months, with the majority of STIs reported being bacterial; chlamydia, gonorrhoea, and syphilis were most prevalent, in line with UK surveillance data.[471,521] Self-reported STIs were most prevalent among MSM who were younger (<30 years), not on ART, had detectable VL, and used recreational drugs (including injection and chemsex-associated drugs). These associations mirror those observed for CLS in Chapter 4. They also emphasize the importance of STI prevention strategies that particularly focus on HIV-diagnosed MSM. All types of CLS and higher partner numbers were strongly associated with reporting any diagnosed STI. Compared to MSM who had condom-protected sex, MSM who had CLS-D were significantly more likely to have an STI; this was independent of socio-demographic factors, drug use, and partner numbers.

The second part of this chapter focussed on HCV, using data from HIV-diagnosed MSM participating in ASTRA who consented to linkage of the questionnaire with routine clinical data. The cumulative prevalence of (chronic/prevalent) HCV was 13% (and 12% when excluding MSM reporting IDU). A strong association was observed between evidence of depressive symptoms and higher prevalence of chronic HCV. While temporality in this association cannot be ascertained due to the cross-sectional nature of our data, these results suggest that screening for and managing depression among HIV-diagnosed individuals may be important. In prospective analysis, the incidence of HCV over follow-up was 0.3 per 100 person years based on 6 HCV seroconversions. Despite the very small number of incident HCV cases, initial results suggested that injection and chemsex-associated drug use, CLS-D, and high partner numbers were predictive of incident HCV.

In terms of assessing and monitoring risk of transmission of STIs among HIV-diagnosed MSM, 'any CLS' is likely to be the most relevant measure in research and surveillance. STIs were assessed by self-report, which may have led to recall bias and underreporting; future studies of HIV-diagnosed MSM would benefit from STI screening at study recruitment.

Detection and control of STIs remains critical among HIV-diagnosed MSM; scaling up of routine sexual health assessment with extra-genital screening is important. Barriers to accessing STI testing (concerns about stigma and confidentiality, embarrassment, limited clinic opening hours) could be addressed with development of accurate, rapid smartphone-enabled diagnostic self-testing kits for multiple STIs, linked to online clinical management pathways.[595] While bacterial STIs are mostly curable, managing the spread of antimicrobial resistant gonorrhoea is a public health priority. With the advent of DAAs, HCV cure rates have improved dramatically.[579] It will remain key to expand access to HCV treatment. Routine HCV screening of HIV-diagnosed MSM, in particular those who report high partner numbers, chemsex use, and traumatic sex practices, will be beneficial in preventing incident HCV infections. There is emerging evidence among HIV-negative MSM enrolled in PrEP trials that on demand antibiotic post-exposure prophylaxis (PEP) for STIs reduces the incidence of bacterial STIs[596]; the long term efficacy of this strategy and its impact on antibiotic resistance remains to be assessed.

9.3 Limitations

Interpretation of findings from this thesis requires careful consideration of bias, in addition to confounding and chance, and considerations relating to causality. Bias in the estimate of the causal effect of the exposure on the dependent variable is mainly categorised into selection and measurement (information) bias.

9.3.1 Selection bias

Selection bias arises from the procedures by which study participants are selected from the source population, or self-selected by consenting to participate; it occurs when there is a difference between characteristics of people selected and those not selected for the study, arising when the sample selected is not random. In ASTRA, the recruitment strategy may have been biased and led to over-recruitment of particular social groups. For example, health-conscious patients may have been more frequent clinic attendees and therefore more likely to be invited to participate during the recruitment period. Individuals interested in sexual behaviour research may have been more likely to participate and may not necessarily be representative of the clinic population as a whole. However, an effort was made to account for this by having long recruitment periods in each participating clinic (mean of 8.2 months, see Table 3.4). This would have ensured that even infrequent attendees would be approached to participate in the study. Selection bias may also have occurred during the process of approaching and inviting patients to participate and in terms of which patients were approached by the recruiters. However, recruiters were encouraged to approach consecutive patients during the specific clinical sessions in which ASTRA recruitment was taking place.

Another component of selection bias is non-response bias. Thirty-six percent of those invited to participate in ASTRA did not complete a questionnaire. Non-responders could have differed from responders in terms of sexual behaviour, as it was clear from the information sheet that the study included questions on sex. Two possible groups of non-responders would emerge in this case: MSM who had 'higher risk' sex and are reluctant to admit it and MSM to whom this section would not be relevant (perhaps because they do not have sex). In addition, non-responders could also differ in terms of factors associated with sexual behaviours, such as age and recreational drugs use. While selection bias in this case can result in biased estimates of the prevalence of factors, it would be expected to have less of an impact on the association between factors. It was not possible to compare responders and non-responders in ASTRA, but respondents could be compared with the group who consented to participate but did not return a questionnaire with respect to selected key factors, such as CD4 count and viral load. There were no significant differences in these factors compared between the two groups. This provides some reassurance that the respondents were broadly representative of all HIV-diagnosed individuals who initially agreed to participate but did not complete the questionnaire. Among MSM, the vast majority of participants consented to data linkage and there were few significant differences between those who provided consent to linkage and those who did not.

Comparison of ASTRA MSM participants to the HIV-diagnosed MSM population receiving care in the UK (SOPHID) in 2011-2012 showed differences in the distribution of age and area of residence, but broadly similar distribution of ethnicity, ART status, and CD4 count. (section 9.2.2). As ASTRA may under-represent younger HIV-diagnosed MSM, it may be that results underestimate the prevalence of factors that are associated with younger age, such as CLS, recreational drug use, and STI co-infections. The study is limited in not recruiting participants in other areas of England (Midlands, South West) as well as other UK countries, and this has implications for the representativeness of findings.

9.3.2 **Information bias**

Information bias results from misclassification of study participants with respect to the information collected about them. Differential misclassification occurs when the probability of misclassification of the dependent (outcome) variable is reliant on exposure status. For example, MSM who were recently diagnosed with HIV in ASTRA (≤3 months prior to questionnaire completion) may have been more likely to report CLS (one of the dependent variables under study), which may have resulted in a spurious association between time since HIV diagnosis and CLS. Thus, MSM who were recently diagnosed were excluded from analyses.

Self-completed questionnaires may be subject to information bias due to missing responses or inaccurate recall or reporting. In addition, participants may provide inaccurate answers on sensitive or stigmatising behaviours (such as depression or CLS) in order to present more favourable or socially 'acceptable' attitudes and behaviours, referred to as social desirability bias. To limit social desirability bias, the questionnaire was self-administered in a private space and participants were reminded that

their answers would not be viewed by clinic staff. In addition, to minimise misclassification of exposure variables at the study design stage, pre-validated instruments and standard questionnaires were selected for inclusion in the questionnaire where possible, which have been shown to have high validity (such as the CAGE, WHO-AUDIT-C, PHQ-9, and GAD-7). At the data management stage, extensive data checks were done to ensure consistency between variables and within subsections of questions. Where applicable, for a limited number of variables, missing information on the questionnaire was completed using information from linked clinical records. While it is possible that the prevalence of sexual behaviour measures may be underestimated due to social desirability bias and missing data, there is likely to be less bias in the examination of associations between sexual behaviour and other factors.

9.3.3 Lack of qualitative data

As this thesis used data from a quantitative cross-sectional study, it lacks insight from qualitative data. Qualitative studies are valuable in exploring subjective experiences of sexual behaviour and enhancing contextual understanding of behaviours that cannot be easily accessed in quantitative studies.[597] Semi-structured and in-depth interviews are particularly suited to the study of sexual attitudes and behaviours, as well as in examining lifestyle issues (e.g. recreational drug use). For instance, a qualitative study of 30 chemsex-using MSM in South London used semi structured interviews to examine the motivations for engaging in chemsex in 2013-2014.[598] This study was the first to describe the phenomenon formally in London, and highlighted the motivations (increasing libido) and capabilities of chemsex drugs (reducing inhibitions and increasing confidence and stamina) for MSM to engage in the kind of sexual behaviour they value.[598] In 2017, a narrative review drew on worldwide literature to synthesise evidence on use and impacts of drug use among all MSM (regardless of HIV-serostatus).[599] The review highlighted that the cultural norms and social context for recreational drug and alcohol use are particularly pervasive among MSM, especially among young men; that MSM may use drugs as a coping strategy in managing "internal conflict about sexuality and its concealment, or the stigma experienced upon disclosure, [or] to avoid thoughts about personal risk for HIV acquisition". Further, qualitative research is beneficial in uncovering the positive motivations for drug (and chemsex use), which could in turn increase understanding of the social and cultural context of drug use. Such findings, combined with those from quantitative studies such as ASTRA, can allow for planning of culturally sensitive health promotion interventions that are acceptable and effective (discussed further in section 9.5.2.3).

9.4 Strengths of the ASTRA study

ASTRA was the largest and questionnaire study of HIV-diagnosed people in the UK at the time, giving enough power to detect modest differences between groups. Over 48% of new infections among MSM are diagnosed annually in London, and over 67% of MSM in ASTRA were recruited in London, representing 10% of all HIV-diagnosed MSM accessing NHS care in London during 2011-2012.[600]The overall ASTRA response rate (64% of eligible patients approached) was satisfactorily high and comparable to earlier UK studies of people attending for HIV care.[131,133,153,589] Other studies recruiting convenience samples of HIV-diagnosed individuals (using time and location sampling of gay bars, saunas,

gay Pride events etc.) are harder to compare to, as the number of participants eligible cannot be directly determined; the range of questionnaire response rates from such UK studies (as a percentage of estimated MSM attending these venues at specific times) also ranges from 50% to 70%.[97,105,142,143] ASTRA is also unique in that patients' routine clinical HIV data is linked to questionnaire data. A very high proportion (92%) of respondents agreed to linkage of clinical with questionnaire data. Although linkage was not complete for all clinics by late 2016, data provided were sufficient to conduct longitudinal analyses examining unadjusted trends.

ASTRA collected comprehensive information recreational drug use, sexual behaviours, attitudes, and sexual health, enabling detailed examination of the number of male (and female) sexual partners, including recent, new, long-term, and CLS partners, as well as recent and lifetime STIs, and other behaviours (group sex, seropositioning). Detailed HIV-related information on VL and CD4 counts was collected from multiple sources (the study log, routine clinic data, and self-report), which allowed for examination of markers of engagement in HIV care (such as level of disagreement between self-reported and clinic recorded viral load) and their relationship to sexual behaviour outcomes. Ours was the first study in the UK to date to report on prevalence of higher HIV risk CLS-D based on clinic-recorded VL.

9.5 Implications

This section summarises the main implications for HIV treatment and clinical care, HIV prevention, and future epidemiological studies of sexual behaviour of HIV-diagnosed MSM that arose from this thesis.

9.5.1 Implications for HIV treatment and clinical care

9.5.1.1 Early ART initiation

Results from Chapters 4, 5, 6, 7, and 8 show that the prevalence of condomless sex and other STIs (and especially with HIV-serodifferent partners) tended to be higher among MSM who were not on ART. This supports the strategy of early ART initiation for all individuals with diagnosed HIV, regardless of CD4 count or clinical staging for preventing HIV transmission. As of 2015, the WHO and BHIVA recommend early ART initiation not only for the net clinical benefit of the patient but also for the public health benefit of decreasing HIV transmission.[17,601]

However, the benefits of early ART cannot be realised fully without linkage to clinical HIV care. Addressing barriers to access and retention in HIV care is thus important. For MSM, these barriers can include perceived or enacted homophobia and stigma associated with attending an HIV clinic, lack of a supportive network, fears of breach in confidentiality, beliefs in alternative therapies as more effective than ART, chaotic lifestyles linked to drug use, among others. Community support (in the form of ongoing post-test counselling by community health workers) has been shown to have an overall positive impact on retention to care, ART adherence, and virological outcomes.[602] For this reason, strengthening the role of community support is a good investment in the care of HIV-diagnosed people and in subsequent prevention of HIV transmission.

9.5.1.2 Prevention and management of sexually transmitted co-infections

Results from Chapters 6 and 8 show the relatively high prevalence of condomless sex and STI co-infections, associated with high partner numbers and chemsex-associated drug use in this population of HIV-diagnosed MSM. These findings highlight the need for continued focus on STI prevention among HIV-diagnosed MSM. In the UK, HIV-diagnosed MSM are disproportionally affected by acute bacterial STIs and hepatitis C (compared to HIV-negative MSM), which suggests that STI transmission is occurring in sexual networks of HIV-positive MSM. The continuing risk of syphilis among MSM, particularly in London, is also of concern, and has been shown to be associated with condomless sex between HIV-positive partners.[603] Therefore, screening, diagnosis, treatment of STIs and contact tracing should continue to be offered routinely as part of open access comprehensive HIV prevention and care for all MSM. Promotion of condom use and of awareness of STIs should continue (where available) and expand through sexual health campaigns targeted at MSM.

9.5.1.3 Harm reduction for HIV-diagnosed MSM who use drugs

Chapters 6, 7, and 8 highlight the high prevalence of recreational drug, chemsex, and polydrug use and extremely strong associations with measures of condomless sex, non-disclosure of HIV-serostatus, STIs, and HCV co-infection among HIV-diagnosed MSM in ASTRA.

There is a need for expansion of integrated sexual health and drug services for all MSM (regardless of HIV serostatus in regions where recreational drug use is most common. MSM who inject drugs (for example as part of chemsex) should have access to sterile injecting equipment. A London sexual health clinic now provides free “slamming packs” for men engaging in chemsex, containing colour-coded syringes and needles, dosing syringes for measuring GHB safely, sterilised spoons for mixing drugs, a thermometer, and a sharps bin.[604] This clinic sets an example for health promotion and harm reduction that is grounded in innovative thinking and prompt action, which should be extended throughout areas of the UK in which chemsex occurs.

Providing achievable goals in chemsex use can help to define and structure progress. Qualitative studies show that among MSM who wish to make changes around their chemsex use, healthcare providers and peer-workers can help identify achievable goals.[605,606] While certain men may wish to abstain from chemsex entirely, others may have more short-term goals, such as reducing use, managing sexual risk-taking and boundaries more effectively during chemsex, safer drug-dosing, or abstaining for a specific period of time, among other goals. In MSM who may not wish to make changes, it is important that a risk assessment is made, both to the health and wellbeing of the chemsex user and of their sexual partners.

Psychosocial support should also be available to MSM who experience mental health issues as a result of their chemsex use. This can include psychological and physical dependence on chemsex drugs, withdrawal symptoms, depression, anxiety, and paranoia, as well as post-traumatic stress disorder induced by non-consensual sex or sexual assault occurring during chemsex-induced “black outs”.

The possibility of recreational drug and ART interactions should also be stressed, particularly given that over half of HIV-diagnosed MSM on ART in ASTRA had used recreational drugs in the past three months. The potential for drug-drug interactions (DDIs) is highest between ritonavir-boosted PI regimens and EDDs, benzodiazepines, ketamine, and chemsex drugs.[320] Hence, clinicians need to not only expand their knowledge and understanding of DDIs, but also need to be aware of all recreational and prescribed substances their HIV-diagnosed patients are using. National HIV treatment guidelines could benefit from inclusion of potential DDIs with specific recreational drugs and guidance on choice of regimen, dosage adjustment, monitoring, and provision of information to patients.

9.5.1.4 Mental health and wellbeing

In Chapter 4 it was shown that the prevalence of symptoms of depression and anxiety was significantly higher among HIV-diagnosed MSM who did not have sex and was also high among MSM who had CLS-D. In Chapter 8 symptoms of depression were also prospectively associated with incident hepatitis C among HIV-diagnosed MSM, although findings were based on a very small number of HCV seroconversions. Nevertheless, provision of routine screening and management of depression in HIV-diagnosed MSM remains an important part of integrated routine HIV care.

9.5.2 Implications for HIV prevention

To respond effectively to HIV among MSM, a comprehensive package of interventions is needed to assist with programming for HIV prevention.

9.5.2.1 Reducing the prevalence of undiagnosed HIV infection

As discussed in section 1.3, the majority of HIV transmissions in the UK are estimated to derive from HIV-undiagnosed MSM. Hence, a reduction in the prevalence of undiagnosed HIV in this population (currently estimated to be 12%), will be key in decreasing the number of new HIV diagnoses. This can be achieved by increasing HIV testing availability and uptake (including self-sampling and self-testing options). Voluntary HIV testing and counselling should be routinely offered to all MSM in community and clinical settings, and by a variety of providers, including community outreach workers and general practitioner surgeries. In community-based testing, it is important that linkages are in place, to care and treatment services for those who test positive as well as to prevention services for those who test negative. In addition to testing, pre- and post-test counselling provides a unique opportunity for health promotion and behavioural interventions. Pre-test counselling should provide accurate information about the test and the implications of each respective result; post-test counselling should provide a supportive discussion of personal choices on disclosure of HIV-serostatus, risk reduction for HIV and other STI transmission, and personalised treatment choices.

9.5.2.2 Strategies for reducing HIV transmission

9.5.2.2.1 Condom use

A quarter of HIV-diagnosed MSM in ASTRA reported always using condoms during anal sex in the past three months. This sizeable proportion shows that the correct and consistent use of condoms remains

an important message in preventing sexual transmission of HIV and of other STIs. Increasing the availability, affordability, and accessibility of condoms and condom-compatible lubricants not only in sexual health clinics but also through targeted distribution programmes (e.g. in sex-on premises venues, chemsex parties, nightclubs) remains an essential component of the HIV response. Promotional campaigns can not only increase awareness but also promote the acceptability of using condoms, as a way to overcome personal and social barriers to their use. As shown in Chapter 4, 7% of ASTRA HIV-diagnosed MSM reported low condom self-efficacy and almost 16% reported difficulty negotiating condom use, which may contribute to the high prevalence of condomless sex overall in this population. Hence, along with promotion and supply of condoms, health providers and community groups should develop programmes offering skills-building in negotiating condom use in those who need it.

9.5.2.2.2 Pre-Exposure Prophylaxis (PrEP)

In the last five years, the field of primary HIV prevention research has made dramatic achievements, particularly with the use of antiretroviral medications by HIV-uninfected individuals to prevent HIV acquisition (PrEP). As discussed in section 1.3.5.2, a number of large, well-conducted randomised trials have demonstrated the substantial protective effect conferred by oral PrEP in reducing the risk of HIV acquisition across genders, types of sexual exposure, regimens, and dosing schemes.[607] There is, so far, no evidence of increased adverse safety events with PrEP use.[607] The risk of PrEP drug resistance is also low, and must be weighed against the overall benefits. However, the effect of large-scale PrEP implementation on resistance levels overall, remains unknown. A meta-analysis of 18 studies found no evidence that PrEP led to behavioural risk compensation, meaning a reduction in condom use or increases in numbers of sexual partners. However, recent results from real-world PrEP implementation in the USA show a relatively high incidence of other STIs along with a 41% decrease in reported condom use among a subset of PrEP users.[608]

Therefore, oral PrEP should be an additional prevention choice for MSM at higher risk of HIV infection, as part of combination HIV prevention. A number of PrEP modelling and implementation studies in high-income countries have evaluated the impact of PrEP on HIV diagnoses among MSM since 2010 (with time horizons from 10 to 40 years). A review of six of these studies showed that PrEP alone will not be able to reduce HIV diagnoses to zero, regardless of the time horizon.[609] The UNAIDS goal of eliminating HIV by 2030 can be achieved with a combination of PrEP uptake and regular HIV testing in HIV-negative individuals, early ART initiation in HIV-diagnosed individuals, and promotion of condom use.[609] This message is now promoted in the local authority-supported 'Do It London' sexual health initiative (http://doitlondon.org/), which aims to increase HIV testing and to promote more prevention choices to people in London. Expansion of such campaigns outside London would be beneficial.

The overall observed decreases in the number of potentially infectious HIV-positive MSM seen in the UK, coupled with increased use of PrEP among HIV-negative MSM, may translate to potential population increases in condomless sex. This is a concern for the detrimental spread and impact of antimicrobial resistant gonorrhoea, which is no longer susceptible to most available therapies.[432] MSM who report

condomless sex, chemsex, high partner turnover (regardless of HIV-serostatus) should have prioritised access to prevention measures such as PrEP and regular STI screening (or re-testing in cases of a prior STI diagnosis).[610,611]

9.5.2.3 The role of qualitative studies

Findings from qualitative studies are able to bring forth the challenges and opportunities of developing strategies for reducing HIV transmission. Evidence from focus groups of HIV-diagnosed MSM attending for HIV care in the UK and the USA shows that sexual risk reduction interventions are more appealing when they address the broader life context of living with HIV, including psychosocial stressors, stigma, and disclosure, as well as community beliefs regarding HIV treatment and normalisation.[597,612] Qualitative work is especially useful in informing the formulation of hypotheses and data collection procedures for the development of sexual risk assessment tools (such as the indicator of higher HIV risk CLS-D developed in Chapter 5) to be used in sexual health care settings.[605] A pertinent example is that of the Fenway Study group (USA), which used semi-structured interviews among HIV-negative men who use chemsex drugs; this study identified acceptable strategies for use of PrEP while 'high' on drugs, detailing men's dosing and regimen preferences according to level of drug use.[606]

In addition, qualitative studies have highlighted inequalities in HIV literacy, which could be barriers to effective use of ART as prevention.[613,614] For instance, a recent qualitative study (interview and focus groups) of HIV-diagnosed MSM receiving care in the USA found that only a small minority of men perceived that ART reduced infectivity; this study showed that interventions need to be specifically tailored to populations' needs.[615] Among HIV-negative men, a Scottish focus group and in-depth interview study explored men's understandings of PrEP effectiveness, finding that concerns about maintaining PrEP adherence and low perception of HIV risk were barriers to potential PrEP uptake.[616] Findings from this study draw attention to how PrEP rollout must include diverse communication methods given differences in HIV literacy.

Mixed methods exploratory approaches from the UK also underscore the acceptability of and barriers to implementation of prevention approaches among MSM and healthcare providers.[617,618] For example, combination of focus group thematic analysis and cross-sectional questionnaires among MSM in Scotland showed that self-testing awareness was prevalent, but associated with specific socio-demographic factors, and that willingness to self-test was high and associated with finding sex online.[619] Lastly, evidence-based health promotion benefits greatly from the contributions of qualitative methods in assessing delivery of interventions. As an instance, the SELPHI RCT examines whether free HIV self-testing leads to increased rates of HIV diagnosis in England and Wales (2017-2020); the trial embedded a qualitative feasibility study and process evaluation, which captured the perspectives of MSM in relation to HIV self-testing, and specifically how the trial components impacted on acceptability to self-test for HIV.[617]

9.5.3 Implications for future epidemiological studies

The thesis results have implications for definitions of variables in research studies that aim to capture risk behaviour in relation to HIV and STI transmission.

9.5.3.1 Mutual classification of sexual behaviour

Firstly, findings from Chapters 4, 6, and 7 show that adoption of the mutually exclusive classification of sexual behaviours is beneficial as it captures different types of condomless sex, CLS, (with HIV-serodifferent or other HIV-positive partners only) and allows for separate analysis of condom-protected sex versus no sex. This classification brings insights into serosorting and associated factors, and leads to better evaluation of complex associations between socio-demographic, health, and lifestyle factors with different types of sexual behaviour.

9.5.3.2 Higher HIV risk CLS-D indicator

Secondly, epidemiological studies of sexual behaviour among HIV-diagnosed MSM would benefit from further refining the concept of CLS-D with a higher risk of HIV transmission, incorporating VL level. Results from Chapter 5 were the first to formally examine higher HIV risk CLS-D in the UK, at a time when HIV transmissions were high and ongoing among MSM, and 'any CLS' was used in research as a marker of HIV transmission risk. While the concept of 'any CLS' remains the most appropriate indicator for measuring risk of transmission of other (non-HIV) STIs, it is no longer the most useful measure of HIV transmission risk sex. The landscape of HIV has changed substantially during the course of this study, which has implications for the use of the 'higher HIV risk CLS-D' indicator in studies and surveillance of sexual behaviours. For the first time ever, the UK saw an 18% decline in newly-diagnosed HIV between 2015 and 2016, particularly among MSM in London.[620] PrEP use has expanded among HIV-negative men since 2012 (when ASTRA completed recruitment), and treatment guidelines changed in 2015 to recommend initiation of ART at HIV diagnosis. As a result, the proportion of HIV-diagnosed MSM likely to contribute to HIV transmission in the current era of the epidemic is likely to be small, and to continue declining as more men achieve virological suppression on ART. As PrEP use further expands, studies and surveillance systems will need to address ways to incorporate preventative measures taken by HIV-negative partners, too. For example, while 4.5% of ASTRA MSM had higher HIV risk CLS-D, the proportion of HIV-negative partners on PrEP is unknown. The proportion of men who had higher HIV risk CLS-D accounting for PrEP may thus be much lower, and will continue to decline. In the context of new HIV prevention methods, a broader range of sexual risk indicators is needed. Future studies of HIV-diagnosed men will still benefit from using the indicator proposed in this thesis, but they could also enquire about HIV-negative partners' use of PrEP; a new indicator could thus measure CLS-D with detectable viral load and no reported PrEP use.

9.5.3.3 Self-perceived viral load

In Chapters 4 and 7 there was some evidence that men who were on ART with self-reported undetectable VL (versus without self-reported undetectable VL) tended to report more CLS-D and were less likely to disclose their HIV serostatus to new sex partners. This may be due to increased awareness of the extremely low risk of HIV transmission when the HIV-diagnosed partner is on effective ART, and

thus overall lower condom use. Although the results presented are reassuring in showing that any effect of perceived undetectable viral load on sexual behaviour of HIV-diagnosed MSM would not impact adversely on HIV or STI transmission risk, it will be important to continue monitoring these associations as ART use expands.

9.6 Concluding remarks

The '90-90-90' targets set by UNAIDS reflect key points in the continuum of HIV care, with respect to HIV testing, treatment, and viral load suppression.[621] The UK has made significant progress towards these goals, having already reached the second and third '90' targets among MSM, with 94% of HIV-diagnosed MSM being on ART, and 96% of those having suppressed viral load. For the first time ever in 2016, there was an observed decline in new HIV diagnoses in the UK. This exciting development must be met with consolidated combination prevention, consisting of innovations in scaling up of HIV testing and access to early ART across the UK for all individuals at highest risk of HIV.[85] As ART use expands among the HIV-diagnosed population, it will be crucial to continue promoting sustained high ART adherence, regular VL monitoring, and ongoing awareness of personal VL level among people with diagnosed HIV.[182] Reaching all three '90' targets in the UK would undoubtedly deliver immense benefits to people living with HIV; it is also important in increasing population-level HIV VL suppression and thus reducing onward transmission of HIV. However, the '90-90-90' strategy does not provide a target for ensuring good health-related quality of life among HIV-diagnosed MSM, both in terms of co-morbidities and of self-perceived quality of life, including sexual wellbeing. Hence, apart from reducing HIV transmission and related morbidity, treatment, policy, and research will need to address a comprehensive set of issues in virally suppressed MSM living with HIV including: psychological and sexual well-being, harm reduction in recreational drug use, and comprehensive management of co-morbidities and STI co-infections.

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Appendix I. ASTRA study documents

ASTRA INFORMATION SHEET
Version 2.0 07/01/2011

This information sheet and the other study documents are also available in French. Just ask the clinic nurse if you would prefer a French copy.

ASTRA Questionnaire Study

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, looking at how HIV and HIV treatment (antiretroviral treatment) affects people's lives, including their health, quality of life, and lifestyle. In particular, the study will investigate the link between HIV treatment and sexual lifestyles. The results will be used to help decide what the effects would be of offering immediate treatment to all people in the UK who are diagnosed with HIV.

Who is taking part?

This study is being conducted at five HIV clinics in the UK. Everyone coming to each of these clinics is eligible to take part. This includes people who are not taking HIV treatment as well as those who are on treatment. We would like as many people as possible to participate, and so your contribution is important.

What will I have to do?

If you agree to take part, you will be asked to complete a questionnaire about your health and well-being, your lifestyle, your experience of having HIV, and your views on HIV treatment. The questionnaire includes some personal questions about your sex life. You can complete the questionnaire on your own. It should take 15 to 30 minutes to complete.

When will I complete the questionnaire?

We would like you to complete the questionnaire today, while you are here in the clinic, either before or after seeing the doctor. 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 with the doctor.

Will my questionnaire responses be confidential?

Yes, completely. Your name or clinic number will NOT be written on the questionnaire. Your answers will NOT be seen by the doctors and nurses in the clinic, and your answers will NEVER be recorded in your clinic notes. Your completed questionnaire can be placed in a sealed envelope which will not be opened by the clinic staff.

What clinical information will be recorded?

If you agree to take part in the study, we will record your latest viral load and CD4 count as part of the study data.

Will any other information about me be gathered?

You will be asked if you agree to us adding your routine HIV clinical information (from this clinic only) to the questionnaire information. This is so we can see how peoples' questionnaire responses relate to their current and future situation. The HIV clinical information would be:

- Your laboratory test results (e.g. viral load and CD4 count)
- Your HIV treatment details
- Other routine information on your HIV care (e.g. any illnesses or hospital admissions)

This is a standard procedure for research studies. The clinical information is added in such a way that your questionnaire responses remain completely confidential, and are NEVER put together with your name or clinic number. You do not have to agree to this, and you can still participate in the study if you do not agree. If you do agree, the clinical information will be collected once when everyone has completed the questionnaire, and on several more occasions over the next few years.

What will happen to the information?

Your anonymised responses will be added to everyone else's responses, 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 ASTRA study website (www.astra-study.org).

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 may keep this information sheet and you will be asked to sign the consent form. If you agree to take part you can still change your mind and decide not to complete and submit the questionnaire. If you choose not to take part in the study, this will not affect the standard of care you receive.

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 nurse to arrange for you to speak to *[insert appropriate clinic/local health professional……..]*

Who is leading this research?

A team of HIV specialists and researchers from the UK is leading this study. The study is being coordinated by the Research Department of Infection and Population Health, University College London, and is funded by the National Institute for Health Research (NIHR). This study has been reviewed and approved by a research ethics committee.

Site lead ……..
Site……

Dr Fiona Lampe
Research Department of Infection and Population Health, University College London.
http://www.ucl.ac.uk/iph/ **f.lampe@ucl.ac.uk**

CONSENT FORM for ASTRA Questionnaire Study
Version 2.1 21/01/2011

Clinical centre: ……..
ASTRA Study ID: _____
Clinic Number: _____

1. I confirm that I have read and understand the information sheet (version 2.0, dated 07/01/2011) for this study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily.	☐ **Please initial**
2. I agree to take part in this study.	☐ **Please initial**
3. 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**
4. I agree / do not agree that information from this clinic on my laboratory test results, HIV treatment and clinical care can be added to my questionnaire responses.	**Please initial one box only** ☐ **YES, I agree** ☐ **NO, I do not**

_____ __ __ /__ __ / __ __ __ __
_____
Name of patient Date Signature

_____ __ __ /__ __ / __ __ __ __
_____

Name of person taking consent Date Signature

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes

Astra

MEN'S QUESTIONNAIRE

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 or clinic number on this questionnaire. Your answers will NOT be seen by the doctors and nurses in the clinic, and your answers will NEVER be recorded in your clinic notes.

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!

SECTION A: GENERAL INFORMATION

A1. What is your date of birth? Month: __ __ __ Year: __ __ __ __

A2. 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

A3. Were you born in the UK?

- ☐ **Yes → PLEASE GO TO QUESTION A4**
- ☐ **No**

If NO, which country were you born in?.....

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

A4. 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).....

A5. 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).....

A6. 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

A7. At what level did you COMPLETE your 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).....

A8. Do you regard yourself as belonging to any particular religion?

- ☐ No religion
- ☐ Islam / Muslim
- ☐ Christianity
- ☐ Judaism
- ☐ Hinduism
- ☐ Buddhism
- ☐ Sikhism
- ☐ Other (please specify).....

If YES, do you regularly (at least once a month) **attend religious meetings?**
(not including weddings and funerals)

☐ Yes ☐ No

A9. How would you describe your sexuality?

- ☐ Gay / homosexual
- ☐ Straight / heterosexual
- ☐ Bisexual
- ☐ Other (please specify).....

A10. Are you currently in an ongoing relationship with a partner (wife / husband 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?

__ __ months __ __ years

Does your partner have HIV? ☐ Yes ☐ No ☐ Don't know

A11. Do you have any children?

- ☐ Yes
- ☐ No

A12. What is your immigration status in the UK? This information is completely confidential and WILL NOT be released to any other organisation. (Please tick one only)

- ☐ I am a British citizen
- ☐ I am a citizen of another EU (European Union) country
- ☐ I have a right to stay for an indefinite amount of time (Indefinite Leave to Remain – ILR)
- ☐ I have a right to stay for a fixed amount of time (Exceptional Leave to Remain – ELR)
- ☐ I am a refugee seeking asylum
- ☐ I have a student visa
- ☐ I have a work permit
- ☐ I have no papers to be in the UK
- ☐ Other (please specify).....

SECTION B: YOU AND HIV

B1. When did you first find out you were HIV positive?
If you are unsure of the month, please give the year only

Month: __ __ __ Year: __ __ __ __

B2. How long have you been attending this HIV clinic?

☐ Less than 1 year ☐ 1 to 3 years ☐ 3 years or longer

B3. 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
- ☐ Unknown
- ☐ Other (please specify).....

B4. At your last test what was your CD4 count?

- ☐ Less than 200
- ☐ 200-350
- ☐ 351-500
- ☐ More than 500
- ☐ Don't know / can't remember

B5. Apart from health care staff, have you told anyone that you have HIV?

- ☐ Yes
- ☐ No → **PLEASE GO TO QUESTION C1**

If YES, who have you told?

I have told a 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
			☐ Not applicable

SECTION C: YOUR HEALTH AND WELLBEING

In this part of the questionnaire, we are using some standard sets of questions to ask you about your health. We apologise if some of the questions seem repetitive, but please take the time to answer each section, as each one is important. Thank you for your help!

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.

C1. 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. Difficulty concentrating	☐	☐	☐	☐	☐
2. Difficulty sleeping	☐	☐	☐	☐	☐
3. Lack of energy	☐	☐	☐	☐	☐
4. Feeling drowsy / tired	☐	☐	☐	☐	☐
5. Trouble remembering things	☐	☐	☐	☐	☐
6. Pain	☐	☐	☐	☐	☐
7. Headache	☐	☐	☐	☐	☐
8. Numbness, tingling or pain in hands or feet	☐	☐	☐	☐	☐
9. Muscle aches or joint pains	☐	☐	☐	☐	☐
10. Nausea	☐	☐	☐	☐	☐
11. Vomiting	☐	☐	☐	☐	☐
12. Diarrhoea	☐	☐	☐	☐	☐
13. Constipation	☐	☐	☐	☐	☐
14. Feeling bloated	☐	☐	☐	☐	☐
15. Dizziness	☐	☐	☐	☐	☐
16. Sweats / fever	☐	☐	☐	☐	☐
17. Cough	☐	☐	☐	☐	☐
18. Shortness of breath	☐	☐	☐	☐	☐
19. Problems with sexual interest / activity	☐	☐	☐	☐	☐

C1. Continued

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 symptoms and was bothered / distressed QUITE A BIT	Yes, had symptoms and was bothered / distressed VERY MUCH
20. Skin problems (e.g. rash, itching, dryness)	☐	☐	☐	☐	☐
21. Dry mouth	☐	☐	☐	☐	☐
22. Mouth sores	☐	☐	☐	☐	☐
23. Lack of appetite	☐	☐	☐	☐	☐
24. Changes in way food tastes	☐	☐	☐	☐	☐
25. Weight loss	☐	☐	☐	☐	☐
26. Changes in fat in face or body	☐	☐	☐	☐	☐

C2. 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			

C3. Please indicate which statements best describe your own state of health TODAY. Please tick one box in each section

a) Mobility

- ☐ I have no problems in walking about
- ☐ I have some problems in walking about
- ☐ I am confined to bed

b) 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

c) 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

d) Pain / discomfort

- ☐ I have no pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have extreme pain or discomfort

e) Anxiety / depression

- ☐ I am not anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am extremely anxious or depressed

C4. 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	☐	☐	☐	☐	☐

C5. In the PAST 3 MONTHS, have you been diagnosed with a sexually transmitted infection (not including HIV)?

☐ Yes ☐ No → **PLEASE GO TO QUESTION C6**

If YES, have you had any of the following in the PAST 3 MONTHS?
Please tick MORE THAN ONE box, if applicable

☐ Syphilis
☐ Gonorrhoea
☐ Chlamydia
☐ LGV
☐ New Hepatitis B
☐ New Hepatitis C
☐ Genital herpes (new or recurrent)
☐ Genital warts (new or recurrent)
☐ Trichomonas
☐ NSU (Non Specific Urethritis), NGU (Non Gonococcal Urethritis)
☐ Other (please specify) .....

C6. Do you currently have any of the following symptoms?
For each symptom, please tick Yes or No

a) Abnormal discharge from penis ☐ Yes ☐ No
b) Anal discharge ☐ Yes ☐ No
c) Pain on passing urine ☐ Yes ☐ No
d) Pain in the genital area or anus ☐ Yes ☐ No
e) Red sores or rash on the genital area or anus ☐ Yes ☐ No

C7. In the PAST 2 YEARS, have you had a sexual health screen (tests for sexually transmitted infections, not including HIV)**?**

☐ Yes ☐ No ☐ Don't know

C8. Have you ever been told by a doctor that you have Hepatitis C?

☐ Yes ☐ No

C9. Are you currently receiving treatment (medicine or other therapy) **for depression?**

☐ Yes ☐ No

C10. Are you currently receiving treatment (medicine or other therapy) **for any other mental health problem?**

☐ Yes (please specify condition).....

☐ No

SECTION D:
YOUR VIEWS ON HIV TRANSMISSION RISK

D1. During the PAST 6 MONTHS, did any of the HIV clinic staff discuss with you condom use and safe sex?
Please tick MORE THAN ONE box, if applicable

- ☐ Yes, discussed with HIV doctor
- ☐ Yes, discussed with HIV nurse
- ☐ Yes, discussed with other clinic staff (e.g. HIV health advisor, HIV counsellor)
- ☐ No, did not discuss with any of the HIV clinic staff
- ☐ Don't remember

D2. 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 or no opinion	Tend to disagree	Strongly disagree
a) Better HIV treatment means that people are less worried about catching HIV	☐	☐	☐	☐	☐
b) Better HIV treatment means that people with HIV are less worried about infecting others	☐	☐	☐	☐	☐
c) An undetectable HIV viral load makes someone less infectious to a sexual partner than if they had a high viral load	☐	☐	☐	☐	☐
d) When viral load is undetectable, a condom is not needed to prevent HIV transmission	☐	☐	☐	☐	☐

SECTION E: HIV TREATMENT

E1. Have you ever taken HIV treatment (antiretroviral treatment / HAART)**?**

☐ Yes ☐ No → **PLEASE GO TO QUESTION E12**

Questions E2 to E11 are for all patients who are taking or have ever taken HIV treatment

E2. When did you start taking HIV treatment?
If you are unsure of the month, please give the year only

Month: __ __ __ Year: __ __ __ __

E3. Did you start antiretroviral treatment because HIV was making you ill?

☐ Yes ☐ No

E4. 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

E5. When did you get your last viral load test results?

- ☐ Today
- ☐ Less than 3 months ago
- ☐ 3 to 6 months ago
- ☐ Over 6 months ago
- ☐ Don't know

E6. What was your viral load the last time you got your test results?

- ☐ 50 copies/mL or less ('undetectable' or 'suppressed')
- ☐ More than 50 copies/mL ('detectable' or 'raised')
- ☐ Don't know

E7. Have you ever changed your HIV treatment because it was not keeping your viral load down?

- ☐ Yes
- ☐ No
- ☐ Don't know

E8. Are you currently taking HIV treatment?

- ☐ Yes → **PLEASE GO TO QUESTION E9**
- ☐ 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 as part of a clinical trial
- ☐ My HIV doctor advised me to stop taking treatment
- ☐ I stopped because of treatment side effects
- ☐ I stopped because 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 F1

E9. How often do you need to take your HIV treatment?

- ☐ Once a day
- ☐ Twice a day
- ☐ Other (please specify).....

E10. In the LAST 2 WEEKS, how many doses of HIV treatment have you missed?
Once a day treatment = 14 doses in 2 weeks
Twice a day treatment = 28 doses in 2 weeks

- ☐ Missed no doses in last 2 weeks (took all 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? For each reason please tick Yes or No

a) Treatment was making me feel ill	☐ Yes	☐ No
b) I forgot to take pills	☐ Yes	☐ No
c) I was away from home and forgot to bring my pills	☐ Yes	☐ No
d) I ran out of pills	☐ Yes	☐ No
e) I was in a public place	☐ Yes	☐ No
f) I was with people who did not know I had HIV	☐ Yes	☐ No
g) I was fed up with taking pills	☐ Yes	☐ No
h) I was feeling depressed / low	☐ Yes	☐ No
i) Other (please specify).....	☐ Yes	☐ No

E11. In the PAST 3 MONTHS, have you ever missed your HIV treatment for two or more days at a time?

☐ Yes ☐ No ☐ Don't know / can't remember

If YES, on how many occasions in the past 3 months has this happened?

☐ Once ☐ 2 or 3 times ☐ More than 3 times

PLEASE GO TO QUESTION F1

Questions E12 and E13 are only for patients who have never taken HIV treatment

E12. 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.

	Strongly agree	Tend to agree	Undecided or no opinion	Tend to disagree	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.	☐	☐	☐	☐	☐
b) I would want to start HIV treatment now, if this would slightly reduce my risk of getting a serious illness.	☐	☐	☐	☐	☐
c) I would want to start HIV treatment now, if this would make me less infectious to a sexual partner (even if there was no benefit to my own health).	☐	☐	☐	☐	☐

E13. Has your HIV doctor ever advised you to start HIV treatment?

☐ Yes ☐ No

If YES, please indicate the main reasons for not starting treatment:
For each reason please tick Yes or No

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)..... ☐ Yes ☐ No

SECTION F: LIFESTYLE

F1. Do you smoke cigarettes regularly (at least 1 per day)**?**

☐ Yes → (please give approximate number smoked per day .....)
☐ No – I am an ex-smoker (given up smoking)
☐ No – I have never smoked

F2. How often do you have a drink that contains alcohol?

☐ Never → **PLEASE GO TO QUESTION F8**
☐ Monthly or less
☐ 2 to 4 times a month
☐ 2 to 3 times a week
☐ 4 or more times a week

F3. 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

F4. Have you ever felt you should cut down on your drinking?

☐ Yes ☐ No

F5. Have people annoyed you by criticising your drinking?

☐ Yes ☐ No

F6. Have you ever felt bad or guilty about your drinking?

☐ Yes ☐ No

F7. Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?

☐ Yes ☐ No

F8. In the PAST 3 MONTHS, have you used recreational drugs?
(e.g. poppers, cannabis, cocaine)

☐ Yes ☐ No

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)
.....

F9. In the past 3 months, have you injected recreational drugs
(e.g. heroin, crystal meth)**?**

☐ Yes ☐ No

If YES, after you injected yourself, did you share needles, syringes or 'works' with anyone who did not have HIV or whose HIV-status you didn't know?

☐ Yes ☐ No

SECTION G: SEXUAL LIFESTYLE (MEN)

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 NEVER be seen by the clinic staff.

SEX WITH WOMEN

The questions ask about **vaginal sex** and **anal sex.** 'Vaginal sex' means a man's penis 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.

G1. In the past 3 months, have you had sex (vaginal or anal sex) **with a woman?**

☐ Yes ☐ No → **PLEASE GO TO QUESTION G6**

If YES, how many women have you had sex with in the past 3 months?
☐ 1 woman - my long-term partner
☐ 1 woman - NOT long-term partner
☐ More than 1 woman (please give approximate number _____)
→ **Was one of these women your long-term partner?**
☐ Yes ☐ No ☐ I don't have a long-term partner

G2. In the past 3 months, have you ever used a condom when you had sex (vaginal or anal sex) **with a woman?**

☐ Yes ☐ No

G3. In the past 3 months, have you had sex (vaginal or anal sex) **with a woman without a condom?**

☐ Yes ☐ No → **PLEASE GO TO QUESTION G6**

G4. In the past 3 months, have you had sex (vaginal or anal sex) **without a condom, with a woman who you knew also had HIV?**

☐ Yes ☐ No → **PLEASE GO TO QUESTION G5**

IF YES: How many HIV-positive women have you had sex with, without a condom in the past 3 months?
☐ 1 woman - my long-term partner
☐ 1 woman - NOT long-term partner
☐ More than 1 woman (please give approximate number _____)
→ **Was one of these women your long-term partner?**
☐ Yes ☐ No ☐ I don't have a long-term partner

G5. In the past 3 months, have you had sex (vaginal or anal sex) **without a condom with a woman who did not have HIV or whose HIV-status you didn't know**

☐ Yes ☐ No → **PLEASE GO TO QUESTION G6**

IF YES:
(i) In the past 3 months, how many women did you have sex (vaginal or anal sex) **with, without a condom? Count only women who did not have HIV, or whose HIV-status you didn't know.**

☐ 1 woman - my long-term partner
☐ 1 woman - NOT long-term partner
☐ More than 1 woman (please give approximate number _____)
→ **Was one of these women your long-term partner?**
☐ Yes ☐ No ☐ I don't have a long-term partner

(ii) In the past 3 months, overall, how many times did you have sex (vaginal or anal sex) **without a 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) In the past 3 months, did you have anal sex without a condom? Count only anal sex with women who did not have HIV, or whose HIV-status you didn't know.

☐ Yes, at least once ☐ No, never

(iv) In the past 3 months, when you had sex (vaginal or anal sex) **without a condom, 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) **without a 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.**

For each reason please tick Yes or No

a) Trying for pregnancy	☐ Yes	☐ No
b) I believe the risk of HIV transmission is very low	☐ Yes	☐ No
c) Didn't think about using a condom	☐ Yes	☐ No
d) Don't like using condoms	☐ Yes	☐ No
e) My partner didn't want to use a condom	☐ Yes	☐ No
f) Felt unable to discuss condom use	☐ Yes	☐ No
g) Did not have a condom	☐ Yes	☐ No
h) It's more enjoyable / close without a condom	☐ Yes	☐ No
i) Got carried away	☐ Yes	☐ No
j) Under the influence of alcohol or drugs	☐ Yes	☐ No
k) Difficult to keep erection or ejaculate using a condom	☐ Yes	☐ No
l) Feel relaxed about having unprotected sex	☐ Yes	☐ No
m) Other, please specify	☐ Yes	☐ No

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

G6. In the past 3 months, have you had anal sex with a man?

☐ Yes ☐ No → **PLEASE GO TO QUESTION J1**

If YES, how many men have you had anal sex with in the past 3 months?

☐ 1 man - my long-term partner
☐ 1 man - NOT long-term partner
☐ More than 1 man (please give approximate number _____)

→ **Was one of these men your long-term partner?**

☐ Yes ☐ No ☐ I don't have a long-term partner

G7. In the past 3 months, have you ever used a condom when you had anal sex with a man?

☐ Yes ☐ No

G8. In the past 3 months, have you had anal sex with a man, without a condom?

☐ Yes ☐ No → **PLEASE GO TO QUESTION J1**

G9. In the past 3 months, have you had anal sex without a condom, with a man you knew also had HIV?

☐ Yes ☐ No → **PLEASE GO TO QUESTION G10**

If YES, how many HIV-positive men have you had sex with, without a condom in the past 3 months?

☐ 1 man - my long-term partner
☐ 1 man - NOT long-term partner
☐ More than 1 man (please give approximate number _____)

→ **Was one of these men your long-term partner?**

☐ Yes ☐ No ☐ I don't have a long-term partner

G10. 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 → **PLEASE GO TO QUESTION J1**

If YES:

(i) In the past 3 months, how many men did you have anal sex with, without a condom? Count only men who did not have HIV, or whose HIV-status you didn't know.

☐ 1 man - my long-term partner
☐ 1 man - NOT long-term partner
☐ More than 1 man (please give approximate number _____)

→ **Was one of these men your long-term partner?**

☐ Yes ☐ No ☐ I don't have a long-term partner

(ii) In the past 3 months, overall, how many times did you have 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.

☐ Once
☐ 2 to 10 times
☐ 11 to 30 times
☐ More than 30 times (please give approximate number _____)

(iii) In the past 3 months, when you had anal sex without a 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) In the past 3 months, when you had anal sex without a 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.

☐ Yes – some or all of the times
☐ No – none of the times

(v) The last time you had anal sex 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.

For each reason please tick Yes or No

a) I believe the risk of HIV transmission is very low	☐ Yes	☐ No
b) Didn't think about using a condom	☐ Yes	☐ No
c) Don't like using condoms	☐ Yes	☐ No
d) My partner didn't want to use a condom	☐ Yes	☐ No
e) Felt unable to discuss condom use	☐ Yes	☐ No
f) Did not have a condom	☐ Yes	☐ No
g) It's more enjoyable / close without a condom	☐ Yes	☐ No
h) Got carried away	☐ Yes	☐ No
i) Under the influence of alcohol or drugs	☐ Yes	☐ No
j) Difficult for me / partner to keep erection or ejaculate when using a condom	☐ Yes	☐ No
k) Feel relaxed about having unprotected sex	☐ Yes	☐ No
l) Other, please specify	☐ Yes	☐ No

SECTION J: SEXUAL LIFESTYLE (GENERAL)

J1. 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 disagree	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	☐	☐	☐	☐	☐
b) I'd expect to ask a new partner their HIV status before we have sex	☐	☐	☐	☐	☐
c) I'd expect to tell a new partner that I'm HIV-positive before we have sex	☐	☐	☐	☐	☐
d) I find it difficult to discuss condom use with a new sexual partner	☐	☐	☐	☐	☐
e) I am less likely to use a condom with a casual partner	☐	☐	☐	☐	☐
f) I am worried that I could have infected someone else with HIV in the past few months	☐	☐	☐	☐	☐

J2. In the past 3 months, have you used the internet to find a sexual partner?

☐ Yes ☐ No

J3. In the past 3 months, have you participated in group sex? (sex with more than one other person on the same occasion)

☐ Yes ☐ No

J4. In the past 3 months, have you received money for having sex?

☐ Yes ☐ No

J5. In the past 3 months, have you received drugs for having sex?

☐ Yes ☐ No

J6. In the past 3 months, if you have had any HIV-negative sexual partners, have any of them taken HIV drugs to reduce the risk of getting HIV?

- ☐ Yes, a partner has taken PrEP (antiretroviral drugs taken before sex)
- ☐ Yes, a partner has taken PEPSE (antiretroviral drugs taken after sex)
- ☐ No or don't know
- ☐ Have not had sex with an HIV-negative partner in past three months

If YES, did you give your antiretroviral drugs to this partner?

☐ Yes ☐ No

J7. Finally we would like to ask about the past 12 MONTHS. In the past 12 months, how many NEW sexual partners have you had?
(this means people you have not had sex with before)

- ☐ No new sexual partners in past 12 months
- ☐ One or more new sexual partners in past 12 months → (please give approximate number .....)

Please use this space to raise any issues you want to

27

Thank you very much for completing this questionnaire.

Please seal the questionnaire in the envelope provided and put it 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.

Further information about HIV and AIDS is available from:

THT DIRECT HELPLINE: **0845 122 1200**
From 10am to 10pm Monday to Friday & 12pm to 6pm Saturday & Sunday.
Telephone advice, information and support service about HIV and AIDS information can also be found on the Terence Higgins Trust website at:
http://***www.tht.org.uk***

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Astra

Appendix II. Search strategy used in MEDLINE and EMBASE for systematic literature review of condomless sex among HIV-diagnosed MSM in high-income countries (1995-2016)

#	Search terms	**Number retrieved**
1	HIV/ or HIV infections/ or HIV seropositivity/ or HIV-positive/ or "HIV positive"/ or HIV-infected/ or "HIV infected"/ [Title/Abstract]	189884
2	Sexual Behaviour.mp. or exp Sexual Behavior/ or Unprotected/ or Risk/ or Unsafe Sex/ or "unprotected anal intercourse".mp.	199676
3	risk reduction behavior/ or HIV serosorting/ or safe sex/ or condomless sex/ [Title/Abstract]	12115
4	Homosexuality, Male/ or Homosexuality/ or gay/ or MSM/ or "men who have sex with men".mp.	26475
5	2 or 3	208319
6	1 and 5	24211
7	6 and 4	9253
8	Great Britain/ or UK or Scotland.mp. or United States/ or America/ or Canada/ or Western europe.mp. or Europe/ or Australia/	1349429
9	7 and 8	1989
10	Limit 9 to English language and publication range 1996-2016	1664
11	Limit 10 to journal articles only (excludes newspaper articles, editorials)	1426
12	Limit 11 to exclude literature reviews or opinion papers	449

Appendix III. Results of literature search on EMBASE and MEDLINE

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
Aghaizu A	Ovid MEDLINE(R)	UK	Sexual behaviours, HIV testing, and the proportion of men at risk of transmitting and acquiring HIV in London, UK, 2000-13: a serial cross-sectional study.	The Lancet. HIV. 3(9):e431-40, 2016 Sep.	Yes
Beer L	Ovid MEDLINE(R)	USA	Disparities in HIV transmission risk among HIV-infected black and white men who have sex with men, United States, 2009.	AIDS. 28(1):105-14, 2014 Jan 2.	Yes
Bolding G	Ovid MEDLINE(R)	UK	Gay men who look for sex on the Internet: is there more HIV/STI risk with online partners?.	AIDS. 19(9):961-8, 2005 Jun 10.	Yes
Bouhnik A-D	Ovid MEDLINE(R)	FR	Unprotected sex in regular partnerships among homosexual men living with HIV: a comparison between sero-nonconcordant and seroconcordant couples (ANRS-EN12-VESPA Study).	*AIDS* 2007; **21 Suppl 1**: S43–8.	Yes
Bourne A	SigmaResearch website	UK	Relative safety II: risk and unprotected anal intercourse among gay men with diagnosed HIV.	London, UK; 2009.	
Bruce D	Ovid MEDLINE(R)	USA	Sexual risk behavior and risk reduction beliefs among HIV-positive young men who have sex with men.	AIDS & Behavior. 17(4):1515-23, 2013 May.	Yes
Colfax GN	Ovid MEDLINE(R)	USA	Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion.	*AIDS* 2002; **16**: 1529–35.	Yes
Dodds JP	Embase	UK	Increasing risk behaviour and high levels of undiagnosed HIV infection in a community sample of homosexual men.	*Sex Transm Infect* 2004; **80**: 236–40.	Yes
Dodds JP	Embase	UK	A tale of three cities: persisting high HIV prevalence, risk behaviour and undiagnosed infection in community samples of men who have sex with men.	*Sex Transm Infect* 2007; **83**: 392–6.	Yes
Durham MD	Ovid MEDLINE(R)	USA	Sexual risk behavior and viremia among men who have sex with men in the HIV Outpatient Study, United States, 2007-2010.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 63(3):372-8, 2013 Jul 1.	Yes
Elford J	Embase	UK	Peer led HIV prevention among homosexual men in Britain.	*Sex Transm Infect* 2002; **78**: 158–9.	Yes
Elford J	Embase	UK	High-risk sexual behaviour increases among London gay men between 1998 and 2001: what is the role of HIV optimism?	*AIDS* 2002; **16**: 1537–44.	Yes
Elford J	Embase	UK	HIV treatment optimism and high-risk sexual behaviour among gay men: the attributable population risk	*AIDS* 2004; **18**: 2216–7.	Yes
Elford J	Embase	UK	Sexual behaviour of people living with HIV in London: implications for HIV transmission.	*AIDS* 2007; **21 Suppl 1**: S63–70.	Yes
Elford J	Embase	UK	High-risk sexual behaviour among London gay men: no longer increasing.	*AIDS* 2005; **19**: 2171–4.	Yes
Elford J	Embase	UK	HAART, viral load and sexual risk behaviour.	*AIDS* 2005; **19**: 205–7.	Yes
Elford J	Ovid	UK	HIV in East London: ethnicity, gender and risk. Design and methods.	BMC Public Health. 6:150, 2006.	

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
	MEDLINE(R)				
Elford J	Ovid MEDLINE(R)	UK	Barebacking among HIV-positive gay men in London.	*Sex Transm Dis* 2007; **34**: 93–8.	Yes
Elford J	Ovid MEDLINE(R)	UK	The Internet and HIV study: design and methods.	BMC Public Health. 4:39, 2004 Sep 1.	No: protocol paper
Elford J	Ovid MEDLINE(R)	UK	Sexual health of ethnic minority MSM in Britain (MESH project): design and methods.	BMC Public Health. 10:419, 2010.	No: protocol paper
Diamond C	Ovid MEDLINE(R)	USA	Use of and adherence to antiretroviral therapy is associated with decreased sexual risk behavior in HIV clinic patients.	J Acquir Immune Defic Syndr. 2005 Jun 1;39(2):211–8.	Yes: in factors section
Glass TR	Embase	SW	Is unsafe sexual behaviour increasing among HIV-infected individuals?	*AIDS* 2004; **18**: 1707–14.	Yes
Golin C	Ovid MEDLINE(R)	USA	Psychosocial characteristics and sexual behaviors of people in care for HIV infection: an examination of men who have sex with men, heterosexual men and women.	AIDS & Behavior. 13(6):1129-42, 2009 Dec.	Yes
Gorbach P.M.	Ovid MEDLINE(R)	USA	Behaviors of recently HIV-infected men who have sex with men in the year postdiagnosis: Effects of drug use and partner types.	Journal of Acquired Immune Deficiency Syndromes. 56 (2) (pp 176-182), 2011. Date of Publication: 01 Feb 2011.	Yes
Halkitis PN	Ovid MEDLINE(R)	USA	Seroconcordant sexual partnerings of HIV-seropositive men who have sex with men.	AIDS. 2005 Apr;19 Suppl 1:S77-86.	
Halkitis PN	Ovid MEDLINE(R)	USA	Barebacking identity among HIV-positive gay and bisexual men: demographic, psychological, and behavioral correlates.	AIDS. 2005 Apr;19 Suppl 1:S27-35.	
Hart GJ	Ovid MEDLINE(R)	UK	Sexual risk behaviour of men who have sex with men: emerging patterns and new challenges.	*Curr Opin Infect Dis* 2010; **23**: 39–44.	Yes
Hickson F	SigmaResearch website	UK	HIV testing and HIV serostatus-specific sexual risk behaviour among men who have sex with men living in England and recruited through the internet in 2001 and 2008.	*Sex Res Soc Policy* 2013; **10**: 15–23.	Yes
Hickson F	SigmaResearch website	UK	State of Play: findings from the England Gay Men's Sex Survey 2014.	Sigma Research London, 2016.	Yes
Hickson F	SigmaResearch website	UK	Tactical dangers: findings from the United Kingdom Gay Men's Sex survey 2008.	London, UK; 2010.	
Hickson F	SigmaResearch website	UK	HIV, sexual risk, and ethnicity among men in England who have sex with men.	Sex Transm Infect. 2004 Dec;80(6):443–50.	
Hirshfield S	Ovid MEDLINE(R)	USA	Social media use and HIV transmission risk behavior among ethnically diverse HIV-positive gay men: results of an online study in three U.S. states.	Archives of Sexual Behavior. 44(7):1969-78, 2015 Oct.	Yes: in factors section
Holt M	Ovid MEDLINE(R)	AUS	Brief Report: HIV Prevention by AUSn Gay and Bisexual Men With Casual Partners: The Emergence of Undetectable Viral Load as One of a Range of Risk Reduction Strategies.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 70(5):545-8, 2015 Dec 15.	Yes
Khosropo	Embase	USA	Trends in serosorting and the association with HIV/STI risk over time among men who have sex	Journal of Acquired Immune	Yes

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
ur C.M.			with men.	Deficiency Syndromes. 72 (2) (pp 189-197), 2016. Date of Publication: 01 Jun 2016.	
Kozal MJ	Ovid MEDLINE(R)	USA	Antiretroviral resistance and high-risk transmission behavior among HIV-positive patients in clinical care.	*AIDS* 2004; **18**: 2185–9.	Yes
Kramer SC	Embase	EU	Factors associated with unprotected anal sex with multiple non-steady partners in the past 12 months: results from the European Men-Who-Have-Sex-With-Men Internet Survey (EMIS 2010).	BMC Public Health. 16:47, 2016.	No - no info on HIV+ UK MSM
Kouyos RD	Ovid MEDLINE(R)	SW	Increases in Condomless Sex in the Swiss HIV Cohort Study.	Open forum Infect Dis. 2015 Apr;2(2):ofv077.	Yes
Kravcik S	Ovid MEDLINE(R)	CA	Effect of antiretroviral therapy and viral load on the perceived risk of HIV transmission and the need for safer sexual practices.	*J Acquir Immune Defic Syndr Hum Retrovirol* 1998; **19**: 124–9.	Yes
Lattimore S	Ovid MEDLINE(R)	UK	Changing patterns of sexual risk behavior among London gay men: 1998-2008.	*Sex Transm Dis* 2011; **38**: 221–9.	Yes
Magidson JF	Ovid MEDLINE(R)	INTL	Engagement in HIV care and sexual transmission risk behavior among men who have sex with men using online social/sexual networking in Latin America.	*AIDS Care* 2015; **27**: 1055–62.	Yes
Magidson JF	Embase	INTL	Antiretroviral Medication Adherence and Amplified HIV Transmission Risk Among Sexually Active HIV-Infected Individuals in Three Diverse International Settings.	*AIDS Behav* 2016; **20**: 699–709.	Yes
Margolis AD	Ovid MEDLINE(R)	USA	Anal intercourse without condoms among HIV-positive men who have sex with men recruited from a sexual networking web site, United States.	Sexually Transmitted Diseases. 41(12):749-55, 2014 Dec.	Yes
Mattson CL	Embase	USA	Sexual risk behaviour and viral suppression among HIV-infected adults receiving medical care in the United States.	*AIDS* 2014; **28**: 1203–11	Yes
Mayer KH	Embase	USA	Ongoing sexually transmitted disease acquisition and risk-taking behavior among US HIV-infected patients in primary care: implications for prevention interventions.	Sexually Transmitted Diseases. 39(1):1-7, 2012 Jan.	Yes
Mayer KH	Ovid MEDLINE(R)	USA	Factors associated with amplified HIV transmission behavior among American men who have sex with men engaged in care: implications for clinical providers.	*Ann Behav Med* 2014; **47**: 165–71.	Yes
Mitchell KR	Ovid MEDLINE(R)	UK	Sexual function in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3).	*Lancet* 2013; **382**: 1817–29.	Yes
Nardone A	Ovid MEDLINE(R)	UK	A comparison of high-risk sexual behaviour and HIV testing amongst a bar-going sample of homosexual men in London and Edinburgh.	European Journal of Public Health. 11(2):185-9, 2001 Jun.	Yes
Nardone A	Ovid MEDLINE(R)	UK	Active surveillance of sexual behaviour among homosexual men in London.	*Commun Dis Public Health* 1998; **1**: 197–201.	Yes
Ostrow DE	Ovid MEDLINE(R)	USA	Attitudes towards highly active antiretroviral therapy are associated with sexual risk taking among HIV-infected and uninfected homosexual men.	AIDS. 2002;16(5):775-780.	Yes
Parsons JT	Embase	USA	Correlates of sexual risk behaviors among HIV-positive men who have sex with men.	*AIDS Educ Prev* 2003; **15**: 383–400.	Yes

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
Parsons JT	Ovid MEDLINE(R)	USA	Sexual harm reduction practices of HIV-seropositive gay and bisexual men: serosorting, strategic positioning, and withdrawal before ejaculation.	*AIDS* 2005; **19 Suppl 1**: S13–25.	Yes
Paz-Bailey G.	Ovid MEDLINE(R)	USA	Trends in condom use among MSM in the United States: The role of antiretroviral therapy and seroadaptive strategies.	AIDS. 30 (12) (pp 1985-1990), 2016. Date of Publication: 31 Jul 2016.	Yes
Prestage G	Ovid MEDLINE(R)	AUS	Use of viral load to negotiate condom use among gay men in Sydney, AUS.	AIDS & Behavior. 13(4):645-51, 2009 Aug.	Yes
Prestage G	Ovid MEDLINE(R)	AUS	How has the sexual behaviour of gay men changed since the onset of AIDS: 1986-2003.	*Aust N Z J Public Health* 2005; **29**: 530–5.	Yes
Remien RH	Ovid MEDLINE(R)	USA	Risk Perception and sexual risk behaviors among HIV-positive men on antiretroviral therapy.	*AIDS Behav* 2005; **9**: 167–76.	Yes
Remien RH	Ovid MEDLINE(R)	USA	The association between poor antiretroviral adherence and unsafe sex: differences by gender and sexual orientation and implications for scale-up of treatment as prevention.	AIDS & Behavior. 18(8):1541-7, 2014 Aug.	Yes: in factors section
Rodger AJ	Ovid MEDLINE(R)	EU	Transmission risk behaviour at enrolment in participants in the INSIGHT Strategic Timing of AntiRetroviral Treatment (START) trial.	HIV Medicine. 16 Suppl 1:64-76, 2015 Apr.	Yes
Semple S.J.	Ovid MEDLINE(R)	USA	Factors associated with sex in the context of methamphetamine use in different sexual venues among HIV-positive men who have sex with men.	BMC public health. 10 (pp 178), 2010. Date of Publication: 2010.	
Sherr L	Ovid MEDLINE(R)	UK	Successive switching of antiretroviral therapy is associated with high psychological and physical burden.	*Int J STD AIDS* 2007; **18**: 700–4.	Yes
Sherr L	Ovid MEDLINE(R)	UK	Adherence to antiretroviral treatment in patients with HIV in the UK: a study of complexity.	*AIDS Care. 2008 Apr;20(4):442–8.*	Yes
Siegler A.J.	Embase	USA	The role of intent in serosorting behaviors among men Who have sex with men sexual partnerships.	Journal of Acquired Immune Deficiency Syndromes. 64 (3) (pp 307-314), 2013. Date of Publication: 01 Nov 2013.	Yes
Stephenson JM	Ovid MEDLINE(R)	UK	Is use of antiretroviral therapy among homosexual men associated with increased risk of transmission of HIV infection?	*Sex Transm Infect* 2003; **79**: 7–10.	Yes
Suzan-Monti M	Ovid MEDLINE(R)	FR	The burden of HIV experience and care among MSM having an HIV-positive seroconcordant steady partner: a possible research hypothesis. Results from the French VESPA ANRS EN-12 study.	*Sex Transm Infect. 2011 Aug;87(5):396–8.*	Yes
Suzan-Monti M	Embase	FR	Sexual risk behaviour among people living with HIV according to the biomedical risk of transmission: results from the ANRS-VESPA2 survey.	*J Int AIDS Soc* 2016; **19**: 20095.	Yes
Suzan-Monti M	Embase	FR	Sexual Behavior with Serodiscordant Partners Among HIV-Positive Men Who Have Sex with Men Followed Up in Hospitals Between 2003 and 2011 in France: Results from a Repeated National Representative Survey (ANRS VESPA and VESPA2).	*AIDS Patient Care STDS. 2016 May;30(5):193–6.*	Yes
The EMIS Network	SigmaResearch website	EU	EMIS 2010: The European Men-Who-Have-Sex-With-Men Internet Survey. Findings from 38 Countries.	Stockholm:The European Centre for Disease Prevention and Control.	No: UK data not presented by HIV-

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
				Stockholm; 2013.	serostatus, all MSM aggregated
Van de Ven P	Ovid MEDLINE(R)	AUS	Sexual practices in a broad cross-sectional sample of Sydney gay men.	AUSn & New Zealand Journal of Public Health. 21(7):762-6, 1997 Dec.	Yes
Van de Ven P	Ovid MEDLINE(R)	AUS	Sexual risk behaviour increases and is associted with HIV optimism among HIV-negative and HIV-positive gay men in Sydney over the 4 year period to February 2000.	AIDS. 14(18):2951-3, 2000 Dec 22.	Yes
Van de Ven P	Ovid MEDLINE(R)	AUS	In a minority of gay men, sexual risk practice indicates strategic positioning for perceived risk reduction rather than unbridled sex.	*AIDS Care* 2002; **14**: 471–80.	Yes
Vanable PA	Embase	USA	Impact of combination therapies on HIV risk perceptions and sexual risk among HIV-positive and HIV-negative gay and bisexual men.	*Health Psychol* 2000; **19**: 134–45.	Yes
Velter A	Embase	FR	Sexual and prevention practices in men who have sex with men in the era of combination HIV prevention: results from the Presse Gays et Lesbiennes survey, France, 2011.	*Euro Surveill. 2015 Jan;20(14).*	
Wallace LA	Embase	UK	HIV prevalence and undiagnosed infection among a community sample of gay and bisexual men in Scotland, 2005-2011: implications for HIV testing policy and prevention.	*PLoS One* 2014; **9**: e90805.	Yes
Weatherburn	SigmaResearch website	UK	"What Do You Need?": Findings from a national survey of people with diagnosed HIV.	London, UK; 2009.	Yes
Weatherburn	SigmaResearch website	EU	The European Men-Who-Have-Sex-With-Men Internet Survey (EMIS): Design and Methods.	Sex Res Soc Policy. Springer US; 2013 Dec 7;10(4):243–57.	
Williamson LM	Ovid MEDLINE(R)	UK	Sexual risk behaviour and knowledge of HIV status among community samples of gay men in the UK.	AIDS. 22(9):1063-70, 2008 May 31.	Yes
Wilson P.A.	Ovid MEDLINE(R)	USA	Fluctuations in depression and well-being are associated with sexual risk episodes among HIV-positive men.	Health Psychology. 33 (7) (pp 681-685), 2014. Date of Publication: July 2014.	Yes: in factors section
Wilson PA	Embase	USA	Sexual Risk Behavior Among Virologically Detectable Human Immunodeficiency Virus-Infected Young Men Who Have Sex With Men.	JAMA Pediatrics. 170(2):125-31, 2016 Feb.	Yes
Wolitski RJ	Embase	USA	The Emergence of Barebacking Among Gay and Bisexual Men in the United States: A Public Health Perspective	*J Gay Lesbian Psychother* 2005; **9**: 9–34.	Yes
Wolitski RJ	Embase	USA	Prevention with gay and bisexual men living with HIV: rationale and methods of the Seropositive Urban Men's Intervention Trial (SUMIT).	AIDS. 2005 Apr;19 Suppl 1:S1-11.	Yes
Xia Q	Embase	USA	Knowledge of sexual partner's HIV serostatus and serosorting practices in a California population-based sample of men who have sex with men.	AIDS. 2006 Oct 24;20(16):2081–9.	Yes
Zablotska IB	Ovid MEDLINE(R)	AUS	Behavioural surveillance among gay men in AUS: methods, findings and policy implications for the prevention of HIV and other sexually transmissible infections.	Sexual Health. 8(3):272-9, 2011 Sep.	Yes
Allen VC Jr	Ovid MEDLINE(R)		The Association Between Alcohol Consumption and Condom Use: Considering Correlates of HIV Risk Among Black Men Who Have Sex with Men. [Review]	AIDS & Behavior. 19(9):1689-700, 2015 Sep.	No: review
Bachman	Ovid		Impact of a computer-assisted, provider-delivered intervention on sexual risk behaviors in HIV-	AIDS Education & Prevention.	No: not relevant

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
n LH	MEDLINE(R)		positive men who have sex with men (MSM) in a primary care setting.	25(2):87-101, 2013 Apr.	
Bancroft J	Ovid MEDLINE(R)		Unprotected anal intercourse in HIV-positive and HIV-negative gay men: the relevance of sexual arousability, mood, sensation seeking, and erectile problems.[Erratum appears in Arch Sex Behav. 2005 Aug;34(4):479-80]	Archives of Sexual Behavior. 34(3):299-305, 2005 Jun.	No: sample size <90
Bavinton BR	Ovid MEDLINE(R)		Willingness to Act upon Beliefs about 'Treatment as Prevention' among AUSn Gay and Bisexual Men.	PLoS ONE [Electronic Resource]. 11(1):e0145847, 2016.	No: qualitative
Bavinton BR	Ovid MEDLINE(R)		The Opposites Attract Study of viral load, HIV treatment and HIV transmission in serodiscordant homosexual male couples: design and methods.	BMC Public Health. 14:917, 2014.	No: protocol paper
Bavinton BR	Embase		Homosexual men in HIV serodiscordant relationships: implications for HIV treatment as prevention research.	J Int AIDS Soc. 2015 Jan;18:19884.	No: HIV-negative only
Begley K	Ovid MEDLINE(R)		Correlates of unprotected anal intercourse in HIV positive men attending an HIV/AIDS clinic in Sydney.	Current HIV Research. 6(6):579-84, 2008 Nov.	No: small sample size (<40)
Begley K	Ovid MEDLINE(R)		Factors associated with unprotected anal intercourse between HIV-positive men and regular male partners in a Sydney cohort.	International Journal of STD & AIDS. 20(10):704-7, 2009 Oct.	No: small sample size (<40)
Bocour A.	Embase		Differences in risk behaviors and partnership patterns between younger and older men who have sex with men in New York City.	Journal of Acquired Immune Deficiency Syndromes. 58 (4) (pp 417-423), 2011. Date of Publication: 01 Dec 2011.	No: no CLS estimates
Bogowicz P	Ovid MEDLINE(R)		HIV testing behaviour and use of risk reduction strategies by HIV risk category among MSM in Vancouver.	International Journal of STD & AIDS. 27(4):281-7, 2016 Mar.	No: HIV-undiagnosed only
Bonell CP	Ovid MEDLINE(R)		Methamphetamine use among gay men across the UK.	International Journal of Drug Policy. 21(3):244-6, 2010 May.	No: results not by HIV-serostatus (lumps all + and -)
Bourne A	Ovid MEDLINE(R)		Problems with sex among gay and bisexual men with diagnosed HIV in the United Kingdom.	BMC Public Health. 12:916, 2012.	No: no CLS estimates
Brennan DJ	Ovid MEDLINE(R)		HIV treatment optimism and unsafe anal intercourse among HIV-positive men who have sex with men: findings from the positive connections study.	AIDS Education & Prevention. 22(2):126-37, 2010 Apr.	No: no CLS estimates
Breskin A	Ovid MEDLINE(R)		Factors Associated With Hepatitis C Infection Among HIV-Infected Men Who Have Sex With Men With No Reported Injection Drug Use in New York City, 2000-2010.	Sexually Transmitted Diseases. 42(7):382-6, 2015 Jul.	No: no CLS estimates
Burnham KE	Ovid MEDLINE(R)		Trauma symptoms, internalized stigma, social support, and sexual risk behavior among HIV-positive gay and bisexual MSM who have sought sex partners online.	AIDS Care. 28(3):347-53, 2016.	No: no CLS estimates
Carballo-Dieguez A	Ovid MEDLINE(R)		Sexual negotiation, HIV-status disclosure, and sexual risk behavior among Latino men who use the internet to seek sex with other men.	Archives of Sexual Behavior. 35(4):473-81, 2006 Aug.	No: <50 HIV+
Carvalho C.	Embase		HIV testing among Portuguese men who have sex with men - results from the European MSM Internet Survey (EMIS).	HIV Medicine. 14 (SUPPL.3) (pp 15-18), 2013. Date of Publication: 2013.	No: results not by HIV-serostatus (lumps all + and -)

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
CDC	Ovid MEDLINE(R)		High-risk sexual behavior by HIV-positive men who have sex with men--16 sites, United States, 2000-2002.	MMWR - Morbidity & Mortality Weekly Report. 53(38):891-4, 2004 Oct 1.	No
CDC	Ovid MEDLINE(R)		HIV testing and risk behaviors among gay, bisexual, and other men who have sex with men - United States.	MMWR - Morbidity & Mortality Weekly Report. 62(47):958-62, 2013 Nov 29.	No: HIV-negative only
Chen S.Y.	Embase		Unprotected anal intercourse between potentially HIV-serodiscordant men who have sex with men, San Francisco.	Journal of Acquired Immune Deficiency Syndromes. 33 (2) (pp 166-170), 2003. Date of Publication: 01 Jun 2003.	No: CLS only no other estimates
Chew K.W.	Embase		Low prevalence of hepatitis C co-infection in recently HIV-infected minority men who have sex with men in Los Angeles: A cross-sectional study.	BMC Infectious Diseases. 15 (1) (no pagination), 2015. Article Number: 538. Date of Publication: November 20, 2015.	No: phylogenetic study
Cox J	Embase		HIV status of sexual partners is more important than antiretroviral treatment related perceptions for risk taking by HIV positive MSM in Montreal, CA.	*Sex Transm Infect* 2004; **80**: 518–23.	No: only attitudes to CLS, no CLS estimates
Crawford JM	Ovid MEDLINE(R)		Negotiated safety and other agreements between men in relationships: risk practice redefined.	International Journal of STD & AIDS. 12(3):164-70, 2001 Mar.	No: data not by HIV serostatus
Crepaz N	Embase		Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review.	*JAMA* 2004; **292**: 224–36.	No: lit review & meta-analysis
Crepaz N	Embase		Prevalence of unprotected anal intercourse among HIV-diagnosed MSM in the United States: a meta-analysis.	*AIDS* 2009; **23**: 1617–29.	No: lit review & meta-analysis
Crosby R	Ovid MEDLINE(R)		Correlates of recent unprotected anal sex among men having sex with men attending a large sex resort in the South.	Sexually Transmitted Diseases. 30(12):909-13, 2003 Dec.	No: biased sample
Crosby R	Ovid MEDLINE(R)		Condom Use Errors and Problems: A Comparative Study of HIV-Positive Versus HIV-Negative Young Black Men Who Have Sex With Men.	Sexually Transmitted Diseases. 42(11):634-6, 2015 Nov.	No: not relevant
Danta M	Ovid MEDLINE(R)		Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours.	AIDS. 21(8):983-91, 2007 May 11.	No: phylogenetic case control study
Denning PH	Ovid MEDLINE(R)		Unprotected anal intercourse among HIV-positive men who have a steady male sex partner with negative or unknown HIV serostatus.	American Journal of Public Health. 95(1):152-8, 2005 Jan.	No: stable partner data only
Doerner R	Ovid MEDLINE(R)		Circumcision and HIV infection among men who have sex with men in Britain: the insertive sexual role.	Archives of Sexual Behavior. 42(7):1319-26, 2013 Oct.	No: focus is circumcision
Dukers NH	Embase		Sexual risk behaviour relates to the virological and immunological improvements during highly active antiretroviral therapy in HIV-1 infection.	*AIDS* 2001; **15**: 369–78.	No: no CLS estimates
Evans AR	Ovid		Central and east European migrant men who have sex with men: an exploration of sexual risk	Sexually Transmitted Infections.	No: data not by HIV

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
	MEDLINE(R)		in the U.K.	87(4):325-30, 2011 Jun.	serostatus
Ferrer L	Embase		Undiagnosed HIV infection in a population of MSM from six European cities: results from the Sialon project.	European Journal of Public Health. 25(3):494-500, 2015 Jun.	No: HIV-undiagnosed only
Fields E.L.	Ovid MEDLINE(R)		Association of discrimination-related trauma with sexual risk among HIV-positive African American men who have sex with men.	American journal of public health. 103 (5) (pp 875-880), 2013. Date of Publication: May 2013.	No: not relevant
Flagg E.W.	Embase		Bacterial sexually transmitted infections among HIV-infected patients in the United States: Estimates from the Medical Monitoring Project.	Sexually Transmitted Diseases. 42 (4) (pp 171-179), 2015. Date of Publication: 30 Apr 2015.	No: not relevant
Forney JC	Embase		Risk and protective factors related to HIV-risk behavior: a comparison between HIV-positive and HIV-negative young men who have sex with men.	AIDS Care. 24(5):544-52, 2012.	No: Young MSM (15yrs)
Grov C	Embase		HIV risk and substance use in men who have sex with men surveyed in bathhouses, bars/clubs, and on Craigslist.org: venue of recruitment matters.	AIDS & Behavior. 16(4):807-17, 2012 May.	No: no CLS estimates, results not by HIV serostatus
Grov C	Ovid MEDLINE(R)		Characteristics of men who have sex with men (MSM) who attend sex parties: results from a national online sample in the USA.	Sexually Transmitted Infections. 90(1):26-32, 2014 Feb.	No: no CLS estimates, results not by HIV serostatus
Grov C	Ovid MEDLINE(R)		HIV Serosorting, Status Disclosure, and Strategic Positioning Among Highly Sexually Active Gay and Bisexual Men.	AIDS Patient Care STDS. 2015 Oct;29(10):559–68.	
Grulich AE	Ovid MEDLINE(R)		HIV serostatus of sexual partners of HIV-positive and HIV-negative homosexual men in Sydney.	AIDS. 12(18):2508, 1998 Dec 24.	
Grulich AE	Ovid MEDLINE(R)		HIV Transmission in Male Serodiscordant Couples in AUS, Thailand and Brazil.	Conference on Retroviruses and Opportunistic Infections. Seattle, WA, 2015: Abstract number: 1019LB.	No: interim results from HIV-serodifferent couples cohort (but discussed throughout thesis)
Gullette DL	Ovid MEDLINE(R)		Stages of change and condom use among an Internet sample of gay and bisexual men.	Journal of the Association of Nurses in AIDS Care. 15(2):27-37, 2004 Mar-Apr.	No: not relevant
Hall HI	Ovid MEDLINE(R)		HIV transmission in the United States: considerations of viral load, risk behavior, and health disparities.	AIDS & Behavior. 17(5):1632-6, 2013 Jun.	no: modelling study
Harawa NT	Ovid MEDLINE(R)		Associations of race/ethnicity with HIV prevalence and HIV-related behaviors among young men who have sex with men in 7 urban centers in the United States.	Journal of Acquired Immune Deficiency Syndromes: JAIDS.	No: HIV-negative only

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
				35(5):526-36, 2004 Apr 15.	
Hart GJ	Ovid MEDLINE(R)		Homosexual men's HIV related sexual risk behaviour in Scotland.	Sexually Transmitted Infections. 75(4):242-6, 1999 Aug.	No: data before 1996, not by HIV serostatus
Hasse B	Ovid MEDLINE(R)		Frequency and determinants of unprotected sex among HIV-infected persons: the Swiss HIV cohort study.	*Clin Infect Dis* 2010; **51**: 1314–22.	No: CLS as % of clinic visits
Hatfield LA	Ovid MEDLINE(R)		Comparison of substance use and risky sexual behavior among a diverse sample of urban, HIV-positive men who have sex with men.	Journal of Addictive Diseases. 28(3):208-18, 2009 Jul.	No: not specifically about CLS, reviewed in drugs chapter
Hays RB	Ovid MEDLINE(R)		Actual versus perceived HIV status, sexual behaviors and predictors of unprotected sex among young gay and bisexual men who identify as HIV-negative, HIV-positive and untested.	AIDS. 11(12):1495-502, 1997 Oct.	No: data prior to 1992
Heijman T	Ovid MEDLINE(R)		Less decrease in risk behaviour from pre-HIV to post-HIV seroconversion among MSM in the combination antiretroviral therapy era compared with the pre-combination antiretroviral therapy era.	AIDS. 2012 Feb 20;26(4):489–95.	No: no CLS estimates
Hirshfield S	Ovid MEDLINE(R)		Crystal methamphetamine use predicts incident STD infection among men who have sex with men recruited online: a nested case-control study.	Journal of Medical Internet Research. 6(4):e41, 2004 Nov 29.	No: in drugs chapter
Holt M	Ovid MEDLINE(R)		The prevalence and correlates of undiagnosed HIV among AUSn gay and bisexual men: results of a national, community-based, bio-behavioural survey.[Erratum appears in J Int AIDS Soc. 2016;19(1):21154]	Journal of the International AIDS Society. 18:20526, 2015.	No: HIV-undiagnosed only
Holt M	Ovid MEDLINE(R)		The converging and diverging characteristics of HIV-positive and HIV-negative gay men in the AUSn Gay Community Periodic Surveys, 2000-2009.	AIDS Care. 25(1):28-37, 2013.	No: Comparison between HIV+ and HIV- on characteristics
Horvath KJ	Ovid MEDLINE(R)		Discussions of viral load in negotiating sexual episodes with primary and casual partners among men who have sex with men.	AIDS Care. 24(8):1052-5, 2012.	No: not relevant and <30 HIV+
Hughes G	Ovid MEDLINE(R)		Lymphogranuloma venereum diagnoses among men who have sex with men in the U.K.: interpreting a cross-sectional study using an epidemic phase-specific framework.	Sexually Transmitted Infections. 89(7):542-7, 2013 Nov.	No: in STI chapter
Jin F	Ovid MEDLINE(R)		Unprotected anal intercourse, risk reduction behaviours, and subsequent HIV infection in a cohort of homosexual men.	AIDS. 2009 Jan 14;23(2):243–52.	No: seroconversion cohort
Jin F	Ovid MEDLINE(R)		Anal sexually transmitted infections and risk of HIV infection in homosexual men.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 53(1):144-9, 2010 Jan.	No: HIV-negative only
Joseph Davey DL	Ovid MEDLINE(R)		Sexual behavior during acute HIV infection among men who have sex with men in Los Angeles, California.	J Infect Dis. 2016 Mar 28;	No: CLS recall prior to seroconversion
Kahler	Ovid		Daily associations between alcohol use and unprotected anal sex among heavy drinking HIV-	AIDS & Behavior. 19(3):422-30, 2015	No: review

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
CW	MEDLINE(R)		positive men who have sex with men. [Review]	Mar.	
Kalichman SC	Ovid MEDLINE(R)		HIV treatment adherence and unprotected sex practices in people receiving antiretroviral therapy.	Sex Transm Infect. BMJ Group; 2003 Feb;79(1):59–61.	No: qualitative
Khan M.R.	Ovid MEDLINE(R)		Social and behavioral correlates of sexually transmitted infection- and HIV-discordant sexual partnerships in Bushwick, Brooklyn, New York.	Journal of Acquired Immune Deficiency Syndromes. 51 (4) (pp 470-485), 2009. Date of Publication: August 2009.	No: <35 HIV+
Knight KR	Embase		Sexual transmission risk behavior reported among behaviorally bisexual HIV-positive injection drug-using men.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 46 Suppl 2:S80-7, 2007 Nov 1.	No: small population of IDUs,not relevant here but added to drugs chapter
Knussen C.	Ovid MEDLINE(R)		Factors associated with recency of HIV testing amongst men residing in Scotland who have sex with men.	AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV. 26 (3) (pp 297-303), 2014. Date of Publication: 04 Mar 2014.	No: very small sample <40 HIV+
Lacefield K	Embase		Comparing Psychosocial Correlates of Condomless Anal Sex in HIV-Diagnosed and HIV-Nondiagnosed Men Who Have Sex with Men: A Series of Meta-Analyses of Studies from 1993-2013.	*LGBT Heal. 2015 Sep;2(3):200–20.*	No: meta-analysis
Landovitz R.J.	Embase		Epidemiology, sexual risk behavior, and HIV prevention practices of men who have sex with men using GRINDR in Los Angeles, California.	Journal of urban health : bulletin of the New York Academy of Medicine. 90 (4) (pp 729-739), 2013. Date of Publication: 01 Aug 2013.	No: CLS estimates not by HIV serostatus
Law MG	Embase		Modelling HIV incidence in gay men: increased treatment, unsafe sex and sexually transmissible infections.	AIDS. 16(3):499-501, 2002 Feb 15.	no: modelling study
Lea T	Ovid MEDLINE(R)		HIV and hepatitis C virus co-infection among men who have sex with men in Sydney, and associations with sexual and drug use practices.	Sexual Health. 10(5):448-51, 2013 Nov.	No: in drugs and STI chapters
Lea T	Ovid MEDLINE(R)		Injecting drug use among gay and bisexual men in Sydney: prevalence and associations with sexual risk practices and HIV and hepatitis C infection.	AIDS & Behavior. 17(4):1344-51, 2013 May.	No: in drugs chapter
Lightfoot M	Ovid MEDLINE(R)		The influence of partner type and risk status on the sexual behavior of young men who have sex with men living with HIV/AIDS.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 38(1):61-8, 2005 Jan 1.	No: data before 1996
Lin X	Embase		Erectile Dysfunction Medication Prescription and Condomless Intercourse in HIV-Infected Men Who have Sex with Men in the United States.	AIDS Behav. 2016 Sep 16;	No: not relevant
Lyons A	Ovid MEDLINE(R)		Versatility and HIV vulnerability: patterns of insertive and receptive anal sex in a national sample of older AUSn gay men.	AIDS & Behavior. 17(4):1370-7, 2013 May.	No: not by serostatus

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
Macdonald N	Ovid MEDLINE(R)		Factors associated with HIV seroconversion in gay men in England at the start of the 21st century.	Sexually Transmitted Infections. 84(1):8-13, 2008 Feb.	
MacKellar DA	Ovid MEDLINE(R)		Unrecognized HIV infection, risk behaviors, and perceptions of risk among young men who have sex with men: opportunities for advancing HIV prevention in the third decade of HIV/AIDS.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 38(5):603-14, 2005 Apr 15.	No: undiagnosed HIV+
Mansergh G	Ovid MEDLINE(R)		Alcohol and drug use in the context of anal sex and other factors associated with sexually transmitted infections: results from a multi-city study of high-risk men who have sex with men in the USA.	Sexually Transmitted Infections. 84(6):509-11, 2008 Nov.	No: Not HIV+ , in drugs chapter
Mansergh G	Ovid MEDLINE(R)		Internalised homophobia is differentially associated with sexual risk behaviour by race/ethnicity and HIV serostatus among substance-using men who have sex with men in the United States.	Sexually Transmitted Infections. 91(5):324-8, 2015 Aug.	No: Not HIV+ , in drugs chapter
Mao L	Ovid MEDLINE(R)		Self-reported sexual difficulties and their association with depression and other factors among gay men attending high HIV-caseload general practices in AUS.	Journal of Sexual Medicine. 6(5):1378-85, 2009 May.	No: not relevant
Maulsby C	Ovid MEDLINE(R)		Individual-Level and Partner-Level Predictors of Newly Diagnosed HIV Infection Among Black and White Men Who Have Sex with Men in Baltimore, MD.	AIDS & Behavior. 19(5):909-17, 2015 May.	No: seroconversion cohort
Maung Maung T.	Ovid MEDLINE(R)		Risks for HIV and other sexually transmitted infections among Asian men who have sex with men in Vancouver, British Columbia: a cross-sectional survey.	BMC public health. 13 (pp 763), 2013. Date of Publication: 2013.	No: not specifically HIV+
Mayer KH	Ovid MEDLINE(R)		Concomitant socioeconomic, behavioral, and biological factors associated with the disproportionate HIV infection burden among Black men who have sex with men in 6 U.S. cities.	PLoS ONE [Electronic Resource]. 9(1):e87298, 2014.	No: no sexual behaviour data
McDaid L.M.	Ovid MEDLINE(R)		Serosorting and strategic positioning during unprotected anal intercourse: Are risk reduction strategies being employed by gay and bisexual men in Scotland?.	Sexually Transmitted Diseases. 39 (9) (pp 735-738), 2012. Date of Publication: September 2012.	No: <10 HIV+
Metsch LR	Ovid MEDLINE(R)		HIV transmission risk behaviors among HIV-infected persons who are successfully linked to care.	*Clin Infect Dis* 2008; **47**: 577–84.	No: results not separated by gender/sexual orientation
Mettey A	Embase		Associations between internet sex seeking and STI associated risk behaviours among men who have sex with men.	Sexually Transmitted Infections. 79(6):466-8, 2003 Dec.	No: MSM from sex resort and data not by HIV serostatus
Miner MH	Ovid MEDLINE(R)		How do social norms impact HIV sexual risk behavior in HIV-positive men who have sex with men?: multiple mediator effects.	Journal of Health Psychology. 14(6):761-70, 2009 Sep.	
Mirandola M	Ovid MEDLINE(R)		HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009.	Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin. 14(48), 2009.	No: data not by HIV serostatus

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
Mitchell JW	Ovid MEDLINE(R)		Relationship characteristics differ based on use of substances with sex among an urban internet sample of HIV-discordant and HIV-positive male couples.	Journal of Urban Health. 92(1):136-50, 2015 Feb.	
Moore DM	Ovid MEDLINE(R)		HIV Community Viral Load and Factors Associated With Elevated Viremia Among a Community-Based Sample of Men Who Have Sex With Men in Vancouver, CA.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 72(1):87-95, 2016 May 1.	No: respondent-driven sampling estimates (and <100 HIV+)
Morin SF	Ovid MEDLINE(R)		Predicting HIV transmission risk among HIV-infected men who have sex with men: findings from the healthy living project.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 40(2):226-35, 2005 Oct 1.	No: population part of RCT aimed at reducing transmission risk
Newcomb ME	Ovid MEDLINE(R)		Partner Disclosure of PrEP Use and Undetectable Viral Load on Geosocial Networking Apps: Frequency of Disclosure and Decisions About Condomless Sex.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 71(2):200-6, 2016 Feb 1.	No: qualitative
Noor SW	Ovid MEDLINE(R)		Factors influencing HIV serodisclosure among men who have sex with men in the US: an examination of online versus offline meeting environments and risk behaviors.	AIDS & Behavior. 18(9):1638-50, 2014 Sep.	No: no CLS estimates, in disclosure chapter
Nostlinger C	Ovid MEDLINE(R)		Implementation and Operational Research: Computer-Assisted Intervention for Safer Sex in HIV-Positive Men Having Sex With Men: Findings of a European Randomized Multi-Center Trial.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 71(3):e63-72, 2016 Mar 1.	No: RCT on increasing condom use
Nostlinger C.	Ovid MEDLINE(R)		Computer-assisted intervention for safer sex in HIV-positive men having sex with men: Findings of a European randomized multi-center trial.	Journal of Acquired Immune Deficiency Syndromes. 71 (3) (pp e63-e72), 2016. Date of Publication: 2016.	No: RCT on increasing condom use
O'Byrne P	Embase		HIV status and sexual behaviour among gay men in Ottawa: considerations for public health.	BMJ Open. 4(9):e005065, 2014.	No: HIV-negative only
Parsons JT	Ovid MEDLINE(R)		Positive, negative, unknown: assumptions of HIV status among HIV-positive men who have sex with men.	AIDS Education & Prevention. 18(2):139-49, 2006 Apr.	No: <80 and no CLS estimates
Patterson T.L.	Ovid MEDLINE(R)		Sexual Risk Reduction among HIV-Positive Drug-Using Men Who Have Sex with Men.	Journal of Urban Health. 80 (4 SUPPL. 3) (pp iii77-iii87), 2003. Date of Publication: December 2003.	No: review
Paz-Bailey G	Ovid MEDLINE(R)		Using the National HIV Behavioral Surveillance System to inform HIV prevention efforts in the United States.	AIDS & Behavior. 18 Suppl 3:S233-6, 2014 Apr.	No: protocol paper
Pedrana AE	Embase		High rates of undiagnosed HIV infections in a community sample of gay men in Melbourne, AUS.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 59(1):94-9, 2012 Jan 1.	No: HIV-undiagnosed
Peterson	Ovid		HIV treatment optimism and sexual risk behaviors among HIV positive African American men	AIDS Education & Prevention.	No: qualitative

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
JL	MEDLINE(R)		who have sex with men.	24(2):91-101, 2012 Apr.	
Poppen PJ	Ovid MEDLINE(R)		Serostatus disclosure, seroconcordance, partner relationship, and unprotected anal intercourse among HIV-positive Latino men who have sex with men.	AIDS Education & Prevention. 17(3):227-37, 2005 Jun.	No: in disclosure chapter
Price H	Ovid MEDLINE(R)		Hepatitis C in men who have sex with men in London--a community survey.	HIV Medicine. 14(9):578-80, 2013 Oct.	No: in HCV chapter
Qvist T	Embase		Predictors of unsafe sex among HIV patients in Denmark: a population-based cohort study.	Scandinavian Journal of Infectious Diseases. 43(3):181-7, 2011 Mar.	No: aggregate estimates (not by gender/sexual orientation)
Ridge D	Ovid MEDLINE(R)		Positive prevention: contemporary issues facing HIV positive people negotiating sex in the UK.	Social Science & Medicine. 65(4):755-70, 2007 Aug.	No: qualitative
Ritchie AJ	Ovid MEDLINE(R)		Comparison of sexual behavior and HIV risk between two HIV-1 serodiscordant couple cohorts: the CHAVI 002 study.	PLoS ONE [Electronic Resource]. 7(5):e37727, 2012.	No: risk quantification model
Rodger A	Ovid MEDLINE(R)		Partners of people on ART - a New Evaluation of the Risks (The PARTNER study): design and methods.	BMC Public Health. 12:296, 2012.	No: protocol paper
Rodger AJ	Ovid MEDLINE(R)		Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy.	JAMA. 316(2):171-81, 2016 Jul 12.	No: discussed throughout thesis, no CLS estimates here
Rogers G.	Ovid MEDLINE(R)		Depressive disorders and unprotected casual anal sex among AUSn homosexually active men in primary care.	HIV Medicine. 4 (3) (pp 271-275), 2003. Date of Publication: July 2003.	No: not by HIV serostatus and v small sample
Ross MW	Embase		The relationship of internalized homonegativity to unsafe sexual behavior in HIV-seropositive men who have sex with men.	AIDS Education & Prevention. 20(6):547-57, 2008 Dec.	No: not relvenat
Safran MA	Ovid MEDLINE(R)		Sexual behaviour and desire to discuss mental health as reported by HIV-infected men who have sex with men.	International Journal of STD & AIDS. 24(2):93-9, 2013 Feb.	No: any sex not cls
Satinsky S	Ovid MEDLINE(R)		USA study of sex toy use by HIV-positive men who have sex with other men: implications for sexual health.	International Journal of STD & AIDS. 22(8):442-8, 2011 Aug.	No: not about CLS
Scott HM	Ovid MEDLINE(R)		Age, race/ethnicity, and behavioral risk factors associated with per contact risk of HIV infection among men who have sex with men in the United States.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 65(1):115-21, 2014 Jan 1.	No: HIV prevention trials
Seng R			Trends in unsafe sex and influence of viral load among patients followed since primary HIV infection, 2000-2009.	AIDS. 2011 Apr 24;25(7):977–88.	No: recently infected (<=6months) sub-cohort of VESPA1

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
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Simon Rosser BR	Ovid MEDLINE(R)		Predictors of HIV disclosure to secondary partners and sexual risk behavior among a high-risk sample of HIV-positive MSM: results from six epicenters in the US.	AIDS Care. 20(8):925-30, 2008 Sep.	No: not specifically about CLS, reviewed in disclosure chapter
Smith DK	Ovid MEDLINE(R)		Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 68(3):337-44, 2015 Mar 1.	No: HIV prevention trials
Spikes PS	Ovid MEDLINE(R)		Sexual risk behaviors among HIV-positive black men who have sex with women, with men, or with men and women: implications for intervention development.	American Journal of Public Health. 99(6):1072-8, 2009 Jun.	
Starks T.J.	Ovid MEDLINE(R)		Predictors of condom use with main and casual partners among HIV-positive men over 50.	Health Psychology. 34 (11) (pp 1116-1122), 2015. Date of Publication: November 2015.	
Stein R	Embase		Reduced Sexual Risk Behaviors Among Young Men of Color Who Have Sex with Men: Findings from the Community-Based Organization Behavioral Outcomes of Many Men, Many Voices (CBOP-3MV) Project.	Prevention Science. 16(8):1147-58, 2015 Nov.	No: HIV-negative only
Tieu HV	Ovid MEDLINE(R)		Sexual partner characteristics, serodiscordant/serostatus unknown unprotected anal intercourse and disclosure among human immunodeficiency virus-infected and uninfected black men who have sex with men in New York City.	Sexually Transmitted Diseases. 38(6):548-54, 2011 Jun.	No: sample size <60
Turner JM	Ovid MEDLINE(R)		Behavioural predictors of subsequent hepatitis C diagnosis in a UK clinic sample of HIV positive men who have sex with men.	Sexually Transmitted Infections. 82(4):298-300, 2006 Aug.	No: not specifically about CLS
Valleroy LA	Ovid MEDLINE(R)		HIV prevalence and associated risks in young men who have sex with men. Young Men's Survey Study Group.	JAMA. 284(2):198-204, 2000 Jul 12.	No: data from 1994
van Kesteren NMC	Embase		Sexual risk behavior among HIV-positive men who have sex with men: A literature review.	Patient Educ Couns. 2007;65(1):5–20.	No: lit review & meta-analysis
Van de Ven P	Ovid MEDLINE(R)		Change in sexual practice among AUSn men who have sex with men, 1992-1996.	AIDS. 12 Suppl B:S66, 1998.	No: Pre-ART
Van De Ven P	Ovid MEDLINE(R)		Increasing proportions of AUSn gay and homosexually active men engage in unprotected anal intercourse with regular and with casual partners.	AIDS Care. 14(3):335-41, 2002 Jun.	No: data collected in 1992
Van de Ven P	Embase		Undetectable viral load is associated with sexual risk taking in HIV serodiscordant gay couples in Sydney	*AIDS* 2005; **19**: 179–84.	No: grouped estimates for HIV+ and HIV-
Van den Boom	Embase		Undetectable viral load and the decision to engage in unprotected anal intercourse among HIV-positive MSM.	*AIDS Behav. 2013 Jul;17(6):2136–42.*	No
Vanable PA	Embase		Viral load and HIV treatment attitudes as correlates of sexual risk behavior among HIV-positive gay men.	*J Psychosom Res. 2003 Mar;54(3):263-9.*	No: <60 HIV+

1st Author	Database	Country / Title		Source / Included in literature review? Reasoning if not	
Weinhardt LS	Ovid MEDLINE(R)		HIV transmission risk behavior among men and women living with HIV in 4 cities in the United States.	Journal of Acquired Immune Deficiency Syndromes: JAIDS. 36(5):1057-66, 2004 Aug 15.	No: sample includes people recruited from clinics and community venues but doesn't separate results
Wejnert C	Ovid MEDLINE(R)		Age-Specific Race and Ethnicity Disparities in HIV Infection and Awareness Among Men Who Have Sex With Men--20 US Cities, 2008-2014.	Journal of Infectious Diseases. 213(5):776-83, 2016 Mar 1.	No: results not by HIV-serostatus (lumps all + and -)
Welles SL	Ovid MEDLINE(R)		History of childhood sexual abuse and unsafe anal intercourse in a 6-city study of HIV-positive men who have sex with men.	American Journal of Public Health. 99(6):1079-86, 2009 Jun.	No: not specifically about CLS
Wheater CP	Ovid MEDLINE(R)		Re-emerging syphilis: a detrended correspondence analysis of the behaviour of HIV positive and negative gay men.	BMC Public Health. 3:34, 2003 Oct 29.	No: correspondence analysis
Winter A.K.	Ovid MEDLINE(R)		Discussion of HIV status by serostatus and partnership sexual risk among internet-using MSM in the United States.	Journal of Acquired Immune Deficiency Syndromes. 60 (5) (pp 525-529), 2012. Date of Publication: 15 Aug 2012.	No: disclosure paper
Wolitski RJ	Ovid MEDLINE(R)		HIV serostatus disclosure among gay and bisexual men in four American cities: general patterns and relation to sexual practices.	AIDS Care. 10(5):599-610, 1998 Oct.	No: data from pre-1990
Zablotska IB	Ovid MEDLINE(R)		Increases in unprotected anal intercourse with serodiscordant casual partners among HIV-negative gay men in Sydney.	AIDS & Behavior. 13(4):638-44, 2009 Aug.	No: HIV-negative only
Zablotska IB	Ovid MEDLINE(R)		Gay men's current practice of HIV seroconcordant unprotected anal intercourse: serosorting or seroguessing?	AIDS Care. 2009 Apr;21(4):501–10.	No: CLS-C estimates only, no CLS overall or CLS-D
Cove J	Ovid MEDLINE(R)		Factors associated with sexual problems in HIV-positive gay men.	*Int J STD AIDS. 2004;15(11):732-736. doi:10.1258/0956462042395221.*	No: small sample <100
Hospers HJ	Ovid MEDLINE(R)		A new meeting place: chatting on the Internet, e-dating and sexual risk behaviour among Dutch men who have sex with men.	AIDS. 2005;19(10):1097-1101.	No: not by HIV serostatus

CA: Canada; CDC: Centers for Disease Control; FR: France; INTL: International EU: European Union; SW: Switzerland; UK: United Kingdom; USA: United States of America

Appendix IV. Comparison of MSM who had CLS without specifying partners' HIV-serostatus ('CLS-unspecified') to MSM who had 'CLS-C without CLS-D' or CLS-D (N=836)

	CLS-unspecified (N=31)		CLS-C without CLS-D (N=479)			CLS-D (N=326)			Total (N=836)
	n	col %	n	col %	p-value◊	n	col %	p-value†	row n
Age at recruitment, years (N=829)									
<30	1	3.2	32	6.7		23	7.1		56
30-39	8	25.8	150	31.4		75	23.3		233
40-49	15	48.4	195	40.9		144	44.7		354
50-59	7	22.6	85	17.8		62	19.3		154
≥60	0	-	15	3.1	0.799 (F)	18	5.6	0.753 (F)	33
Time since HIV diagnosis (N=829)									
3 months-2 years	3	9.7	40	8.4		29	9.0		72
2-5 years	6	19.4	94	19.7		57	17.6		157
5-15 years	9	29.0	234	49.1		165	50.9		408
>15 years	13	41.9	109	22.9	0.070 (F)	73	22.5	0.057 (F)	195
Recreational drug use (N=835)‡									
No	10	32.3	146	30.5		103	31.6		259
Yes	21	67.7	333	69.5	0.835	223	68.4	0.940	577
Use of chemsex-related drugs* (N=835)‡									
No	22	71.0	316	66.0		253	77.6		591
Yes	9	29.0	163	34.0	0.568	73	22.4	0.401	245
Number of recreational drugs used (N=576)‡									
1	3	14.3	65	19.5		51	22.9		119
2-4	12	57.1	150	45.0		114	51.1		276
≥5	6	28.6	118	35.4	0.635 (F)	58	26.0	0.723 (F)	182
Participant's HIV-negative sexual partner(s) took PEP or PrEP (N=835)‡									
No/missing	31	100.0	473	98.7		312	95.7		816

	CLS-unspecified (N=31)		CLS-C without CLS-D (N=479)			CLS-D (N=326)			Total (N=836)
	n	col %	n	col %	p-value◊	n	col %	p-value†	row n
Yes	0	-	6	1.3	-	14	4.3	-	20
Harmful/hazardous alcohol consumption (N=835)									
No	27	87.1	406	84.8		251	77.0		684
Yes	4	12.9	73	15.2	0.743 (F)	75	23.0	0.195 (F)	152
Stable partner's HIV-serostatus (n=835)									
HIV-positive	9	29.0	253	52.8		47	14.4		309
HIV negative or HIV-unknown (incl.missing partner status)	5	16.1	54	11.3		143	43.9		202
No stable partner	17	54.8	172	35.9	0.037	136	41.7	0.006	325
Sexually transmitted infection (STI) (N=824)‡									
No	28	90.3	397	83.8		247	77.2		672
Yes	3	9.7	77	16.2	0.449 (F)	73	22.8	0.110 (F)	153
Lifetime hepatitis C diagnosis (N=814)									
No	27	87.1	359	77.4		256	80.0		642
Yes	4	12.9	105	22.6	0.265 (F)	64	20.0	0.476(F)	173
Current STI symptoms (N=835)									
No/missing	26	83.9	420	87.7		273	83.7		719
Yes	5	16.1	59	12.3	0.573 (F)	53	16.3	0.985 (F)	117
Group sex (N=820)‡									
No	20	69.0	305	64.1		169	53.5		494
Yes	9	31.0	171	35.9	0.593	147	46.5	0.109	327
Used internet to find sex (N=820)‡									
No	13	44.8	203	42.6		113	35.8		329
Yes	16	55.2	273	57.4	0.818	203	64.2	0.332	492
Transactional sex (N=827)‡									
No	29	100.0	470	98.3		317	98.8		816
Yes	0	-	8	1.7	N/A	4	1.2	-	12
"I feel confident that I can make sure a condom is used with any partner, in any situation" (N=820)									
Strongly/tend to agree or undecided	25	83.3	435	91.8		276	87.1		736
Tend to/strongly disagree	5	16.7	39	8.2	0.169 (F)	41	12.9	0.572 (F)	85
HIV transmission risk beliefs (N=819)									
Most conservative	13	43.3	190	40.3		85	26.6		288

	CLS-unspecified (N=31)		CLS-C without CLS-D (N=479)			CLS-D (N=326)			Total (N=836)
	n	col %	n	col %	p-value◊	n	col %	p-value†	row n
Moderately conservative	15	50.0	254	53.9		200	62.7		469
Least conservative	2	6.7	27	5.7	0.780 (F)	34	10.7	0.180 (F)	63
Viral load agreement (N=694 on ART)									
Agreement	23	82.1	355	90.8		251	91.3		629
Disagreement	5	17.9	36	9.2	0.176 (F)	24	8.7	0.166 (F)	65
"I find it difficult to discuss condom use with a new sexual partner" (N=822)									
Tend to/strongly disagree or undecided	25	83.3	408	85.7		234	73.8		667
Strongly/tend to agree	5	16.7	68	14.3	0.788 (F)	83	26.2	0.379 (F)	156
"I am less likely to use a condom with a casual partner" (N=816)									
Tend to/strongly disagree or undecided	19	65.5	383	81.0		185	58.7		587
Strongly/tend to agree	10	34.5	90	19.0	0.043	130	41.3	0.566 (F)	230
"I am worried I could have infected someone else with HIV in the past few months " (N=815)									
Tend to/strongly disagree or undecided	23	79.3	461	97.5		257	81.6		741
Strongly/tend to agree	6	20.7	12	2.5	<0.001	58	18.4	0.803	76
Number of sexual partners (N=820)‡									
1	11	39.3	193	41.0		78	24.2		282
2-4	8	25.0	133	28.4		93	28.9		234
5-9	2	7.1	71	15.2		56	17.4		129
10-19	2	7.1	45	9.6		41	12.7		88
≥20	6	17.9	20	4.3		44	13.7		70
>1 but exact number missing	1	3.6	7	1.5	0.025 (F)	10	3.1	0.386 (F)	18
10 or more new partners in past 12 months (N=835)									
No/missing	14	45.2	193	40.3		176	54.0		383
Yes or >1 but exact number missing	31	100.0	479	100.0	0.593	326	100.0	0.347	836

*P-values by chi-squared test, chi-squared test for linear trend (T), or Fisher's exact test (F); col %: column percentage; row n: total number by row; ‡ Three month recall period; ◊ p-value comparing CLS-unspecified with CLS-D group; †p-value comparing CLS-unspecified with CLS-C only group; * GHB/GBL, mephedrone, crystal methamphetamine*

Appendix V. Natural history of HIV

Beginning of the HIV epidemic

In 1981 a formerly unknown disease was described in previously healthy gay men in the United States. It was characterised by high incidence of rare opportunistic infections, such as fungal pneumonia and the cancer Kaposi's Sarcoma.[622,623] Surveillance reports of an expanding epidemic continued to rise across the USA during 1982, and new cases were also described among intravenous drug users and recipients of blood transfusions.[624,625] The epidemic was characterised by extremely high mortality rates (85% died within five years of initial diagnosis) and underlying acquired immune deficiency.[626–628] As the epidemic was mostly described among clusters of epidemiologically linked gay men, the emerging hypothesis on the cause of the disease was that of a sexually transmitted infectious agent.[629] By 1983 the etiologic agent had been isolated and identified as a novel human retrovirus, phylogenetically similar to lentiviruses, which were known to cause chronic infections in animals.[630,631] Due to its detrimental effect on human immunity, the virus was named human immunodeficiency virus (HIV). In 1985, serologic assays were developed for the detection of anti-HIV antibodies in blood of asymptomatic individuals; this was catalytic in screening blood donations and paved the way to discovery of therapies.[632,633] The first therapy that became available in 1987 was azidothymidine (AZT, or zidovudine), an antiviral agent found to lower short-term incidence of mortality, and opportunistic infections, and to slow the progression of HIV-related complications among patients with advanced HIV infection.[634] AZT was also found to reduce mother-to-child transmission of HIV (MTCT) among pregnant women from 25.5% to 8.3%.[635] Early treatment of individuals with asymptomatic HIV infection with AZT monotherapy, however, had profound side effects and did not improve overall prognosis.[636] In the early to mid-1990's greater understanding of viral dynamics and of additional drug discovery targets lead to the synthesis of new antiviral drugs (protease inhibitors, PIs).[637,638] Randomised controlled trials among asymptomatic people with HIV also showed that a two-drug combination therapy was superior to monotherapy.[639,640] Landmark studies in 1995-96 demonstrated that triple combination therapy (termed highly active antiretroviral therapy, HAART) was superior to two-drug therapy in reducing both mortality[641] and the amount of HIV found in blood serum (plasma viral load, VL).[642,643] At the same time, VL laboratory assays were developed and paved the way for the discovery of the critical role of low viral load in predicting progression to AIDS and death.[644] HAART became the standard of care in the USA and Western Europe and by 1998 surveillance data showed marked reduction in AIDS morbidity and mortality in countries offering HAART.[645] Since the beginning of the epidemic, a total of 78 million individuals (95%CI 71-87 million) have acquired HIV, and 39 million (35-43) have died of AIDS-related diseases.[1] Thirty-five years after the isolation of HIV, antiretroviral drug therapy, technological and research advances in the understanding of transmission dynamics and determinants have transformed HIV from a 'death sentence' to a treatable chronic condition. [2]

Origins and strains of HIV

Two types of HIV circulate in human populations. The majority of infections globally are caused by HIV-1; a minority of infections in individuals resident in or native to West Africa are caused by HIV-2. Both viruses originated from lentiviruses circulating in African primates (simian immunodeficiency viruses, SIV); HIV-1 originated from SIV in different subspecies of chimpanzees in West-Central Africa, while HIV-2 derived from SIV in mangabey monkeys in West Africa.[626] There is evidence that HIV crossed species between 1885 and 1925 and has been detected in blood samples as far back as 1959.[626]

HIV has enormous genetic diversity and numerous subtypes are distributed across the globe. Three groups of HIV-1 exist: 'M' ('main'), 'O' ('outlier'), and 'N' ('new'), which are all further subdivided into smaller subtypes according to geographical region of endemicity. The first type of HIV recognised during the 1981 outbreak and the majority (90%) of today's HIV-1 infections in North America and Europe are due to group 'M', and specifically subtype 'B', whereas subtype 'C' is more prevalent in Southern Africa, and others ('A' and 'D') are prevalent in sub-Saharan Africa.[626]

Description of the virus

HIV is a retrovirus with two identical copies of single-stranded ribonucleic acid (RNA) genomes within one virion (infectious particle.)[626] The virion is comprised of a protective protein shell, or capsid, which in turn consists of thousands of copies of the viral p24 protein (antigen). HIV preferentially infects immune cells, such as helper T-lymphocytes and macrophages, which carry a CD4+ cell surface antigen (receptor). In order for HIV to replicate, it must bind onto the host cell via surface membrane co-receptors (chemokine receptors CCR5 or CXCR4), fuse into the surface, and penetrate the host cell.[646] Following fusion, the virion's core is uncoated and the two strands of RNA are transcribed into a double-stranded DNA copy of the RNA genome (the 'provirus') by the enzyme reverse transcriptase. The provirus is transported to the host cell's nucleus and integrated into the host's genomic DNA by the viral enzyme integrase. Subsequent provirus transcription leads to expression of new viral RNA for synthesis of viral proteins and assembly of new virions, which exit the host cell by budding through the cell membrane.[636,647] Once viral DNA has integrated into the host genome as a provirus, it can remain dormant and thus go undetected by the immune system for many years. Latently infected CD4 cells have a dormant integrated provirus and are thus not able to produce new virions. This property explains the presence of viral reservoirs (cell types or anatomical sites of accumulated latently infected T-cells) outside of blood, such as lymphoid tissues, the central nervous system, and genital mucosal membranes.[648] Once latently infected CD4 cells are activated, transcription of the provirus genome starts anew and immature virus particles bud from the host cell membrane.[649] Following expulsion, new virions undergo maturation by the enzyme protease, and are able to infect other cells.[650] The rate of HIV replication is extremely rapid; 10^{12} virions are estimated to be produced daily and a similar number of millions of CD4+ lymphocytes being destroyed.[626,636]

Detection of HIV

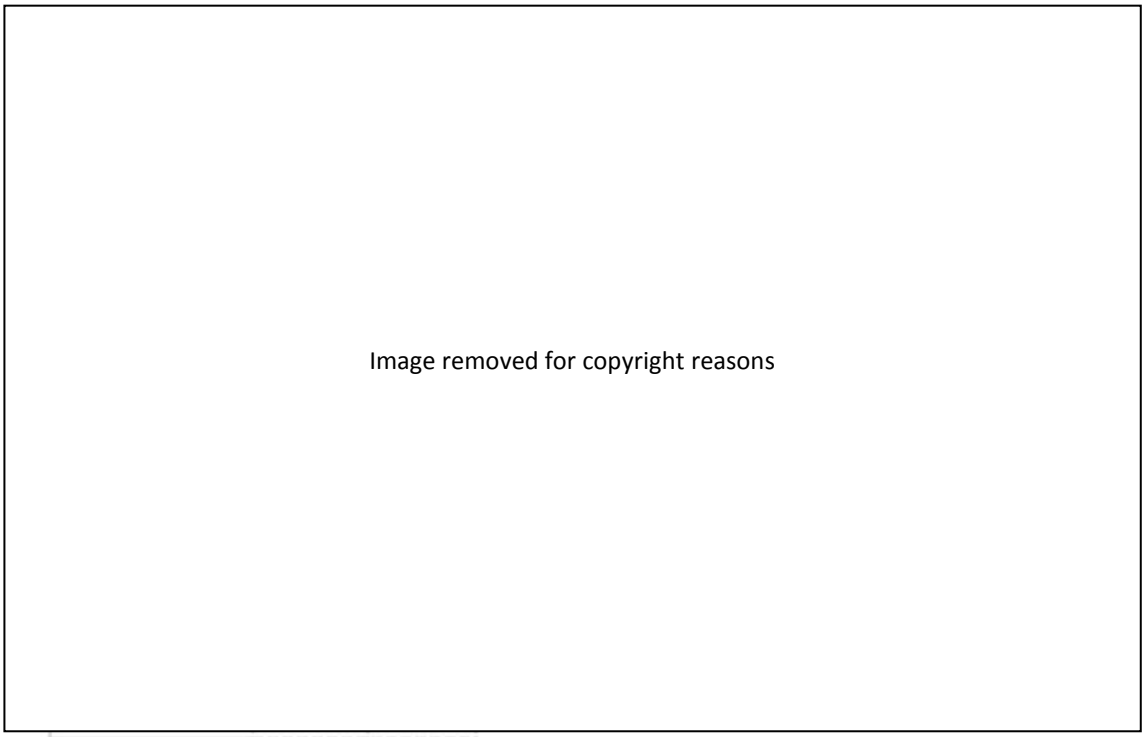
Testing blood plasma for HIV is undertaken by laboratory assays, classified into those that detect HIV-specific antibodies (for screening and confirmation of a new HIV infection), those that identify HIV-specific proteins (antigens), and those which detect or monitor viral nucleic acid (HIV RNA or HIV proteins). In the UK, universal free HIV testing is offered in genitourinary medicine (GUM)/sexual health clinics, antenatal services, and healthcare services for those diagnosed with tuberculosis, hepatitis B or C; as of 2008, testing is also recommended in primary care practices and general medical admissions where diagnosed HIV prevalence is greater than 2 in 1,000 population.[651]

Antibody testing

Antibodies are proteins secreted by white blood cells which identify, bind to, and attempt to neutralise pathogens called antigens (such as p24). Blood plasma concentrations of these biomarkers vary by days since exposure to HIV. (Figure V1)

Following the isolation of HIV-1 in 1983, blood-screening antibody tests (immunoassays) became available for HIV detection. Since then, there have been four successive generations of these tests used for screening and diagnosis.[652] Each new generation of assays achieved a reduction in the window period, improving detection of early infection. (Figure V1) The first-generation test (enzyme-linked immunosorbent assay, ELISA) indicated the presence or absence of the virus within 12 weeks of infection, but suffered from low specificity. The window period was reduced to a mean of six weeks with second-generation immunoassays (introduced in 1987), and further yet to three weeks with third generation assays, (introduced in the early 1990s).[652] Fourth-generation screening assays, introduced in 1997, test blood plasma for anti-HIV antibodies and p24 antigen simultaneously, reducing the window period even further to two weeks.[651,653] They have excellent sensitivity (99.8-100%) and specificity (99.5-99.3%).[654] In the case of a reactive sample (where HIV antibodies are detected), testing of a second sample and three additional confirmatory laboratory assays are required (Western Blot or Immunoblot) to verify infection and differentiate between HIV types (1 or 2) and major groups ('M','O', and 'N').[651,655]

Figure V1: Evolution of viral and immunological markers following HIV infection[656]



Rapid Tests

Assays that can detect specific HIV-antibodies or p24 in thirty minutes or less are referred to as rapid or point-of-care tests (POCT). POCTs are designed to detect biomarkers in serum, plasma, whole blood (from fingerprick), or oral fluid (from a mouth swab), but tend to have lower sensitivity compared to established immunoassays (e.g. fourth-generation ELISA).[657,658] The prevalence of false negatives in POCTs during primary HIV infection makes rapid tests problematic in detecting acute infection.[659] POCTs that use oral fluid have lower sensitivity (81-91%) compared to those which use fingerprick whole blood samples (92-98%).[660] Nevertheless, POCTs facilitate access to testing and are routinely used in GUM clinics in the UK.[651,661]

Detecting recent HIV infection

Since 2009, the Recent Infection Testing Algorithm (RITA) has been used in UK routine surveillance data to distinguish recently acquired from long-standing HIV infections.[662] RITA is based on a modified version of ELISA, called enzyme immunoassay (EIA), which measures the strength in the bond between HIV antibody and antigen (also known as 'avidity index'), which tends to be weaker at the initial stages of infection.[663] RITA also incorporates information on CD4 count, ART status, and AIDS-defining illnesses. Hence, samples with low antibody avidity index (<80%) demonstrate a positive RITA result, meaning a likely recent HIV acquisition (approximately six months prior to HIV diagnosis).

Natural history of HIV

CD4 count

Depletion of CD4 lymphocyte cells is quantified by flow cytometry, a laboratory test used to count the number of CD4 cells in a cubic millimetre of blood (mm^3), referred to as CD4 count;[664] this is a marker of

immunological status and allows for staging of HIV disease. Normal ranges are between 500 and 1200cells/mm^3, with opportunistic infections most prevalent below 200cells/mm^3.

Viral load quantification

The amount of virions circulating in blood plasma (viral load, VL) is considered the single best marker of long-term clinical progression (up to 10 years) to AIDS and death.[665–667] Viral load is measured as copies of virion per millilitre of blood plasma (c/mL) and is usually considered on a log scale. Therefore a change in VL is reported as a log change (in powers of 10, log_{10}). Viral load is used as a marker of the total replication activity of the virus in an individual.[668] A higher VL is associated with a faster rate of CD4 cell decline than a lower VL.

Viral load became quantifiable with the development of nucleic acid-based molecular diagnostic assays in the latter half of the 1990's.[643,669,670] The development of quantitative polymerase chain reaction (PCR) has led to significant improvement in the sensitivity of laboratory techniques to estimate and monitor HIV-1 VL. PCR is now widely used and can have a lower quantification limit of 40c/mL.[650,651] HIV-1 RNA becomes detectable in blood plasma approximately 11 days after exposure to the virus.(Figure V1)[671] In cases of suspected very recent infection (< 15 days), when patients may have early symptoms, fourth generation assays may be negative. In this case only, UK guidelines on testing (2012) recommend viral load testing performed with specialist input.[585]

Immune response to HIV

HIV replication leads to sustained immune activation, which in turn leads to severe immune deficiency.[647,672] Persistent immune activation is characterised by enhanced production of activation markers on CD4 cells and B-lymphocytes as well as by high concentrations of inflammatory cytokines; these proteins promote inflammation in lymphoid tissues by expressing adhesion molecules which trap lymphocytes.[673] During high-level viremia, CD4 responses to HIV antigens are impaired leading to dysregulated immune responses to other opportunistic pathogens. CD4 cell activation induces complete cell cycles, ending in accelerated cellular death, and thus leads to depletion of T-cells and destruction of peripheral lymphoid tissues. With advancing HIV disease, production of other immune system cells (macrophages and natural killer cells) is halted and severe immune deficiency ensues.[672]

Clinical stages of HIV infection

The course of HIV progression varies significantly by individual, but is overall characterised by progressive loss of immune system function.[636] The World Health Organization (WHO) and the Centers for Disease Control (CDC) have developed classification systems for the natural history of HIV disease according to laboratory findings and clinical manifestations, which are mainly used in resource limited settings.[674,675](Table V1) The 2007 WHO staging system relies on clinical presentations of various diseases, conditions, and infections, and it is intended to be used globally across resource settings. The 2008 CDC classification system relies on monitoring of CD4 counts; the lowest CD4 count or the presence of an AIDS-defining condition is used to determine the stage of infection.

Table V1: Classification of HIV disease stages according to the WHO and the CDC[674,675]

WHO stage[676]	Clinical manifestation	CDC stage[674]	AIDS-defining condition	Laboratory-confirmed CD4 count
Clinical stage1		Stage 0 (early HIV infection)	-	-
Asymptomatic	No symptoms reported or upon examination			
Persistent generalised lymphadenopathy	Enlarged lymph nodes for 3 months or longer			
Clinical stage 2	Unexplained weight loss (<10% of body weight), recurrent upper respiratory tract infections, herpes zoster, oral ulceration, papular pruritic lesions, seborrhoeic dermatitis, fungal nail infections	Stage 1	None	≥500 cells/mm^3
Clinical stage 3	Unexplained weight loss (>10% of body weight), unexplained chronic diarrhoea and persistent fever, persistent oral candidiasis, pulmonary TB, severe bacterial infection (e.g. pneumonia, meningitis), acute necrotising gingivitis or periodontitis, unexplained anaemia, neutropaenia, or chronic thrombocytopaenia	Stage 2	None	200-499 cells/mm^3
Clinical stage 4	HIV wasting syndrome, Pneumonia, Chronic herpes simplex virus infection, Extrapulmonary TB, Kaposi sarcoma, HIV encephalopathy	Stage 3 (AIDS)	Yes	<200 cells/mm^3

Primary HIV infection (PHI)

PHI describes the first stage of the disease, from infection with HIV until immune system function achieves balance with viral replication.[677] Seroconversion, the period of time during which HIV-specific antibodies are produced and become detectable in blood plasma tests, begins two to six weeks after infection and lasts five to ten days on average. In over 80% of cases seroconversion is accompanied by flu-like symptoms (fever, fatigue, headache, pharyngitis, lymphadenopathy, and maculopapular skin rash) which resolve over two to four weeks.[636]

PHI is characterised by active viral replication and CD4 cell depletion.[678] The virus continuously replicates in lymphoreticular tissues (lymph nodes, spleen, gut-associated lymphoid cells, and macrophages) and preferentially infects CD4+ T lymphocytes initially in the genital/rectal membranes, spreading via the blood to lymph nodes and lymphoid tissues in the gut.[679] Rapid replication leads to exponentially increasing plasma viremia, with up to millions of virus copies per millimetre of plasma (c/mL) produced. At this point the viral population doubles every six to ten hours.[678] Diagnostic tests using antibody reactivity may be indeterminate or negative during this stage, as anti-HIV antibodies are generated (and thus detectable) two to six weeks after the onset of seroconversion symptoms. Plasma viral load and p24 antigen assays however, are positive from the onset of symptoms.[636]

Clinical latency

Clinical latency describes the asymptomatic phase between PHI and the development of AIDS. Viral replication, CD4 cell loss, and destruction of lymphoid tissue in the gut are continuous throughout infection, but HIV-infected individuals generally remain free from serious illnesses for a number of years.[678] Within four to six months of seroconversion the host's immune system is able to respond to HIV, which leads to a decrease in VL to a plateau ('set point') that varies between individuals.[636]

AIDS

AIDS refers to the point in disease progression when CD4+ T cell counts decline to critical levels (<200 cells/mm^3) resulting in opportunistic infections and clinical immunodeficiency. The 2015 UK guidelines follow CDC classification systems of AIDS-defining illnesses to define progression to AIDS.[17](Table V2) In the absence of ART, an individual's higher viral 'set point' correlates with faster rate of disease progression to AIDS; the average period of time between infection and AIDS is 10 years, but some individuals develop AIDS within two years. Median survival post-AIDS diagnosis in the absence of ART ranges from one to two years.[636] There is strong evidence from meta-analyses that prior to the widespread use of ART, time since and age at seroconversion were the major determinants of risk of AIDS and death among people with HIV in Europe, North America, and Australia.[680]

Table V2: CDC classification of Stage 3 AIDS-defining conditions[674]

AIDS-defining conditions:
Bacterial infections, multiple or recurrent
Candidiasis of bronchi, trachea, or lungs
Candidiasis of esophagus
Cervical cancer, invasive
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1 month's duration)
Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
Cytomegalovirus retinitis (with loss of vision)
Encephalopathy, HIV related
Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1 month's duration)
Kaposi sarcoma
Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex
Lymphoma, Burkitt (or equivalent term)
Lymphoma, immunoblastic (or equivalent term)
Lymphoma, primary, of brain
Mycobacterium avium complex or *Mycobacterium kansasii,* disseminated or extrapulmonary
Mycobacterium tuberculosis of any site, pulmonary, disseminated,or extrapulmonary
Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
Pneumocystis jirovecii pneumonia
Pneumonia, recurrent
Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of brain, onset at age >1 month
Wasting syndrome attributed to HIV

Appendix VI. Background on STI aetiology among males

Table VI.1: Natural history, transmission, clinical manifestation, diagnosis, and treatment of common bacterial STIs among males [442–452]

STI	Aetiology	Sexual transmission	Natural history (untreated)	Clinical features	Diagnostic methods	Treatment/management ‡
Chlamydia (CT)	Bacterial (*C.trachomatis)* serovars D-K	Direct inoculation of infected secretions from mucous membranes	Incubation period 7-21 days. Spontaneous resolution 12 months from diagnosis in 50%. Complications (rare): epididymitis, sterility, prostatitis, reactive arthritis	Urethral discharge and/or dysuria (50%). Remainder asymptomatic. Rectal infection asymptomatic (>60%) but may cause anal discharge/pain.	Positive NAAT on urine or urethral/rectal swab. POCT using EIA.	•Twice daily doxycycline for 7 days or single dose azithromycin. •Avoidance of sex incl. with condoms until treatment and symptoms resolved. • All sexual contacts should be notified (within 2 weeks prior to symptom onset or last 3 months if asymptomatic) and offered testing/treatment.
Gonorrhoea (NG)	Bacterial (*N.gonorrhoeae)*	Direct inoculation of infected secretions from mucous membranes	Incubation period 1-14 days. Spontaneous symptom resolution within 6 months untreated (95%). Complications (rare) as in CT.	Urethral/anal discharge (80%), dysuria (50%) within 5 days of exposure. Pharyngeal symptoms in 10-25%. Asymptomatic in 5-10%. Mild fever, skin rash	Positive NAAT on urine or urethral/rectal/pharyngeal swab, or positive culture from any site	• Single dose intramuscular ceftriaxone plus single dose oral azithromycin • Avoidance of sex including with condoms until treatment and symptoms resolved • Sexual contact tracing as per CT • High levels of multi-drug resistance require alternative regimens
Lymphogranuloma venereum (LGV)	Bacterial (C.trachomatis) - serovars L1-L3	Penetration of skin through lacerations, abrasions	•Primary lesion: painless genital or perianal papule or ulcer and proctitis, 3-12 days after exposure. Occurs in 3-53% and heals rapidly.	Genital lesion/ulcer/bubo and inflammatory proctitis (>90%): rectal pain, bleeding, discharge, constipation. Ulcers in pharynx.	Positive NAAT on urine, bubo pus, or genital/rectal/pharyngeal swabs	• Twice daily doxycycline for 21 days • Contact tracing for all sexual contacts since and during 4 weeks prior to symptom onset

STI	Aetiology	Sexual transmission	Natural history (untreated)	Clinical features	Diagnostic methods	Treatment/management ‡
			•Secondary stage: Lyphadenopathy after 10-30 days, painful anogenital bubo, which may ulcerate (in ~33%) or disappear.			
Non-gonococcal urethritis (NGU)/ Non-specific urethritis (NSU)	•Bacterial: CT (30-50% of cases), *M.genitalium* (6-50%), *U.urealyticum*(11-26%) •Viral: Adenovirus (2-4%), HSV-1/HSV-2 (2-3%) • Parasite: *T.vaginalis* (1-20%)	Sexual (not always)	Incubation period 1-5 weeks. Overall self-limiting. Complications (rare): epididymitis (<2% of untreated), reactive arthritis (% unknown)	Urethral discharge, dysuria, penile irritation. Asymptomatic in up to 25%.	For symptomatic patients only: Confirmed microscopy of urethral smear or urine specimen.	• Twice daily doxycycline for 7 days or single dose azithromycin (or multiple doses for 4 days if *M.genitalium*-positive) • Avoidance of sex including with condoms until treatment and symptoms resolved • Partner notification within past 4 weeks (symptomatic) or up to past 6 months (asymptomatic)
Syphilis	Bacterial (*T.pallidum)*	Direct lesion contact: sexual (only from early syphilis), blood-borne	• Early (infectious) syphilis: - Primary: 9-90 days after infection resolving within 2-8 weeks - Secondary: 6 weeks-6 months after infection with persisting primary lesion (in 33%) - Early latent: within 2 years of infection • Late syphilis: - Late latent: >2 years of infection - Late benign can appear	• Early (infectious) syphilis: -Primary: painless ulcerative lesion where direct contact with infected lesion occurred (genitals,extra-genital) -Secondary: malaise, fever, skin lesions, lymphadenopathy, musculoskeletal, renal, neurological symptoms -Early latent: no signs/symptoms • Late syphilis: - Late latent: no signs/symptoms gumma formation (benign	Positive serology 4 weeks after infection (can take up to 12 weeks to develop).	• Early: single injection of penicillin (or other oral antibiotics for 10 days) and serological review monthly for 3 months • Late or unknown duration latent: weekly injections of penicillin for 3 doses (or other oral antibiotics for 17 days) and serological review until negative • All sexual contacts within past 3 months should be notified (extend to past 2 years if secondary/early latent syphilis)

STI	Aetiology	Sexual transmission	Natural history (untreated)	Clinical features	Diagnostic methods	Treatment/management ‡
			between 10-15 years, musculoskeletal or CVD after 15-20 years (10-30%), meningovascular or neurological disease after 2-25 years (5-12%)	granulation tissue) on skin, bones, oral cavities - CVD, disease associated with early and late neurosyphilis		• Avoidance of sex including with condoms until early lesions fully healed and until 2 weeks following treatment
Trichomonas (TV)	Parasitic (*T.vaginalis)*	Direct genital contact	Incubation period range 3-9 days. Overall self-limiting. Spontaneous resolution in 20-25%	NGU. Asymptomatic in up to 50%.	NAATs, culture, or direct microscopy of urethral smear/urine specimen	• Twice daily metronidazole for 7 days or single dose • Simultaneous treatment of sex partners within past 4 weeks • Avoidance of sex for ≤1 week until patient and partner(s) completed treatment
Not showing details for presentation of STIs in women, focus is on men only. CVD: cardiovascular disease; EIA; Enzyme-linked immunosorbent assay (see chapter 1); NAAT: nucleic acid amplification test;. ‡ Treatment as per UK national guidelines for each STI.						

Table VI.2: Aetiology, transmission, natural history, clinical features, and management of genital herpes and genital warts among males[450,451,453,454]

STI	Aetiology	Sexual transmission pathway	Natural history	Clinical features	Diagnostic methods	Management ‡
Genital herpes	Herpes simplex virus (HSV) type 1 and 2	Direct skin contact with infected oral mucosa (HSV-1) or genital mucosa (HSV-2)	Symptoms at acquisition of HSV-2 in up to 33%: incubation among them ranges 2 days-2 weeks. • Primary: 1st infection without pre-existing antibodies. Latency established in local sensory ganglia. • Recurrent: intermittent reactivation of latent virus with lesions (4-15 days) or asymptomatic shedding (18-55% of HSV-2, 10-29% of HSV-1). Significant morbidity if left untreated.	• Primary: Asymptomatic in >60%. Fever, malaise, myalgia within first week (50%). Painful blistering, ulcerative lesions in ano-, orogenital membranes. Urethral discharge/disuria (33%). Can also cause neurological involvement. • Recurring within first year in 90% of those with HSV-2, 60% HSV-1. Prodrome (skin tingling, nerve pain) up to 48 hours prior to lesion appearance (50%). Lesions confined to affected anogenital site.	• Clinical presentation • NAATS or PCR of genital lesion or rectal swab • Serology • Virus typing	• Primary: general advice, analgesics, antiviral management within 5 days of onset for 5 days. • Recurrent: typically mild and self-limiting, antiviral treatment can partially control symptoms and antiviral prophylaxis reduces recurrences. General advice and support. • Avoidance of sex during lesion recurrence or prodromes. Advice: transmission may occur with asymptomatic shedding; condom use may not completely prevent transmission. Disclosure encouraged.
Genital warts*	Human papillomavirus (HPV) - anogenital lesions caused by HPV types 6,11	Direct skin contact	Incubation period 3 weeks to 8 months for development of anogenital warts (benign epithelial skin tumours). Spontaneous clearance within 6 months (30%). Persistent infection with ≥1 high-risk HPV type can cause high grade dysplasia and progression to anogenital/oropharyngeal cancers.	• Majority asymptomatic. • New lumps/growths in anogenital area, local irritation, bleeding, discomfort, perianal lesions.	• Clinical presentation	• Topical cream/gel for 1 week (or up to 16 weeks depending on wart clearance rate) • Physical ablation (excision, cryotherapy, electrosurgery, laser treatment) • Consistent condom use advised • Prophylactic HPV vaccine

*Not showing details for presentation of STIs in women, focus is on males only. * Does not include oral warts. NAATs: nucleic acid amplification tests; PCR: polymerase chain reaction; ‡ Management as per UK national guidelines for each STI.*

Appendix VII. List of publications and conference presentations arising from this thesis

Publications

Daskalopoulou M, Rodger AJ, Phillips AN, Sherr L, Speakman A, Collins S, et al. Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: results from the cross-sectional ASTRA study. Lancet HIV. 2014 Sep;1(1):e22–31. **(Chapter 6)**

Lampe FC, Daskalopoulou M, Phillips AN, Speakman A, Johnson M, Gilson R, et al. Sexual behaviour among people with HIV according to self-reported antiretroviral and viral load status. Results from the ASTRA study. AIDS. 2016 Mar 31;30(11):1745–59. **(Chapters 4 and 5)**

Daskalopoulou M, Rodger AJ, Phillips AN, Speakman A, Lampe FC. Prevalence of recreational drug use is indiscriminate across antiretroviral regimens of differing drug–drug interactions among MSM. AIDS. 2016;30(5):810–2. **(Chapter 6)**

Daskalopoulou M, Lampe FC, Sherr L, Phillips AN, Johnson MA, Gilson R, et al. Non-Disclosure of HIV Status and Associations with Psychological Factors, ART Non-Adherence, and Viral Load Non-Suppression Among People Living with HIV in the UK. AIDS and Behavior. 2016 Jan 1;1–12. **(Chapter 7)**

Sewell J, Daskalopoulou M, Nakagawa F, Lampe FC, Edwards S, Perry N, et al. Accuracy of self-report of HIV viral load among people with HIV on antiretroviral treatment. HIV Med. 2016 Dec 22; DOI: 10.1111/hiv.12477 **(Chapter 4)**

Daskalopoulou M, Rodger AJ, Phillips AN, Sherr L, Elford J, McDonnell J, et al. Condomless sex in HIV-diagnosed men who have sex with men in the UK: prevalence, correlates, and implications for HIV transmission. Sex Transm Infect. In press. DOI: 10.1136/sextrans-2016-053029 **(Chapters 4 and 5)**

Conference presentations

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Daskalopoulou M, Rodger A, Thornton A, Phillips A, Sherr L, Gilson R, et al. Sexual behaviour, recreational drug use and hepatitis C co-infection in HIV-diagnosed men who have sex with men in the United Kingdom: results from the ASTRA study. J Int AIDS Soc. 2014 Jan;17(4 Suppl 3):19630. **(Chapter 8)**

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