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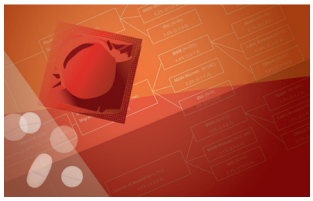

Illustration of a condom and different pills

European men who have sex with men still at risk of HIV infection despite three decades of prevention efforts

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More than 30 years have passed since the first description of Pneumocystis pneumonia in homosexual men in Los Angeles in 1981 [1], as one manifestation of a supposedly Gay-Related Immune Deficiency Syndrome and since the discovery of the underlying pathogen, the human immunodeficiency virus (HIV) in 1983 [2]. Since then countries have spent considerable resources to set up surveillance systems to obtain a better overview of the HIV/AIDS epidemic and to define the most affected population groups. In Europe, EuroHIV coordinated the surveillance of AIDS and later also HIV infection between 1984 and 2007. Since 2008, the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Regional Office for Europe have jointly coordinated HIV/AIDS surveillance in Europe and published an annual analysis of the data [3].

Men who have sex with men (MSM) have been identified as the group most at risk of HIV infection in the European Union (EU)/European Economic Association (EEA) and in the United States despite specifically targeted prevention programmes since the early years of the epidemic [4,5]. This can be explained by various factors. In this special issue of *Eurosurveillance*, published in two parts, articles from different European countries highlight a variety of factors and demonstrate how they impact the HIV/AIDS and sexually transmitted infections (STI) epidemics in MSM.

Frequent HIV testing among MSM was promoted already in the early stages of the HIV/AIDS epidemic as an important prevention measure and as having a significant benefit for the individual MSM [4,6]. Also today, the limited available evidence suggests that HIV testing uptake is higher in MSM than in other groups, such as heterosexuals, injecting drug users (IDU) and migrants in Europe [5]. Increasing numbers of newly diagnosed HIV infections in MSM could possibly be explained by increased testing, however, as seen in the trend analysis of 37,560 MSM from the United Kingdom (UK) in this issue, a true increase in incidence has taken place over the past 15 years [7]. Late presentation, defined as presenting with a CD4 count of <350 cells/mm^3 at date of diagnosis, was associated with increased risk of death within one year of diagnosis, particularly in MSM over 50 years in the UK [7]. Although the authors found that linkage to care had improved in recent years in the UK, culturally and linguistically appropriate services still need to be improved to enhance testing and to reduce late presentation of disease. Similarly, Diaz et al. studying determinants of late presentation (LP) with HIV infection among MSM presenting to 15 STI/HIV counselling and testing clinics in Spain, found that late presentation was particularly common among migrants from Latin America with low levels of education. The authors recommend targeted efforts to increase HIV testing uptake in those at risk groups [8]. In another Spanish study, Belza et al., showed that street-based rapid HIV testing can reduce the time of undiagnosed infections due to the high visibility and low threshold of the testing facilities, however, they recommend concentrating this type of testing in locations highly frequented by persons at higher risk [9].

Certain practices and behaviours increase the risk of MSM becoming infected with HIV or STIs. In a study investigating the diversity of practices and behaviours to prevent HIV with casual sexual partners in a large convenience sample of almost 7,000 MSM in France, Velter et al. found that many MSM persisted in engaging in high-risk practises and that seroadaptive strategies became common in the antiretroviral treatment (ART) era [10]. Seroadaptive practises are risk-reduction practises developed in order to reduce the risk of transmission, such as serosorting, where unprotected anal intercourse (UAI) is practiced with partners with same serostatus, and seropositioning, where the HIV-negative partner represents the insertive part in anal intercourse [10]. Within the Lisbon cohort, participants enrolled in an open cohort of HIV-negative MSM enrolled after testing at a community-based voluntary HIV counselling and testing centre in Lisbon. The authors followed 804 MSM for a total of 893 person-years and found that newly adopted UAI with a regular partner as well as persistent UAI with occasional partners and new syphilis infections were significantly associated with increased HIV seroconversion [11].

Presence of a STIs increases the risk of HIV transmission and infection [12], thus acting as another catalyst for the increase in HIV infections in MSM. In England, an analysis of the Genitourinary Medicine Clinic Activity Dataset for the years 2008 to 2013, found that HIV-positive MSM had high rates of STI, with almost one in five of all diagnosed HIV-positive MSM having an acute STI in 2013 and increasing trends since 2009. Numbers were four times higher than in HIV-negative or undiagnosed MSM. Malek et al. conclude based on their findings that the sexual health of MSM is worsening in England [13].

More efforts are needed in certain societies where this risk group is harder to reach to better understand the epidemic and its drivers. Internet-based sampling (IBS) and recruitment can be used to gather data and improve HIV and STI testing in countries without dedicated STI services for MSM, as shown by Ruutel et al. from Estonia [14]. The authors managed to attract 301 respondents of whom 88% self-identified as MSM. Although only 26% of these went on to accept the offer of testing, this study demonstrated the feasibility of linking the Internet-based collection of behavioural data for MSM with biological sampling for HIV, hepatitis and a variety of STIs. In another study, Wirtz et al. used respondent-driven sampling (RDS) to supplement IBS to recruit 124 MSM for HIV counselling and testing (including for syphilis and human papilloma virus (HPV)) in Moscow, Russia. Taking advantage of a larger cross-sectional study where participants were invited for HIV and syphilis tests after completion of the behavioural, interviewer-administered survey, Wirtz et al. embedded a study to look into anal cytology and HPV genotyping as well as to obtain additional specimens for possible urethral, oral and rectal gonorrhoea and chlamydia infections. Again, infections with high-risk HPV types were more common in HIV-positive MSM and were strongly associated with behavioural risk and low healthcare access [15].

A systematic literature review by Strömdahl et al. [16] looked into the latest available evidence for various interventions aimed at preventing HIV and STIs in MSM in Europe. They looked at twenty-four HIV prevention interventions and of these four interventions were assigned a Highest Attainable Standard of Evidence (HASTE) grade 1: condom use, treatment as prevention, peer-led group interventions and peer outreach within the MSM community. In all, 15 interventions were graded to be strongly, probably or possibly recommended. This review provided the evidence-base and, together with extensive rounds of expert opinions and consultation, formed the basis for the development of a guidance document on this subject by the European Centre for Disease Prevention and Control [17].

The clear and persisting increases in HIV infections and STIs in MSM over the last decade, despite many prevention efforts, are a cause for concern. We see the need for renewed efforts and investment in evidence-based targeted and combined prevention measures among MSM. These targeted interventions, coupled with good monitoring and evaluation of the programmes will be essential if the steady rise in HIV infections and STIs among MSM is to be reversed any time soon.

Conflict of interest

None declared.

Authors' contributions

KH and AJAG jointly drafted the manuscript and both approved the final version.

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An overview of the HIV epidemic among men who have sex with men in the United Kingdom, 1999–2013

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We describe epidemiological trends in HIV among men who have sex with men (MSM) in the United Kingdom (UK) to inform prevention strategies. National HIV surveillance data were analysed for trends. Multivariable analyses identified predictors of late diagnosis (<350 copies/µL) and mortality. Between 1999 and 2013, 37,560 MSM (≥15 years) were diagnosed with HIV in the UK. New diagnoses rose annually from 1,440 in 1999 to 3,250 in 2013. The majority of MSM were of white ethnicity (85%) and UK-born (68%). Median CD4 count increased steadily from 350 cells/µL to 463 cells/µL. HIV testing in England increased from 10,900 tests in 1999 to 102,600 in 2013. One-year death rates after diagnosis declined among late presenters (4.7% to 1.9%). Despite declining late diagnosis (50% to 31%), the number of men diagnosed late annually has remained high since 2004. Older age (≥50 years), and living outside London were predictors of late presentation; older age and late presentation were predictors of one-year mortality. Increases in new diagnoses reflect increased testing and ongoing transmission. Over 900 men present late each year and mortality in this group remains high and preventable. Appropriate prevention and testing strategies require strengthening to reduce HIV transmission and late diagnosis.

Introduction

In the United Kingdom (UK), as in many other western countries with concentrated HIV epidemics, sex between men is the most important mode of HIV transmission [1]. National HIV/AIDS surveillance was established and coordinated at Public Health England (PHE) (formerly the Health Protection Agency) at the beginning of the 1980s, and has allowed comprehensive understanding and description of the epidemic in the UK [2]. Since the first reports of HIV in the early 1980s, men who have sex with men (MSM) have remained the group most at risk of acquiring HIV in the UK. By the time an HIV antibody test became available in 1984, over 2,000 men had been reported with an AIDS diagnosis. In the late 1980s and early 1990s, the annual number of new HIV/AIDS cases plateaued but remained high at 1,620 cases, on average, annually [2]. This period was also marked by a rapid increase in deaths until the availability of effective treatment in the mid-1990s, which resulted in a marked decline in mortality reports.

Trends in new diagnoses must be interpreted in the context of HIV testing patterns. In the UK, HIV testing services are free and confidential, regardless of residency status, and cross-sectional surveys indicate that the large majority of MSM prefer to undergo HIV testing at sexually transmitted infection (STI) clinics (A Nardone, personal communication, August 2014). Once diagnosed, quality of care is excellent with high retention rates and a near-normal life expectancy among persons diagnosed early [3]. We review 15-year epidemiological trends in HIV diagnoses and testing patterns among MSM to assess the success of prevention efforts and testing strategies. We calculate mortality rates within a year of diagnosis, and in a multivariable model we investigate predictors of late presentation and assess its impact on mortality within one year of diagnosis.

Methods

Data sources and quality

We define MSM as men who have ever had sexual contact with another man. The term describes sexual behaviour, regardless of how men perceive their sexual identity. Information on MSM ('men' hereafter) newly diagnosed with HIV between 1999 and 2013 in the UK was obtained from the national HIV and AIDS Reporting System (HARS) held at PHE [4]. HARS has three national surveillance components that collect demographic and clinical information on adults (aged 15 years and older) newly diagnosed with HIV infection from clinicians and/or laboratories and prospective clinical information (CD4 counts, viral loads, antiretroviral therapy (ART) status) annually collated for all adults seen for HIV care and supplementary CD4 counts from laboratories in England, Wales and Northern Ireland. Scottish data are provided separately by Health Protection Scotland, and subsequently incorporated to create a UK dataset.

Although national reporting of HIV is not mandatory, returns are linked to commissioning of HIV services and therefore are timely and of high completeness. From triangulation of the data sources, annual loss-to-follow-up is less than 5% [5], ensuring that HARS' coverage is above 95%. Notification delay is minimal (<2%) and national figures are not adjusted for delay. AIDS diagnoses and deaths are also reported by clinicians. All-cause mortality for people aged up to 65 years is supplemented from the Office for National Statistics (ONS) death register. Data are linked to HARS using limited patient identifiers (sex, date of birth and Soundex (scrambled surname code [6]). No names are collected on HIV databases kept at PHE and data are kept securely within data protection regulations.

Missing information on probable route of transmission is routinely adjusted for by calculating and applying the proportional distribution of each known exposure group to the overall number of new diagnoses in a given year. Missing exposure information is higher in recent years (11.5%, 690/6,000 in 2013 vs 0.9%, 30/3,248 in 1999). We present trends in the overall number of new diagnoses reported annually. Unless specified, we present observed data for all sub-analyses of new diagnoses among men.

Over the past 15 years, completion rates for ethnicity, country of birth and probable country of infection (PCOI) were 99% (35,923/36,340), 86% (31,318) and 70% (25,352), respectively. CD4 counts were available for 89% (32,349) of new diagnoses with 85% (31,000) available within three months of diagnosis. To address potential selection biases in completeness of the country of birth field (particularly evident in the earlier years) we calculated a lower estimate of men born in the UK by assuming that all men with a missing country of birth were born abroad, and an upper estimate by assuming all men with missing data were born in the UK. For men born abroad, a published algorithm incorporating information on age, ethnicity, year of arrival in the UK, and CD4 count at diagnosis was used to ascertain and report whether men were infected abroad or in the UK [7]. These adjusted figures are only produced nationally. Elsewhere, observed data on men infected abroad are presented.

Aggregate data on the number of HIV tests performed in STI clinics reported to PHE were used for the years 1999 to 2008 (known as KC60 returns), and after which testing data were reported as part of a disaggregate dataset (known as Genitourinary medicine clinic activity dataset version 2 (GUMCADv2)). KC60 returns included HIV diagnoses and other services provided by all STI clinics in the UK by risk group and for MSM for all ages only. Since 2008, GUMCADv2 has replaced KC60 returns and captures patient-level data, including demographic and clinical history information, on all STI clinic attendees but for England only [4]. As a result we present trends in overall HIV testing data among men attending STI clinics in England for the past 15 years and by age groups for the period 2009–2013.

Definitions

All persons newly diagnosed with HIV infection have confirmatory laboratory evidence of anti-HIV antibodies. A late HIV diagnosis was defined as having a CD4 count<350 cells/µL within 91 days of diagnosis. One-year mortality was calculated using all-cause mortality within twelve months of a HIV diagnosis among newly diagnosed men in a given year and both measures were expressed as percentages with 95% confidence intervals (CI).

Statistical analysis

Descriptive analyses were conducted on trends in new diagnoses and late diagnoses. Changes over time were investigated using the chi-squared test for trend and non-parametric trend analysis was conducted to investigate changes over time within groups. Non-parametric analysis was conducted to examine trends in median CD4 count at diagnosis.

Univariate analysis was performed to explore associations between demographic attributes and late diagnosis. Variables with marginal associations ($p<0.10$) were included in multivariable logistic regression analyses, where a stepwise backward approach was used to sequentially remove variables not significant ($p\geq0.05$) in order of the p value magnitude. For significant ($p<0.05$) risk factors, adjusted odds ratios (OR) and 95% CI were reported. All statistical analyses were conducted using Stata 13.1 (StataCorp, College Station, TX).

Results

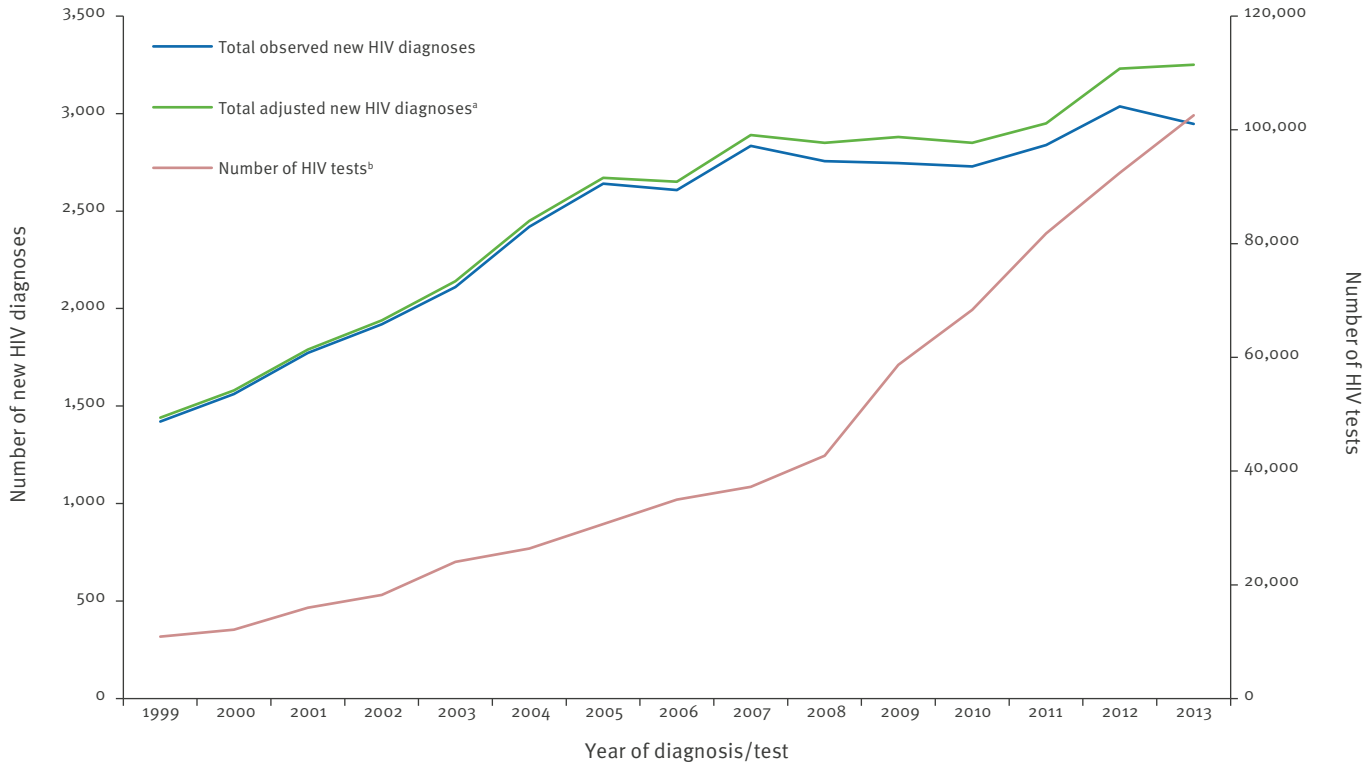
Fifteen-year trends in the demographic profile of new diagnoses and HIV tests in sexually transmitted infection clinics

Between 1999 and 2013, 37,560 (adjusted) new HIV diagnoses were reported among MSM in the UK, representing 61% of all MSM diagnosed since the beginning of the epidemic. New diagnoses rose steadily throughout the 15 years, reaching an estimated 3,250 (adjusted) in 2013 compared with 1,440 (adjusted) in 1999 (Figure 1). Among the 36,340 observed new HIV diagnoses, 33,341 (93%) were diagnosed in England, 1,710 (4.7%) in Scotland, 801 (2.2%) in Wales and 450 (1.2%) in Northern Ireland. The number of HIV tests performed in MSM attending STI clinics across England increased almost 10-fold from 10,900 in 1999 to 102,600 in 2013 (Figure 1), with a steeper rise in testing volume since 2009.

The median age at diagnosis remained constant at 35 years throughout the period (interquartile range (IQR): 28–42)) ($p=0.64$). Annual diagnoses significantly increased in all age groups but increased almost fourfold among younger men (15–24 years, from 131 to 462, $p<0.001$) and almost threefold among men aged ≥50

Figure 1

Numbers of new HIV diagnoses and HIV tests (England only), men who have sex with men, United Kingdom, 1999–2013



[a] Data adjusted for missing risk

[b] Number of HIV tests in England

years (from 115 to 308, p<0.001). Nevertheless, collectively, three quarters of all diagnoses were reported among men aged 25–34 years (38%) and 35–49 years (40%).

Overall, the majority of men were white (85%), with some annual change. While absolute numbers were small, among those of other ethnicities, there has been a significant year-on-year increase in new diagnoses among Asian (including Indian sub-continent, Chinese and other Asian) and black African men (p<0.001). Diagnoses among black-Caribbean men remained low (annual average: 60, standard deviation (SD): 13.2).

Almost half of all new diagnoses were made in London over the period, although the annual proportion has significantly declined over time from 57% (815/1,421) in 1999 to 50% (1,465/2,947) in 2013 (p<0.001). Overall, diagnoses increased by 34% in England compared with 53% in England excluding London.

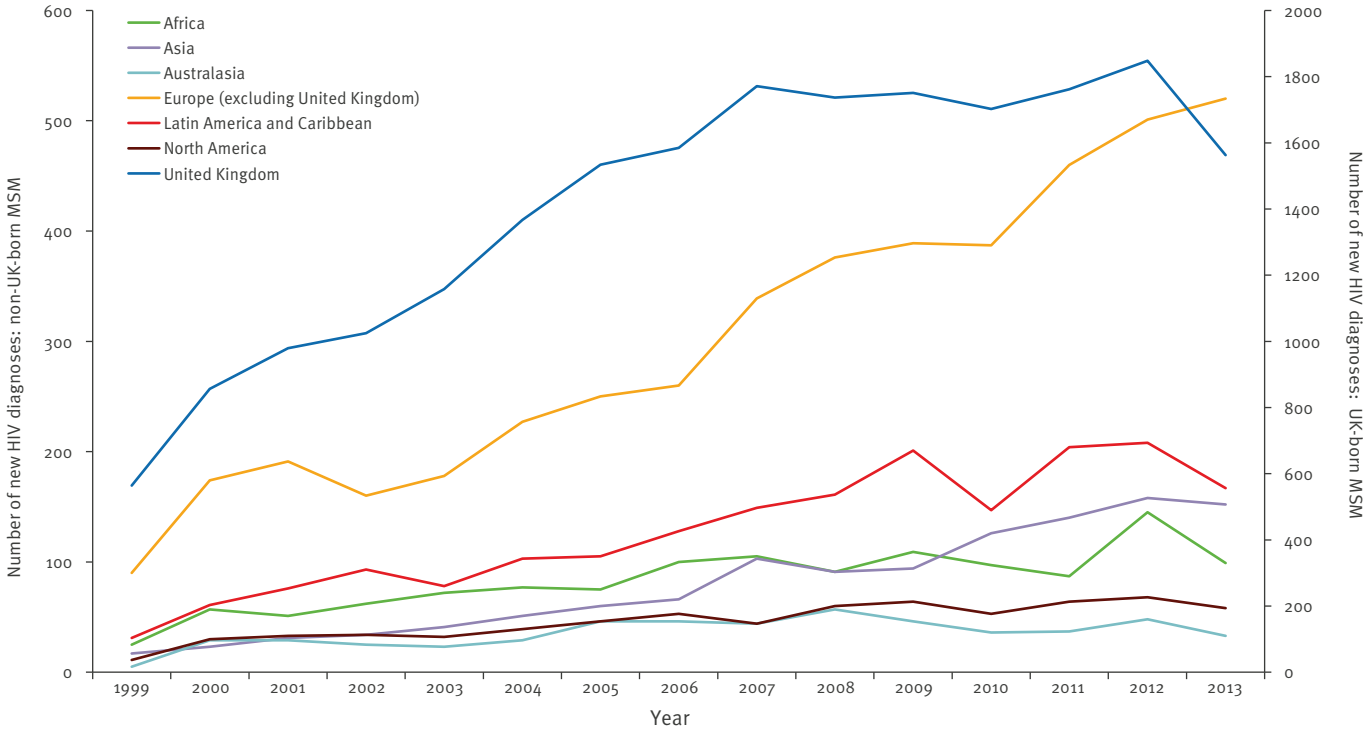
An estimated 68% (21,202/31,318) of new diagnoses were among men born in the UK (range: 58% to 72% when adjusting for missing information). However, diagnoses among men born in other European countries rose from 12% (90/743) of all diagnoses in 1999 to 20% (520/2,593) in 2013 (Figure 2). Over half of all new diagnoses among European men (n=4,502) were among men born in Spain (15%), Italy (13%), Ireland (10%), France (10%) and Poland (10%). Outside Europe, a small but significantly increasing proportion of all diagnosed men was born in Asia (2.2% (n=17/743) in 1999 to 5.9% (n=152/2,593) in 2013, p<0.001) and in Latin America (2.8% (21/743) to 5.3% (n=137/2,593), p=0.01) (Figure 2). Overall, two thirds of non-UK-born men were white compared with 94% of UK-born men.

Over the period, two thirds of diagnoses (15,803/24,082) were in UK-born men who probably acquired their infection in the UK; the figure for 2013 was 59% (1,173/2,005). Of the 1,629 of men diagnosed in 2013 who probably acquired their infection in the UK, 72% were UK-born and 12% were born in other European countries. In comparison, only 16% of men who were probably infected outside the UK were born in the UK (p<0.001).

The median CD4 count at diagnosis steadily increased from 350 cells/mm^3 (IQR: 155–530) to 463 cells/µL (IQR: 307–641) over the 15 years (p<0.001). A statistically significant increase was observed among all age groups except the youngest men and the incline was steepest among men aged ≥50 years (Figure 3). Throughout

Figure 2

Number of new HIV diagnoses by region of birth, men who have sex with men, United Kingdom, 1999–2013



MSM: men who have sex with men; UK: United Kingdom.

the 15 years, median CD4 count at diagnosis remained highest among men aged 15–24 years.

In the last five years, the number of men testing annually has steadily increased in all age groups with the slowest increase among 35–49 year-olds (46% vs 69% among 25–34 and ≥ 50 year-olds and 84% among 15–24 year-olds) (Figure 4). Concurrently, new diagnoses among men of this age group and those aged 50 years and above have remained stable. The greatest increases in testing and new diagnoses were observed among the youngest men.

Late HIV diagnoses

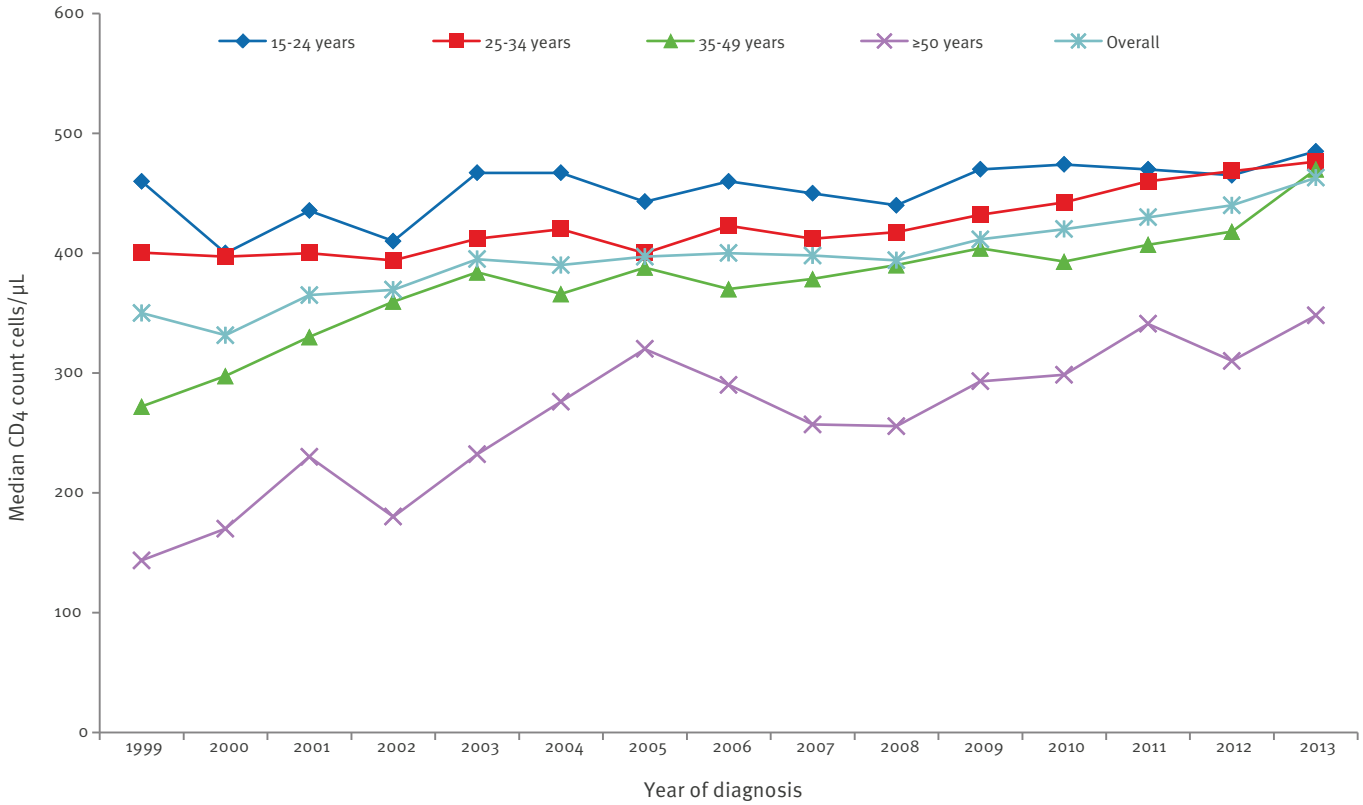
The proportion of men diagnosed late was 40.8% (95% CI: 40.2 to 41.3) overall with a decline observed over time (from 50% (95% CI: 47 to 53) in 1999 to an estimated 31% (95% CI: 29 to 33) in 2013) ($p<0.001$). The decline was particularly striking by age and ethnicity. Among 25–34 year-olds and those aged 50 years and above, late diagnosis declined from 42% (95% CI: 37 to 46) to 26% (95% CI: 24 to 29) and from 78% (95% CI: 69 to 88) to 50% (95% CI: 44 to 56), respectively. Among men of black (Caribbean, African and other black (defined as black ethnicities not captured by Caribbean and African ethnicities e.g. black British, black American)) ethnicity, the proportion declined from 69% (95% CI: 55–82) in 1999 to 35% (95% CI: 27 to 43) in 2013.

The absolute number of annual late HIV diagnoses, however, remained steady (average: 936; SD: 67) since 2004 (Figure 5) including among black men (average: 55; SD: 11). The drop in numbers in 2013 could be due to more missing CD4 count information (2013: 8% vs 2012: 5.6%). There were important differences by demographic variables. The number of late HIV diagnoses increased in men aged 50 years and over from 111 in 2004 to 183 in 2009 and then declined to 140 in 2013. An increase was also evident among men who probably acquired their infection in the UK, from 454 in 2004 to 689 in 2007 (after which the number remained stable). In multivariable analyses, in 2013 older men and those living outside London were more likely to present late (Table 1). Men who acquired their infection outside the UK were no less likely to be diagnosed late.

One-year mortality from HIV diagnosis decreased from 4.6% (95% CI: 3.5–5.8) in 1999 to 0.9% (95% CI: 0.6–1.3) in 2013. The decline was largely due to reduced mortality among men diagnosed late from 4.7% (95% CI: 3.1–6.9) in 1999 to 1.9% (95% CI: 1.1–3.1) in 2013 ($p<0.001$) (Figure 5). Among men diagnosed with CD4 counts < 200 cells/μL, mortality declined from 6.6% (95% CI: 4.1–10.0) in 1999 to 3.8% (95% CI: 2.1–6.3) in 2013 ($p=0.005$), and from 2.0% (95% CI: 0.5–4.9) to 0.2% (95% CI: 0.006–1.3) with CD4 counts between 200 and 349 cells/μL at diagnosis ($p=0.02$). Mortality remained highest among men diagnosed late aged

Figure 3

Median CD4 count at diagnosis by age group, men who have sex with men, United Kingdom, 1999–2013



50+(13%, 95% CI: 5.8–24.2 in 1999 to 8.6%, 95% CI: 4.5–14.4 in 2013), followed by 35–49 year olds (3.9%, 95% CI: 1.8–7.3 to 1.0%, 95% CI: 0.2–2.9). In 2013, in multivariable analyses, older age and a late diagnosis were predictors of dying within a year of being diagnosed (Table 2).

Discussion

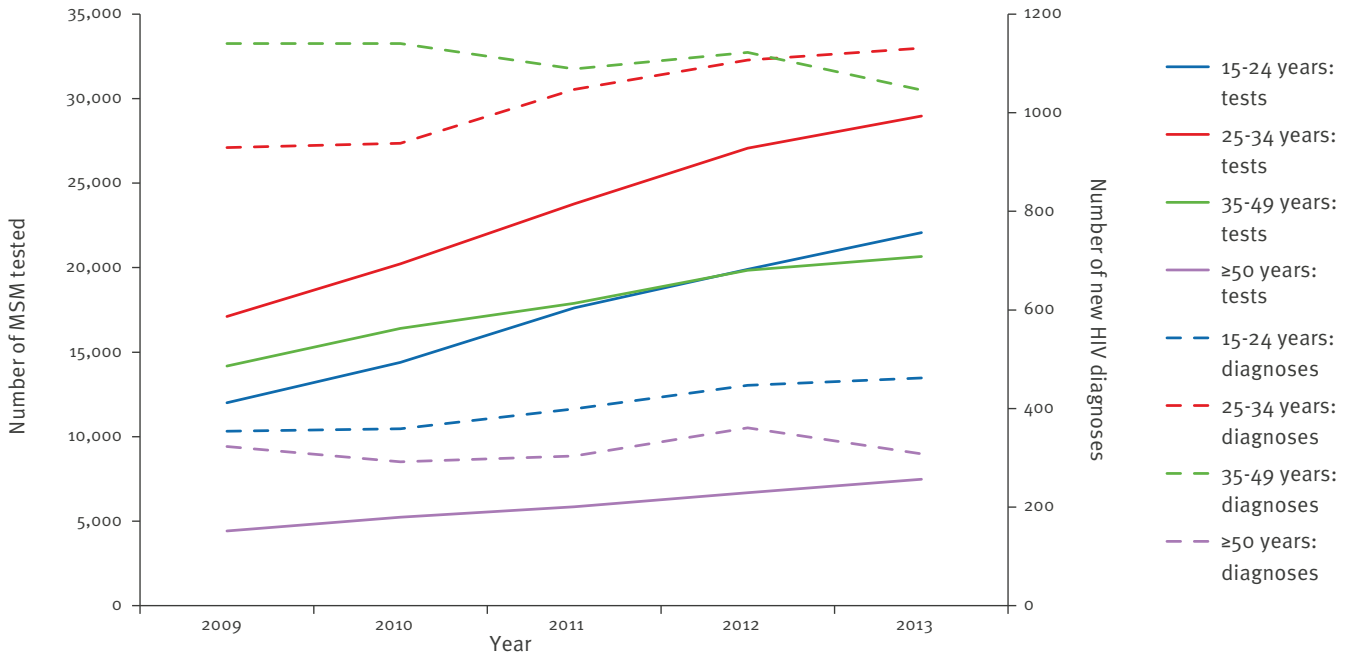
Despite targeted interventions aimed at reducing HIV infections in the UK since the early 1980s, the past 15 years of the epidemic have seen year-on-year rises in new diagnoses among MSM, with a record 3,250 new diagnoses in 2013. On a positive note, alongside this rise, the volume of HIV tests performed in STI clinics also increased to over 100,000 tests in 2013 and the proportion diagnosed late declined to an estimated 31%. Of concern is the continued high numbers of late presenters and high mortality rate in the year following a HIV diagnosis in this group.

We observed the greatest increases in new diagnoses among younger men. This rise is probably due to sustained HIV transmission as well as increased HIV testing. New diagnoses among younger men are often used as a proxy of incidence, as the time interval between diagnosis and infection is shorter than for older ages. This is also supported by the high median CD4 count at diagnosis in this group, which is indicative of recent infection. During the same period, the number of HIV tests performed increased almost 10-fold and this is reflected in the decline in time-to-diagnosis interval from 4 years in 2001 to 3.2 years in 2010 [8]. From the age-specific HIV testing data, testing among younger men has also steadily increased. Despite this increase in HIV testing, the number of HIV tests performed in 2011 only equated to an estimated HIV test coverage of<10% of the male population in England [9]. Safer sex campaigns with HIV testing and other prevention strategies must be promoted to make an impact on the increasing trends in new diagnoses.

Although surveillance systems differ between countries, new diagnosis trends among men in the UK are broadly comparable to those observed in other European countries [10-12]. This has resulted in an overall increase in new HIV diagnoses among men reported by the European Centre for Disease Prevention and Control (ECDC): with a 36% increase in new diagnoses observed between 2003 and 2008 in Europe [13]. While an increase among younger men has been reported in other countries, the pattern in new diagnoses among older men is varied [13]. Without concurrent HIV testing data, it is difficult to interpret the rise in new diagnoses reported in other countries. In Norway, the rise has been attributed to increased transmission rather than HIV testing [10]. A proportional decline in late diagnosis among men has been reported across Europe in recent years [13-15]; in central Europe from

Figure 4

Number of men who have sex with men tested in sexually transmitted infection clinics, England, and number of new HIV diagnoses, United Kingdom, by age group, 2009–2013



MSM: men who have sex with men.

Figure 5

Late HIV diagnosis and one-year mortality, United Kingdom, 1999–2013

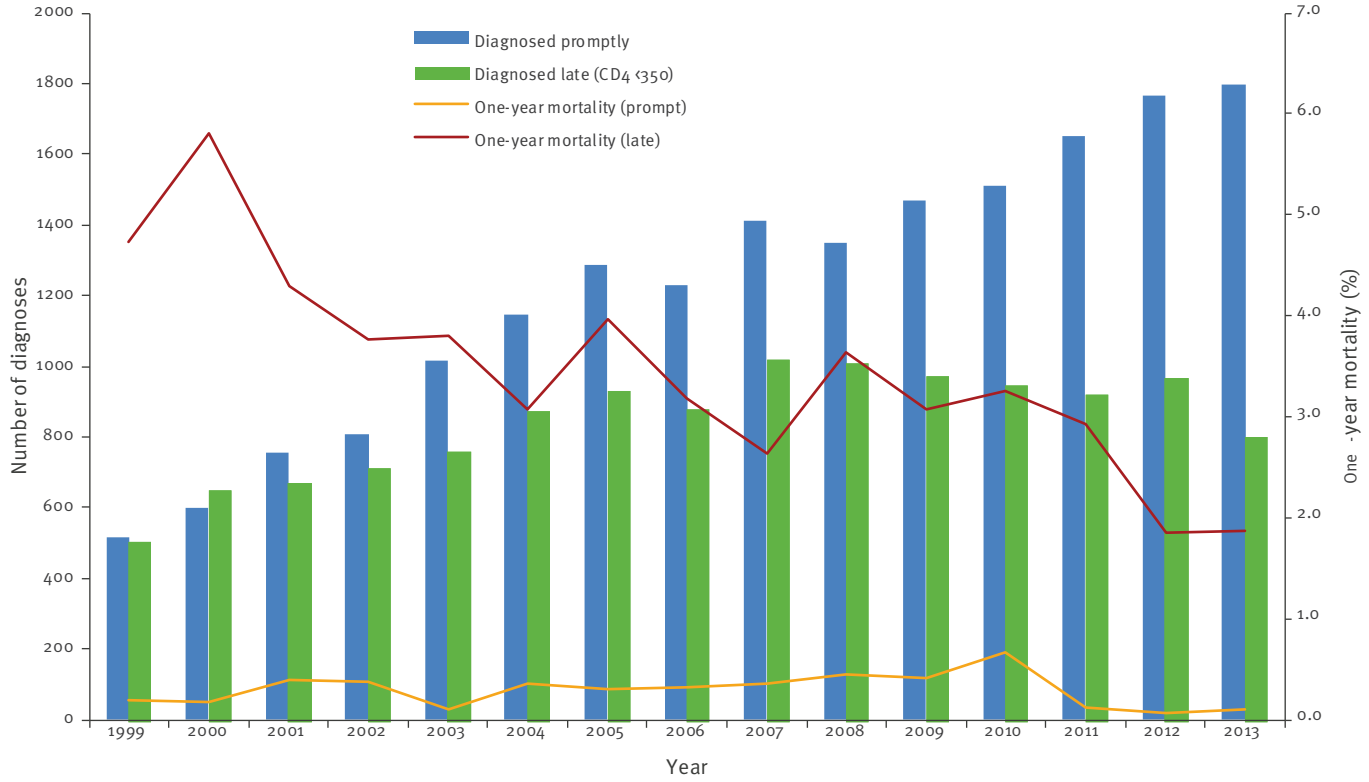


Table 1

Multivariable analyses for late HIV diagnosis among men who have sex with men, United Kingdom, 2013 (n=2,602)

Variable		N[a] (%) (n=2,602)	Number diagnosed late (%)[b] (n=802)	Late HIV diagnosis		
				Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
Residence	Elsewhere, UK	1,231 (47)	457 (37)	1	1	<0.001
	London	1,371 (53)	345 (25)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	
Age group	15–24 years	407 (16)	98 (24)	1	1	<0.001
	25–34 years	1,000 (38)	263 (26)	(0.9–1.5)	1.2 (0.9–1.6)	
	35–49 years	916 (35)	301 (33)	1.6 (1.2–2.0)	1.7 (1.3–2.2)	
	≥50 years	279 (11)	140 (50)	3.2 (2.3–4.5)	3.2 (2.3–4.4))	
Ethnicity[c]	White	2,035 (81)	631 (31)	1	n.a.	n.a.
	Black African	61 (2.4)	22 (36)	1.2 (0.7–2.1)	n.a.	
	Black Caribbean	64 (2.6)	21 (33)	1.1 (0.6–1.8)	n.a.	
	Black other	32 (1.3)	12 (38)	1.3 (0.6–2.7)	n.a.	
	Asian	144 (5.7)	40 (28)	0.8 (0.6–1.2)	n.a.	
	Other	171 (6.8)	50 (29)	0.9 (0.6–1.3)	n.a.	
UK-born	No	924 (40)	245 (27)	1	n.s.	0.102
	Yes	1,372 (60)	481 (35)	1.5 (1.3–1.8)	n.s.	
UK-acquired infection	No	376 (18)	105 (28)	1	n.a.	n.a.
	Yes	1,689 (82)	533 (32)	1.2 (0.9–1.5)	n.a.	

CI: confidence interval; n.a.: not applicable (not included in multivariable analyses); n.s.: not significant; OR: odds ratio; UK: United Kingdom.

[a] Only includes men with CD4 count information.

[b] Late diagnosis defined as a CD4 count <350 cells/µL within 91 days of HIV diagnosis.

[c] Ethnicities as reported by clinicians. 'Black other' includes black ethnicities not captured by Caribbean and African ethnicities e.g. black British, black American. 'Asian' includes Indian sub-continent, Chinese and other Asian ethnicities and 'other' includes mixed ethnicity.

52% in 2000 to 40% in 2008 and in northern Europe from 48% to 39% [14].

Disappointingly, the annual number of men diagnosed late has remained high and stable throughout the decade and in 2013, one in three men was still diagnosed late, at the threshold at which treatment is recommended. As total numbers of new diagnoses have increased, stable numbers of late diagnoses suggest those additional annual diagnoses are probably being diagnosed promptly through repeat testing and/or recent acquisition. In multivariable analysis, older men were more likely to present late and be at increased risk of death within a year of diagnosis. Others have also found increasing age to be a predictor for late diagnosis [15,16]. This finding is likely to reflect both delay in diagnosis and steeper CD4 declines following HIV infection in older men [17]. Poorer health outcomes among older adults diagnosed with HIV infection has been previously documented in this population [18]. Together these findings underscore the importance of reaching men who are not regularly testing for HIV and ensuring a prompt diagnosis and access to HIV care and treatment for all men regardless of age.

Reductions in late diagnoses can be achieved through a higher HIV testing coverage. Since 2008, national HIV testing guidelines recommended expanding and normalising HIV testing beyond STI clinics into medical services in areas where diagnosed HIV prevalence is above the threshold of two per thousand among 15–59 year olds [19], and have advocated the development of local strategies to offer HIV testing to men [20]. In addition, late diagnosis of HIV infection has been selected as a key indicator of Public Health Outcome Framework in England since 2010 [21]. Despite these recommendations, there is little evidence to date of local initiatives to expand HIV testing beyond STI clinics [22] and an estimated 8,000–9,000 men remain undiagnosed annually across the UK [8]. The numbers undiagnosed has remained stable throughout the decade and modelling suggests that the large majority of transmissions come from men unaware of their infection [23].

The decline in one-year mortality is an important achievement as it implies that linkage and retention in HIV care have improved, especially among men diagnosed late. The decline also reflects changes to national recommendations on ART initiation. In 2008, the recommendation to initiate treatment was amended from CD4 cell counts <200 to <350/µL [24]. Nevertheless a mortality of 2% among those diagnosed late is alarmingly high when compared with 0.1% among men diagnosed promptly. These findings highlight the importance of prompt diagnosis and ART initiation.

Table 2

Multivariable analyses for one-year mortality among men who have sex with men, United Kingdom, 2013 (n=2,195)

Variable		Number dying within a year of diagnosis (n=27)	One-year mortality[a] (%)	Late HIV diagnosis		
				Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
Residence	Elsewhere, UK	19	1.2	1	n.s.	0.652
	London	8	0.6	0.4 (0.2–1.0)	n.s.	
Age group	15–24 years	1	0.2	1	n.a.	<0.001
	25–34 years	2	0.2	0.8 (0.07–9.0)	1[b]	
	35–49 years	4	0.4	1.8 (0.2–15.9)	2.8 (0.3–26.9)	
	≥50 years	20	6.5	32.0 (4.2–239.8)	30.9 (4.0–239.8)	
Ethnicity[c]	White	25	1.1	1	n.a.	-
	Black African	0	0	[d]	n.a.	
	Black Caribbean	0	0	[d]	n.a.	
	Black other	0	0	[d]	n.a.	
	Asian	0	0	[d]	n.a.	
	Other	1	0.5	0.5 (0.06–3.5)	n.a.	
UK-born	No	3	0.3	1	n.s.	0.239
	Yes	19	1.2	4.2 (1.2–14.3)	n.s.	
UK-acquired infection	No	1	0.2	1	n.a.	n.a.
	Yes	15	0.8	3.5 (0.5–26.3)	n.a.	
Late diagnosis	No	2	0.1	1	1	0.003
	Yes	15	1.8	17.1 (3.9–74.9)	9.9 (2.2–44.1)	

CI: confidence interval; n.a.: not applicable (not included in multivariable analyses); n.s.: not significant; OR: odds ratio, UK: United Kingdom.

[a] One-year mortality defined as all-cause mortality within twelve months of a HIV diagnosis among newly diagnosed men in a given year.

[b] Men who have sex with men aged 15–24 years old were excluded from multivariable analyses due to missing CD4 information, and 25–34 year-olds were used as the reference group.

[c] Ethnicities as reported by clinicians. Black other includes black ethnicities not captured by Caribbean and African ethnicities e.g. black British, black American. Asian includes Indian sub-continent, Chinese and other Asian ethnicities and other includes mixed ethnicity.

[d] No deaths within a year of diagnosis.

While white, UK-born men aged 25-49 years account for the majority of new HIV diagnoses over the 15 years, the HIV epidemic among MSM has diversified. The largest increases in new diagnoses have been among the youngest and oldest age groups and in 2013 these accounted for 16% and 11% of new diagnoses, respectively. The ethnic composition of the epidemic has also expanded with greater numbers of men originating from Asia and central and eastern Europe; in 2013 more than one third of men diagnosed with HIV infection were born abroad. A similar diversity is apparent among men diagnosed late, where a substantial number were of black ethnicity. Importantly, our estimates of country of infection indicate that 66% of men born abroad probably acquired their HIV infection in the UK. MSM from ethnic minority groups in the UK may face additional challenges including discrimination and isolation. It is therefore vital that prevention programmes provide culturally and linguistically appropriate services for this diverse population of gay and bisexual men and other men who have sex with men.

There are several strengths to our study. The study population is based on comprehensive national surveillance data from multiple sources linked to all-cause deaths reported to the Office of National Statistics. Data quality and completeness are high overall. Nevertheless, there are several limitations. First, some variables were less complete than others. For example, 14% of men did not have information on country of birth and 15% were missing CD4 cell count within three months of diagnosis. Reassuringly, no differences were observed between men with and without country of birth or CD4 information (data not shown). Second, linkage between our national HIV surveillance system and the ONS death register does not capture all deaths. However, the remaining deaths are actively followed up to ensure the surveillance system captures the majority of deaths. Third, HIV testing data were only available for STI clinics. However, STI clinics test over half of all individuals for HIV [25] and the majority of new HIV diagnoses among MSM are made in STI clinics [26]; therefore, although MSM can test at other sites, we do not expect substantial HIV testing outside STI clinic settings. Finally, HIV testing data were not available for UK for the entire period and before 2009, testing data for England were not available by age group. We are therefore unable to fully investigate whether

the increase in new diagnoses among the youngest and oldest men can be accounted for by increases in HIV testing. However, 93% of all new HIV diagnoses between 1999 and 2013 were reported in England with very little variation in recent years. Trends in new HIV diagnoses in Scotland, Wales and Northern Ireland also follow the same trend as in England (data not shown). For these reasons, we do not believe the exclusion of HIV testing data from the other UK countries would have significantly affected our analyses.

In summary, in the past 15 years of the epidemic in the UK, our data indicate that new HIV diagnoses have continued to rise due to increased testing and high rates of ongoing transmission. Late diagnosis and older age are important predictors of mortality. Despite a decline in late diagnosis, over 900 men present late each year and one-year mortality remains high in this group. Culturally appropriate prevention and testing strategies that are sensitive to a diversifying population require strengthening to reduce HIV transmission and late diagnosis.

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Conflicts of interest

None declared.

Authors' contributions

SD led on the data analysis and drafting of the manuscript supported by SC, AB, GH and VD. HM provided HIV testing data. All authors commented on drafts of the manuscript and approved the final version.

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Contribution of transmission in HIV-positive men who have sex with men to evolving epidemics of sexually transmitted infections in England: an analysis using multiple data sources, 2009–2013

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HIV seroadaptive behaviours may have contributed to greater sexually transmitted infection (STI) transmission in HIV-positive men who have sex with men (MSM) and to the global increase in STIs. Using multiple national surveillance data sources and population survey data, we estimated the risk of STIs in HIV-positive MSM and assessed whether transmission in HIV-positive MSM has contributed to recent STI epidemics in England. Since 2009, an increasing proportion of STIs has been diagnosed in HIV-positive MSM, and currently, the population rate of acute bacterial STIs is up to four times that of HIV-negative or undiagnosed MSM. Almost one in five of all diagnosed HIV-positive MSM in England had an acute STI diagnosed in 2013. From 2009 to 2013, the odds of being diagnosed with syphilis increased from 2.71 (95% confidence interval (CI) 2.41–3.05, p<0.001) to 4.05 (95% CI 3.70-4.45, p<0.001) in HIV-positive relative to HIV-negative/undiagnosed MSM. Similar trends were seen for gonorrhoea and chlamydia. Bacterial STI re-infection rates were considerably higher in HIV-positive MSM over a five-year follow-up period, indicative of rapid transmission in more dense sexual networks. These findings strongly suggest that the sexual health of HIV-positive MSM in England is worsening, which merits augmented public health interventions and continued monitoring.

Introduction

The United Kingdom (UK) has seen a steady increase in diagnoses of sexually transmitted infections (STIs) in the last decade, in particular, in men who have sex with men (MSM). From 2012 to 2013, gonorrhoea and syphilis diagnoses in MSM increased by 26% and 12% respectively [1]. The emergence of resistance and reduced sensitivity to frontline treatments of gonorrhoea is of global concern and may have contributed to high levels of gonorrhoea transmission in MSM [2-4]. Additionally, outbreaks of less common STIs such as Lymphogranuloma venereum (LGV) [5], together with shigellosis (which can be sexually transmissible) [6] in this population are of particular concern.

There is increasing evidence that HIV-positive MSM in the UK are disproportionately affected by STIs. Recent data demonstrated that of MSM diagnosed with syphilis, 35% were HIV positive [7]. HIV-positive MSM have also been found to account for more than 80% of LGV cases [5]. In part, these observations may reflect seroadaptive behaviours in HIV-positive MSM [8], in which different sexual practices such as unprotected (i.e. condomless) anal intercourse are adopted according to the reported HIV status of both partners in order to reduce the risk of transmitting or acquiring HIV. Seroadaptive behaviours vary considerably and include serosorting (limiting sexual partners to those with the same HIV status as themselves), strategic positioning (adopting a specific sexual position according to the HIV status of one's partner), withdrawal before ejaculation, and negotiating around viral load [9]. However, seroadaptive behaviours may come at a cost of increased transmission of STIs [10-12].

The UK has a growing population of HIV-positive MSM [13] and recent studies suggest that they may be increasingly adopting seroadaptive behaviours [8,14]. In this study we used multiple surveillance data sources and population survey data to estimate the risk of STIs in HIV-positive MSM and assessed whether transmission in HIV-positive MSM has contributed to recent STI epidemics in England.

Methods

Sources of data

Descriptive and comparative data analyses of the incidence of STIs were undertaken using data from GUMCADv2 (Genitourinary Medicine Clinic Activity Dataset) [15]. The Survey of Prevalent HIV Infections Diagnosed (SOPHID) [16], the third National Survey

of Sexual Attitudes and Lifestyles (Natsal-3) [17] and census data from the Office for National Statistics (ONS) [18] were employed to estimate denominator populations.

GUMCADv2 is a mandatory electronic pseudo-anonymised (i.e. contains the sex, age and hospital/clinic number of each patient but no patient identifiable information such as name, date of birth or postcode of residence is included) [19] patient-level dataset submitted to Public Health England (PHE) by all genitourinary medicine (GUM) clinics in England. The dataset contains information on all STI diagnoses and services provided for each patient as well as information on patient demographic such as sexual orientation, age, sex, ethnicity, area of residence and country of birth [19]. A unique patient identifier is assigned to each patient attending a given GUM clinic, allowing subsequent visits by the same patient to the same clinic to be identified.

SOPHID is a cross-sectional survey of all persons with diagnosed HIV infection who attend for HIV care at an NHS site in England, Wales and Northern Ireland. Age, sex, probable route of HIV infection, ethnicity, antiretroviral therapy (ART) status, CD4 cell count, region of residence and region of care provider are measured for each calendar year.

Natsal-3 is a nationally representative survey conducted between 2010 and 2012 on 15,162 individuals and provides information on key sexual behaviours, risk factors and also includes biological sampling and testing.

ONS is the national statistical institute for the UK and is responsible for collecting and publishing statistics related to the economy, population and society at national, regional and local levels.

Study population

MSM were defined as men who reported a homosexual or bisexual orientation at least once over the study period. MSM were defined as diagnosed HIV positive (hereafter referred to as 'HIV-positive' MSM) if they were diagnosed with HIV at least six weeks before their STI diagnosis, as newly diagnosed with HIV if they were diagnosed within six weeks of their STI diagnosis, and as HIV-negative/undiagnosed if there was no evidence of an HIV diagnosis in their GUMCADv2 record. For the analysis of acute STIs, STI population rates and association between STI outcomes and HIV status, MSM with new HIV diagnoses were grouped with those of negative or unknown status and referred to collectively as 'HIV-negative/undiagnosed', as the newly diagnosed men were assumed to be undiagnosed at the time of their STI exposure.

Data analysis

Acute sexually transmitted infections in known HIV-positive men who have sex with men

Episodes of acute STI diagnoses including gonorrhoea (acute and complicated), syphilis (primary, secondary and early latent), chlamydia, genital warts (first episode) and genital herpes (first episode) and HIV status in MSM were identified using Sexual Health and HIV Activity Property Type (SHHAPT) codes from GUMCADv2 for the years 2008 to 2013. Acute gonorrhoea includes all new cases of uncomplicated gonorrhoea of the lower genitourinary tract, anorectum, mouth, throat and adult conjunctivitis; complicated gonorrhoea includes all upper genitourinary tract complications (such as pelvic inflammatory disease and epididymitis) and systemic complications [20]. The proportion of STI diagnoses which were in HIV-positive MSM was calculated for each STI by year.

Sexually transmitted infection population rates in HIV-negative/undiagnosed and HIV-positive men who have sex with men

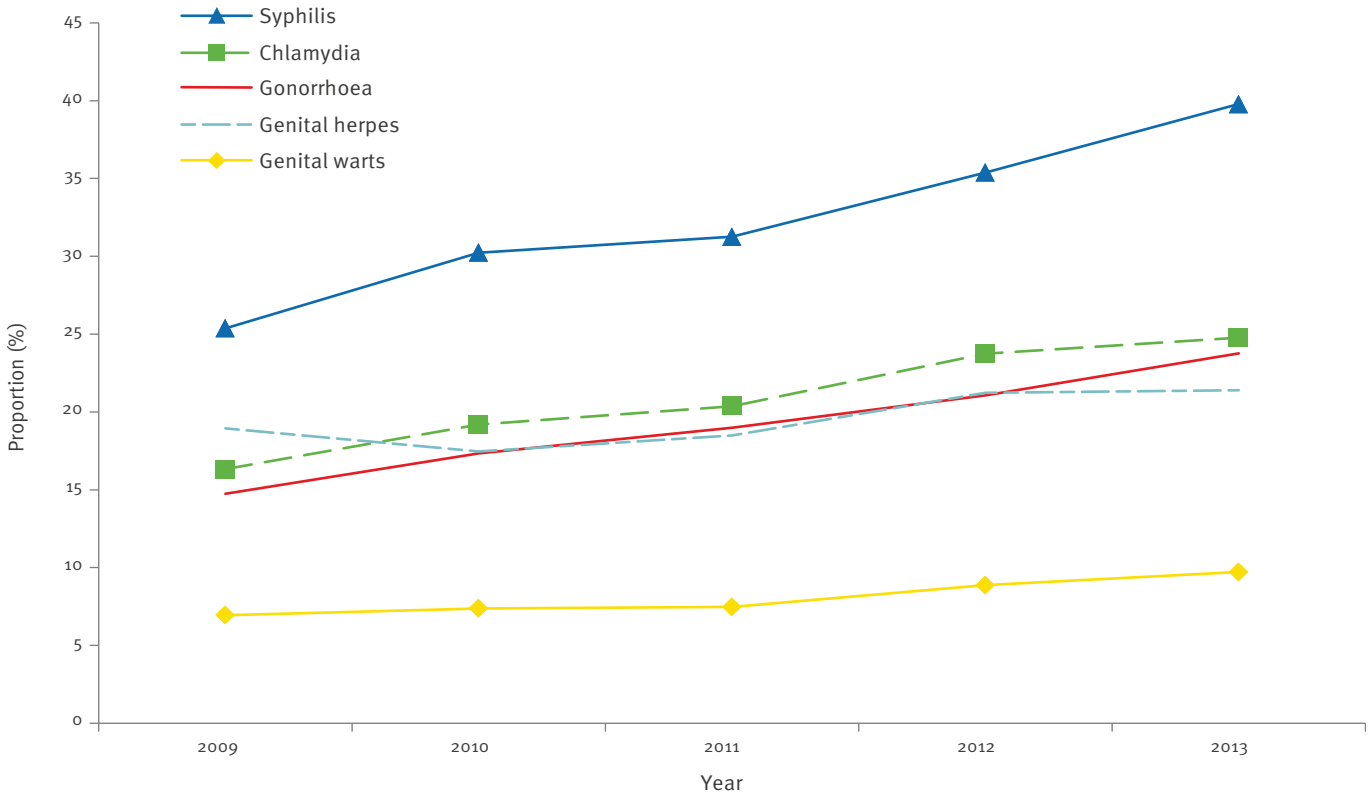
The rates of acute bacterial (gonorrhoea, chlamydia and syphilis) and acute viral STIs (first episode of genital warts and first episode of genital herpes) in HIV-positive and HIV negative/undiagnosed MSM were compared from 2009 to 2013. The numerators were individual HIV-positive and negative/undiagnosed MSM presenting at GUM clinics each year using data from GUMCADv2. The denominator for HIV-positive MSM was identified from SOPHID. The proportion of men aged 15 to 74 years who are MSM was estimated using data from Natsal-3. An estimated 2.6% of men in the UK had at least one male sexual partner in the past five years across all age groups of men [21]. This was applied to the mid-year population estimates from the ONS for the number of men aged 15 to 74 years for each year [22,23], and the estimated number of HIV-positive MSM was subtracted from this to calculate the denominator for HIV-negative/undiagnosed MSM. The results of a sensitivity analysis (data not shown) showed a small effect when using the upper and lower limits of the confidence interval (2.1% and 3% respectively) of the estimation of men in the UK having at least one male sexual partner in the past five years across all ages of men. For the most recent year of analysis, the range for bacterial STIs in HIV-negative MSM was 33 per 1,000 to 48 per 1,000.

Associations between sexually transmitted infection outcomes and HIV status

Univariate and multivariate logistic regression models were prepared for the MSM population attending GUM clinics in England for each individual MSM diagnosed with an acute bacterial STI (gonorrhoea, chlamydia and syphilis) for each year from 2009 to 2013 inclusive. Explanatory variables included all demographic variables from GUMCADv2 (age, ethnicity, continent of birth, and area of residence), diagnosed HIV status, and number of tests in the previous 12-month period

Figure 1

Proportion of acute sexually transmitted infection diagnoses in men who have sex with men which were in HIV-positive men who have sex with men, England, 2009–2013



for each respective bacterial STI; all were included in the final multivariate model.

Gonorrhoea and chlamydia re-infection rates by HIV status

The probability of patients who became re-infected with the most common bacterial STIs (gonorrhoea and chlamydia) within one year was estimated by the Kaplan-Meier method. Patients became at-risk from 42 days after the time of first attendance with gonorrhoea and chlamydia [24] and were censored at the end of the study period (31 December 2013). Data for calculating re-infection rates was obtained from GUMCADv2.

All statistical analyses were undertaken using Stata version 12 (StataCorp, College Station, Texas, US). P values‹0.05 were considered to be statistically significant.

Results

During the study period, the number of MSM attending GUM clinics recorded in GUMCADv2 increased from 78,226 in 2009 to 117,410 in 2013. The total number of MSM attendances increased from 241,676 to 316,250. The number of MSM in England estimated using Natsal-3 and ONS was 501,895 in 2009, increasing to 516,416 in 2013.

Acute sexually transmitted infections in known HIV-positive men who have sex with men

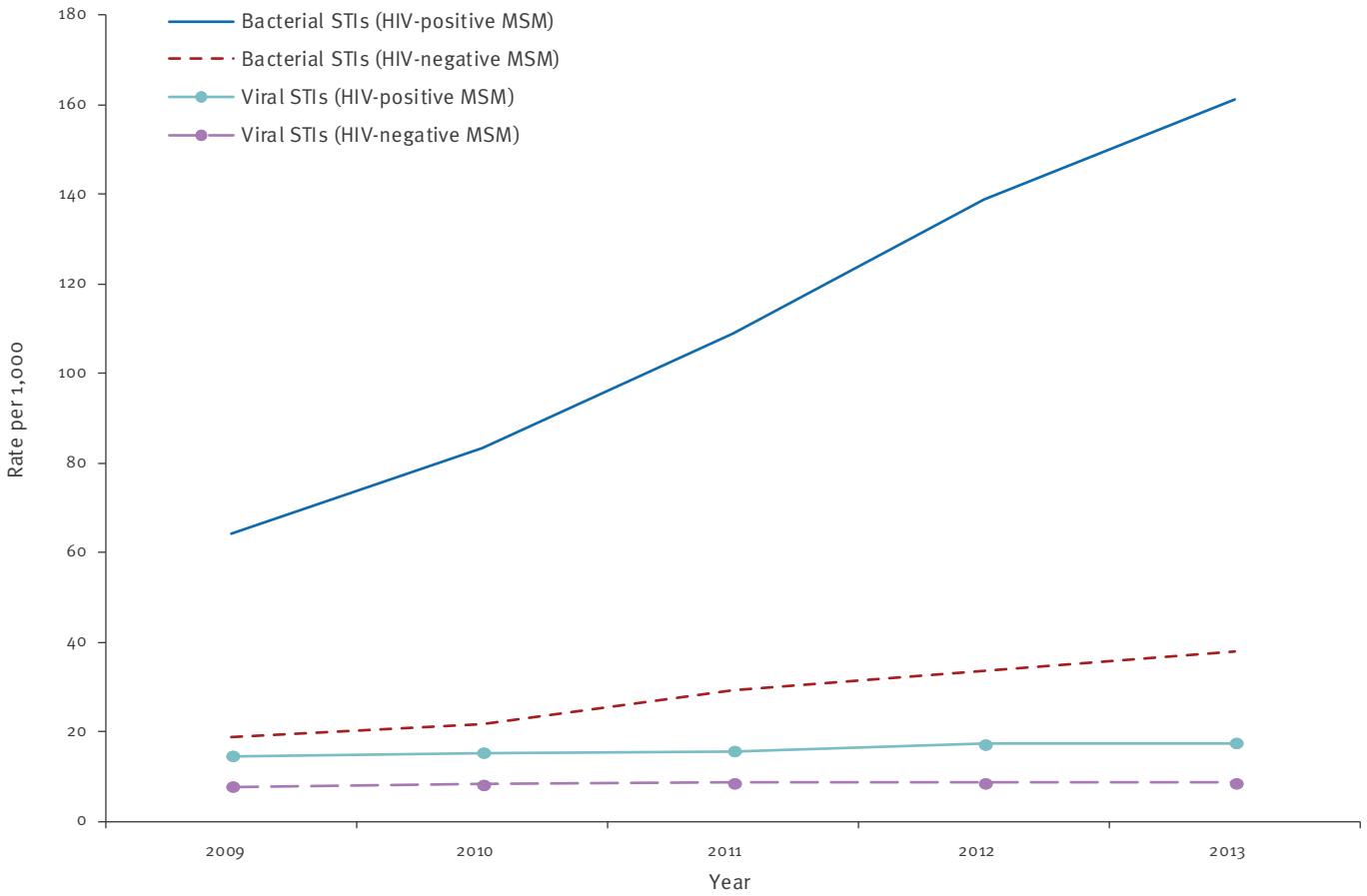
The proportion of acute STI diagnoses in MSM that were in HIV-positive MSM is shown in Figure 1. Overall, from 2009 to 2013, this proportion increased for all acute STIs: from 25% to 40% for syphilis, 16% to 25% for chlamydia, 15% to 24% for gonorrhoea, 19% to 21% for genital herpes and 7% to 10% for genital warts.

Sexually transmitted infection population rates in HIV-negative/undiagnosed and HIV-positive men who have sex with men

The rate of acute bacterial STIs in HIV-positive MSM nearly trebled (64 per 1,000 to 161 per 1,000), and increased from 3.2 times higher than the rate in HIV-negative/undiagnosed MSM in 2009 to 4.2 times higher in 2013 (Figure 2). For HIV-negative/undiagnosed MSM, the rate of acute bacterial STIs also increased to a lesser degree (19 per 1,000 to 38 per 1,000). The rate of acute viral STIs in HIV-positive MSM was approximately twice that observed in HIV-negative/undiagnosed MSM and remained fairly stable over the five year period (15 to 18 per 1,000 in HIV-positive and 8 to 9 per 1,000 in negative/undiagnosed MSM). This indicates that the rate of acute STIs in HIV-positive MSM was close to one in five (179 per 1,000).

Figure 2

Rates of acute bacterial and acute viral sexually transmitted infections in HIV-positive and negative/undiagnosed men who have sex with men per 1,000 men who have sex with men, England, 2009–2013



MSM: men who have sex with men; STI: sexually transmitted infection.

Bacterial STIs: gonorrhoea, chlamydia and syphilis
Viral STIs: first episode of genital warts and first episode of genital herpes

Associations between sexually transmitted infection outcomes and HIV status

Table 1 shows the final multivariate logistic regression models for gonorrhoea, chlamydia and syphilis adjusted for all explanatory variables. Data are presented for the most recent available year only. Table 2 shows the change in the adjusted odds ratio over time by HIV status. When compared with HIV-negative/undiagnosed MSM, the adjusted odds ratio (aOR) of being diagnosed with gonorrhoea, chlamydia and syphilis was significantly higher in HIV-positive MSM in all years analysed and increased over time ($p<0.001$).

Gonorrhoea and chlamydia re-infection rates by HIV status

The estimated probability of gonorrhoea and chlamydia re-infection is shown in Figure 3. A total of 34,090 and 31,206 MSM diagnosed with gonorrhoea and chlamydia respectively were included. The probability of repeat infection with gonorrhoea was estimated at 36.6% in HIV-positive, 33.2% in newly diagnosed and 22.7% in HIV-negative/undiagnosed MSM at the end of the 5 year follow-up period. For chlamydia, the estimated probability of repeat infection was 31.6% in HIV-positive, 23.7% in newly diagnosed and 17.3% in HIV-negative/undiagnosed MSM over the same period.

Discussion

For the first time, we have estimated the relative contribution of HIV-positive MSM to STI transmission over time in England. Since 2009, an increasing proportion of STIs has been diagnosed in HIV-positive MSM, and currently, the population rate of acute bacterial STIs is up to four times that of HIV-negative or undiagnosed MSM. We estimate that almost one in five of all diagnosed HIV-positive MSM in England had an acute STI diagnosed in 2013. The odds of being diagnosed with gonorrhoea, syphilis and chlamydia were significantly higher in HIV-positive relative to HIV-negative/undiagnosed MSM and increased over time. Re-infection rates of bacterial STIs were also considerably higher in HIV-positive MSM over a five-year follow-up period, indicative of rapid transmission in more dense sexual networks.

Table 1

Unadjusted and adjusted odds ratio for gonorrhoea, chlamydia and syphilis diagnoses, men who have sex with men, England, 2013

Variable		Gonorrhoea			Chlamydia				Syphilis			
	Number (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value	Number (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value	Number (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
HIV												
Negative/unaware	9,566 (78.2)	1	1		6,575 (76.4)	1	1		1,400 (60.9)	1	1	
Positive	2,674 (21.8)	1.22 (1.16-1.27)	1.75 (1.67-1.84)	<0.001	2,027 (23.6)	1.34 (1.27-1.41)	1.79 (1.69-1.90)	<0.001	900 (39.1)	2.80 (2.57-3.05)	4.05 (3.70-4.45)	<0.001
IMD score												
1 (least deprived)	883 (7.2)	1	1		689 (8.0)	1	1		159 (6.9)	1	1	
2	1,201 (9.8)	1.02 (0.93-1.11)	0.92 (0.84-1.01)	0.078	1,012 (11.8)	1.10 (0.99-1.21)	1.06 (0.95-1.17)	0.3	222 (9.6)	1.05 (0.85-1.28)	0.96 (0.78-1.19)	0.728
3	1,992 (16.3)	1.15 (1.04-1.21)	0.96 (0.88-1.05)	0.367	1,481 (17.2)	1.09 (0.99-1.20)	1.00 (0.91-1.1)	0.95	396 (17.2)	1.27 (1.05-1.52)	1.09 (0.90-1.32)	0.364
4	4,179 (34.1)	1.47 (1.35-1.55)	1.09 (1.00-1.18)	0.045	2,746 (31.9)	1.24 (1.13-1.35)	1.07 (0.98-1.18)	0.12	803 (34.9)	1.57 (1.32-1.86)	1.22 (1.02-1.46)	0.032
5 (most deprived)	3,985 (32.6)	1.48 (1.37-1.60)	1.11 (1.03-1.20)	0.009	2,674 (31.1)	1.28 (1.17-1.39)	1.10 (1.00-1.20)	0.04	720 (31.3)	1.49 (1.25-1.77)	1.15 (0.96-1.37)	0.138
Region												
Not London	4,827 (39.4)	1	1		4,077 (47.4)	1	1		999 (43.4)	1	1	
London	7,413 (60.6)	1.73 (1.66-1.80)	1.71 (1.64-1.78)	<0.001	4,525 (52.6)	1.25 (1.19-1.31)	1.21 (1.15-1.27)	<0.001	1,301 (56.6)	1.47 (1.35-1.59)	1.29 (1.18-1.42)	<0.001
Ethnic group												
White	9,684 (79.1)	1	1		6,724 (78.2)	1	1		1,778 (77.3)	1	1	
Black African	195 (1.6)	1.20 (1.04-1.40)	0.91 (0.77-1.08)	0.29	134 (1.6)	1.19 (1.00-1.42)	1.02 (0.84-1.25)	0.83	35 (1.5)	1.18 (0.84-1.65)	1.03 (0.70-1.50)	0.884
Black Caribbean	304 (2.5)	1.49 (1.32-1.69)	1.08 (0.95-1.23)	0.233	211 (2.5)	1.49 (1.29-1.73)	1.22 (1.05-1.42)	0.01	60 (2.6)	1.61 (1.24-2.09)	1.01 (0.76-1.33)	0.969
Black other	97 (0.8)	1.18 (0.96-1.47)	0.89 (0.71-1.10)	0.274	70 (0.8)	1.23 (0.96-1.58)	1.05 (0.82-1.35)	0.69	30 (1.3)	2.00 (1.38-2.89)	1.51 (1.03-2.21)	0.034
Asian or Asian British	414 (3.4)	0.87 (0.78-0.96)	0.76 (0.68-0.85)	<0.001	336 (3.9)	1.02 (0.91-1.14)	0.86 (0.75-0.98)	0.02	88 (3.8)	1.01 (0.81-1.25)	1.01 (0.79-1.29)	0.963
Mixed	501 (4.0)	1.33 (1.21-1.46)	1.03 (0.94-1.14)	0.517	337 (3.9)	1.29 (1.15-1.44)	1.12 (0.99-1.26)	0.06	88 (3.8)	1.27 (1.02-1.58)	1.08 (0.86-1.35)	0.507
Other ethnic	499 (4.1)	1.07 (0.97-1.17)	0.91 (0.82-1.01)	0.078	409 (4.7)	1.26 (1.13-1.40)	1.07 (0.95-1.21)	0.24	95 (4.1)	1.11 (0.90-1.36)	0.91 (0.72-1.15)	0.427
Unknown	546 (4.5)	0.90 (0.82-0.98)	1.00 (0.91-1.09)	0.93	381 (4.4)	0.90 (0.81-1.00)	0.97 (0.87-1.09)	0.64	126 (5.5)	1.13 (0.94-1.35)	1.23 (1.02-1.48)	0.033
Continent of birth												
Europe	9,636 (78.7)	1	1		6,687 (77.7)	1	1		1,746 (75.9)	1	1	
Africa	385 (3.2)	1.17 (1.05-1.32)	1.03 (0.91-1.17)	0.608	265 (3.1)	1.16 (1.02-1.32)	1.04 (0.9-1.2)	0.61	69 (3.0)	1.16 (0.91-1.47)	0.91 (0.69-1.19)	0.484
Asia	493 (4.0)	0.93 (0.85-1.02)	0.88 (0.78-0.98)	0.026	453 (5.3)	1.23 (1.11-1.36)	1.19 (1.05-1.35)	0.01	99 (4.3)	1.03 (0.84-1.26)	1.02 (0.79-1.30)	0.901
Australasia	251 (2.1)	1.39 (1.21-1.58)	1.15 (1.00-1.32)	0.044	165 (1.9)	1.31 (1.12-1.54)	1.24 (1.05-1.46)	0.01	32 (1.4)	0.97 (0.68-1.39)	0.84 (0.59-1.21)	0.346
North America	221 (1.8)	1.19 (1.03-1.36)	1.04 (0.90-1.20)	0.363	130 (1.5)	1.00 (0.84-1.20)	0.98 (0.81-1.17)	0.8	28 (1.2)	0.83 (0.57-1.21)	0.76 (0.52-1.11)	0.159
South America	594 (4.8)	1.46 (1.34-1.60)	1.07 (0.97-1.18)	0.153	390 (4.5)	1.38 (1.24-1.54)	1.1 (0.98-1.23)	0.11	162 (7.0)	2.20 (1.87-2.59)	1.53 (1.27-1.84)	<0.001
Unknown	660 (5.4)	0.87 (0.80-0.95)	0.83 (0.76-0.90)	<0.001	512 (6.0)	0.97 (0.89-1.07)	0.93 (0.85-1.03)	0.17	164 (7.1)	1.19 (1.01-1.40)	0.98 (0.83-1.16)	0.842
Number of tests for STI in past 12 months												
1	5,314 (43.4)	1	1		3,803 (44.2)	1	1		1,301 (56.6)	1	1	
2-4	4,854 (39.7)	1.62 (1.55-1.69)	1.56 (1.5-1.63)	<0.001	3,448 (40.1)	1.61 (1.53-1.69)	1.56 (1.48-1.63)	<0.001	906 (39.4)	1.23 (1.13-1.35)	1.14 (1.04-1.24)	0.004
>5	2,072 (16.9)	0.61 (0.58-0.65)	0.56 (0.53-0.59)	<0.001	1,351 (15.7)	0.56 (0.52-0.60)	0.48 (0.45-0.52)	<0.001	93 (4.0)	0.11 (0.09-0.14)	0.07 (0.05-0.08)	<0.001
Age group												
15-24 years	2,706 (22.2)	1	1		1,676 (19.6)	1	1		264 (11.5)	1	1	
25-34 years	5,274 (43.2)	1.11 (1.06-1.17)	0.94 (0.89-0.99)	0.019	3,282 (38.3)	1.12 (1.05-1.19)	1.02 (0.96-1.08)	0.57	766 (33.4)	1.66 (1.44-1.91)	1.37 (1.18-1.58)	<0.001
35-44 years	2,735 (22.4)	0.84 (0.79-0.89)	0.68 (0.64-0.72)	<0.001	2,134 (24.9)	1.06 (0.99-1.13)	0.93 (0.87-1)	0.04	701 (30.5)	2.21 (1.92-2.55)	1.61 (1.39-1.87)	<0.001
45-64 years	1,434 (11.7)	0.49 (0.46-0.53)	0.43 (0.40-0.46)	<0.001	1,388 (16.2)	0.77 (0.72-0.83)	0.71 (0.66-0.77)	<0.001	546 (23.8)	1.93 (1.66-2.24)	1.51 (1.29-1.76)	<0.001
>65 years	65 (0.5)	0.22 (0.16-0.27)	0.21 (0.16-0.27)	<0.001	89 (1.0)	0.47 (0.37-0.60)	0.47 (0.38-0.59)	<0.001	19 (0.8)	0.63 (0.40-1.01)	0.63 (0.39-1.00)	0.052

CI: confidence interval; IMD: Index of Multiple Deprivation; OR: odds ratio; STI: sexually transmitted infection.
Data restricted to men who have sex with men resident in England

Table 2

Adjusted odds ratios for gonorrhoea, chlamydia and syphilis diagnoses by HIV status in men who have sex with men, England, 2009–2013

Year	2009			2010			2011			2012			2013		
	Number (%)	Adjusted OR (95% CI)	p value	Number (%)	Adjusted OR (95% CI)	p value	Number (%)	Adjusted OR (95% CI)	p value	Number (%)	Adjusted OR (95% CI)	p value	Number (%)	Adjusted OR (95% CI)	p value
Gonorrhoea															
HIV neg	3,062 (86.0)	1		4,102 (83.0)	1		6,073 (82.8)	1		8,027 (80.1)	1		9,566 (78.2)	1	
HIV pos	497 (14.0)	1.43 (1.29–1.59)	<0.001	840 (17.0)	1.45 (1.34–1.58)	<0.001	1,258 (17.2)	1.44 (1.34–1.54)	<0.001	1,994 (19.9)	1.61 (1.52–1.70)	<0.001	2,674 (21.8)	1.75 (1.67–1.84)	<0.001
Chlamydia															
HIV neg	3,684 (84.1)	1		4,413 (81.6)	1		5,923 (81.4)	1		6,131 (77.2)	1		6,575 (76.4)	1	
HIV pos	697 (15.9)	1.5 (1.37–1.65)	<0.001	998 (18.4)	1.48 (1.37–1.59)	<0.001	1,356 (18.6)	1.44 (1.35–1.54)	<0.001	1,807 (22.8)	1.80 (1.70–1.91)	<0.001	2,027 (23.6)	1.79 (1.69–1.90)	<0.001
Syphilis															
HIV neg	1,271 (74.5)	1		1,171 (69.7)	1		1,385 (69.6)	1		1,370 (64.9)	1		1,400 (60.9)	1	
HIV pos	436 (25.5)	2.71 (2.41 – 3.05)	<0.001	509 (30.3)	2.74 (2.44–3.07)	<0.001	606 (30.4)	3.09 (2.78–3.43)	<0.001	742 (35.1)	3.66 (3.31–4.04)	<0.001	900 (39.1)	4.05 (3.70–4.45)	<0.001

CI: confidence interval; HIV neg: HIV negative/undiagnosed men who have sex with men; HIV pos: HIV-positive men who have sex with men; OR: odds ratio.
Data restricted to men who have sex with men resident within England

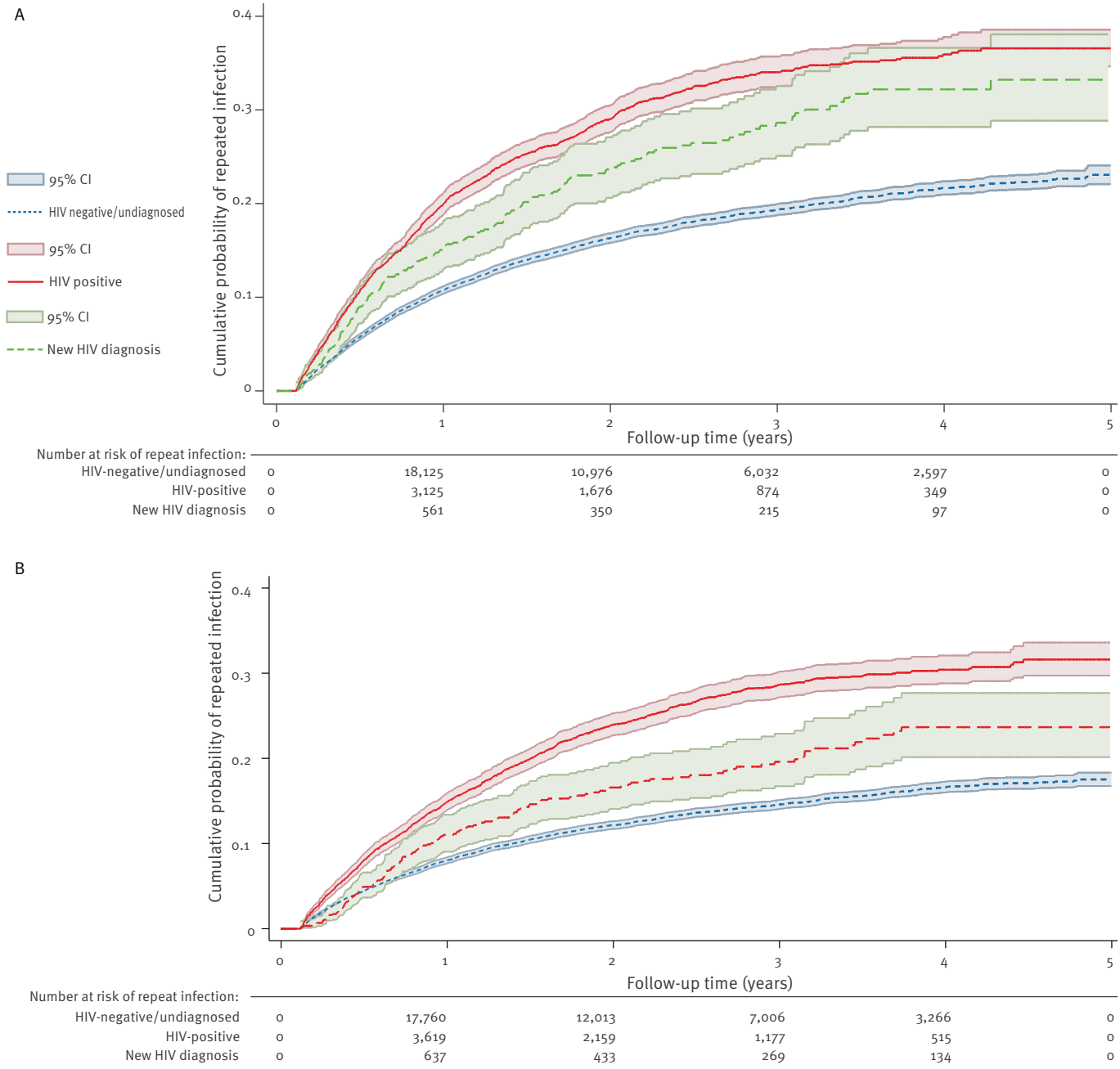
These findings strongly suggest that the sexual health of HIV-positive MSM in England is worsening. They are consistent with data from a cross-sectional survey of men in commercial gay venues in London, Brighton, Manchester, Glasgow and Edinburgh which demonstrated that numbers of STIs diagnosed in the previous 12 months were higher in MSM known to be HIV-infected compared with uninfected men (aOR 7.2, 95% CI 4.63–11.17) [25], and similar studies in Europe [26,27]. A study of LGV re-infection in the UK also found that, at baseline, repeaters were more likely to be HIV-positive compared with non-repeaters [28].

It seems probable that these changes in STI transmission patterns in HIV-positive MSM reflect increasing adoption of HIV seroadaptive behaviours and their impact on sexual network structures. HIV-positive MSM reporting seroadaptive behaviours are at higher risk of STIs compared with HIV-negative MSM [10-12]. One study reported that HIV-positive MSM practising seroadaptive behaviours had a threefold increased risk of bacterial STIs, with almost a third of HIV-positive MSM reporting an STI in the past year, compared with 9% of HIV-negative MSM [11]. However, despite the considerable changes in STI transmission patterns in HIV-positive MSM seen in our study, the degree to which transmission in HIV-positive MSM engaging in seroadaptive behaviours is fuelling current STI epidemics in England is unclear. The recent emergence of relatively rare infections such as LGV and *S. flexneri* in the UK has been strongly and predominantly associated with transmission in HIV-positive MSM [5,6,29]. Likewise for syphilis, our study showed that 39.1% of cases in MSM in England were known to be HIV-positive, and this is consistent with data from the United States, Australia and Europe [26,27,30,31]. The duration of infectiousness with *Shigella*, LGV and syphilis may be short as these infections are typically symptomatic, so it is highly likely that their transmission is being sustained in highly active sexual networks of HIV-positive MSM engaging in seroadaptive behaviours [32]. However, fewer than 25% of MSM diagnosed with chlamydia and gonorrhoea (and even less with viral STIs) in our study were HIV-positive. Therefore, while seroadaptive behaviours in HIV-positive MSM may be making an important contribution to the transmission of chlamydia, gonorrhoea and viral STIs in MSM, they are not necessary to sustain infection at endemic levels in the wider MSM population.

HIV seroadaptive behaviours will likely have other negative or unintended consequences for the sexual health of MSM. The presence of an STI may compromise the health of HIV-positive MSM through several mechanisms including a reduction in CD4 cell count as well as acute increases in HIV viral load, which may compromise effective antiretroviral therapy [33-35]. In addition, STIs may also increase HIV infectiousness by facilitating HIV shedding in the genital tract or rectal mucosa [36]. Further, evidence suggests that a low viral load may reduce the probability of infecting

Figure 3

Estimated probability of repeat gonococcal infection (A) and of repeat chlamydial infection (B) in men who have sex with men attending genitourinary medicine clinics by HIV co-infection, England, 2009–2013



a sexual partner [37-39], thus, HIV-positive MSM may engage in seroadaptive behaviours when they receive highly active antiretroviral therapy (HAART) or have an undetectable viral load. However, surveys of gay commercial venues and gyms in London, Glasgow and Edinburgh suggest the proportion of MSM reporting unprotected anal intercourse with partners of unknown or discordant HIV status has increased, leading to risk of HIV as well as other STI transmission [8,14].

A study by Fox et al. showed significant reduction in self-reported HIV transmission-risk behaviour in MSM recently diagnosed with HIV, with patients reporting greater condom use and fewer sexual partners [40]. However, these may have limited impact on STI incidence due to the various routes of transmission of STIs (such as oral, digital and use of sex toys). Furthermore, in MSM recently diagnosed with HIV, those reporting continued transmission-risk behaviour were more likely to have another STI [40]. Thus, health promotion activities should also consider the broader context around sexual risk-taking in MSM, especially in those diagnosed with HIV. The recent Public Health England framework for promoting the health and well being of MSM highlighted the interaction of mental health, alcohol and drug use, and sexual risk behaviour [41]. There is increasing concern on the interaction between drug use and STIs, especially in HIV-positive

MSM, and that in developing appropriate interventions and services, the specific needs of HIV-positive MSM should be considered [29]. Furthermore, the high incidence of asymptomatic STIs, especially in extra-genital sites [42,43] emphasises the need to promote regular screening for STIs in HIV-positive individuals [44,45]. Nonetheless, surveys of healthcare providers in the US have reported significant barriers, especially in screening for gonorrhoea and chlamydia, which include time constraints, difficulty obtaining a sexual history, language and cultural barriers, and patient confidentiality concerns [46].

There are several limitations of this study. There may be a degree of ascertainment bias in the assessment of HIV status in MSM in patients with a longer history in GUMCADv2. However, sensitivity analysis (data not shown) was performed by identifying HIV-positive MSM from a retrospective review of a single year of GUMCADv2 data, and there was only a minimal impact on the results. The probability of repeat infection may also have been underestimated as, in this analysis, repeat diagnosis was used as a proxy measure for repeat infection. Some patients will have become re-infected but will remain undiagnosed, as only patients who returned to the same clinic for testing were assessed in the analysis. This is a limitation of GUMCADv2, as it allows only longitudinal patient data within a particular clinic or service and attendances by the same patient at different clinics cannot be monitored [19]. However, the data quality and completeness of GUMCADv2 is extremely high with 100% submissions from GUM clinics [19]. HIV-positive MSM engaged in care are also more likely to return regularly for STI screening during clinic visits and this may have contributed to the proportion and rates of STIs observed. Diagnosis of STIs (including HIV) is dependent on screening practices and frequency of screening. It is therefore not a true measure of incidence of infection but provides a good proxy for infection. A further limitation is the estimation of the true size of the MSM population in the UK. However, the methodology employed in Natsal-3 is among the most robust to estimate the size of this population. Furthermore, between Natsal-2 and Natsal-3, there was no significant increase in the proportion of men reporting same sex partners in the past 5 years [21]. Thus, the results of this longitudinal data analysis provide valuable insights into the complexity and evolution of STI epidemics in England.

The presence of an increasing proportion and rates of acute STIs in HIV-positive MSM, a population which also has higher rates of repeat infection and reports higher risk sexual behaviour, presents an increased risk for the sexual health of all MSM. This therefore merits public health action through improved monitoring and intervention. Currently, the collection of behavioural data is being piloted alongside that of clinical and socio-demographic data and this will allow further insights into the impact of seroadaptive practices to be explored in the future. Improved public health interventions with a holistic approach focussing on promoting condom use, reducing high risk behaviour and increasing the frequency of STI testing in MSM should be a priority.

Conflict of interest

None declared.

Authors' contributions

Gwenda Hughes and Anthony Nardone devised the study, advised on data analysis and participated in interpreting the data. Ramona Malek, Holly Mitchell and Martina Furegato carried out statistical analysis, participated in data analysis and intepreting the data. Ian Simms and Hamish Mohammed participated in interpreting the data. Ramona Malek prepared the first draft of the manuscript. All authors contributed to the final manuscript.

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Effects of region of birth, educational level and age on late presentation among men who have sex with men newly diagnosed with HIV in a network of STI/HIV counselling and testing clinics in Spain

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This paper analyses late presentation (LP) of HIV infection, and its determinants, among men who have sex with men (MSM) in Spain, newly diagnosed with HIV (2003–2011) in 15 sexually transmitted infection/HIV counselling and testing clinics. LP was defined as <350 CD4 cells/µL or AIDS. In total, 3,081 MSM were included (2,499 having CD4/AIDS); overall LP was 25.3%. LP was higher in men older than 34 years, those not previously HIV-tested (adjusted odds ratio (aOR):3.1; 95% confidence intervals (CI):2.3–4.2) , and those tested >12 months before diagnosis (12–24 months (aOR:1.4; 95% CI:1.0–2.0); >24 months (aOR:2.2; 95% CI:1.7–3.0)). LP was less likely in MSM reporting a known HIV-infected partner as infection source or symptoms compatible with acute retroviral syndrome. 'Region of birth' interacted with 'educational level' and 'steady partner as infection source': only African and Latin-American MSM with low educational level were more likely to present late; Latin-American men attributing their infection to steady partner, but no other MSM, had LP more frequently. In Spain, HIV testing among MSM should be promoted, especially those > 34 years old and migrants with low educational level. The current recommendation that MSM be tested at least once a year is appropriate.

Introduction

Delayed diagnosis and treatment of HIV infection is a huge problem worldwide, with important individual and public health consequences. People presenting with an impaired immune system at diagnosis have higher rates of morbidity and mortality than those diagnosed earlier [1,2], and treating them is more costly [3]. Moreover, HIV-infected people unaware of their status may inadvertently spread HIV [4].

Different definitions have been used for late presentation of new HIV diagnoses [5], most of them based

on different CD4 count levels at HIV diagnosis and/or simultaneous or recent diagnosis with acquired immunodeficiency syndrome (AIDS) [6–8]. To facilitate data comparisons, a consensus definition was proposed in Europe in 2010 and 2011 defining advanced disease (AD) as presenting a CD4 count below 200 cells/µL or AIDS at diagnosis, and late presentation (LP) as having less than 350/µL or AIDS [8,9].

In the European Union/European Economic Area (EU/EEA) countries, nearly half (49.3%) of new HIV diagnoses reported in 2012 were late presenters (defined as fewer than 350 CD4 cells/µL at diagnosis), with a range of 35–66% across countries [10]. The proportion of LP was higher among heterosexuals (59.1%) and people who inject drugs (PWID) (55.9%) than among men who have sex with men (MSM), (38.4%). In Spain, using the same definition, 48% of new HIV diagnoses reported to the national surveillance system that same year presented late; variations across exposure categories are similar, with MSM having the lowest proportion of LP in comparison to PWID and heterosexuals (39%, 59% and 65% respectively) [11].

In addition to the surveillance system, data on LP are available in Spain from the CoRIS cohort and the EPI-VIH Network. CoRIS is a Spanish cohort of treatment-naïve HIV patients which collects epidemiological/clinical data in a broad setting [12]; LP in this cohort was 48.6% in the period 2004–2006 [2]. The EPI-VIH Network includes all sexually transmitted infections (STI) and HIV counselling and testing (HCT) clinics operating in the main Spanish cities; these are low threshold public facilities attending all key populations at higher risk for HIV [13,14]. Between 2003 and 2010, the proportion of LP in new HIV diagnoses in this network was 27.6% [15], significantly lower than what was found in the comprehensive surveillance system [11].

Both in Spain (cohort and surveillance data) and elsewhere, several socio-demographic and epidemiological factors have been associated with LP, such as male sex, age, migration, low socio-economic status and HIV transmission mode [2,5,16-18]. Also, all the Spanish studies have showed that LP is less common in MSM than in other transmission categories, even after adjusting for other variables. However, little is known about factors affecting LP within this group. The objective of this paper is to analyse LP of HIV infection and its determinants among MSM newly diagnosed with HIV from 2003 to 2011 in the EPI-VIH Network.

Methods

All new HIV diagnoses among MSM testing for HIV between 2003 and 2011 in the EPI-VIH Network were included. The network in this period comprises 21 clinics located in the main Spanish cities: Alicante, Barcelona, Bilbao, Cartagena, Castellón, Gijón, Granada, Logroño, Madrid (two clinics), Málaga, Murcia, Oviedo, Palma de Mallorca, Pamplona, San Sebastián, Santander, Seville, Tenerife, Valencia and Vitoria. Fifteen of these clinics (excluding Castellon, Gijón, Granada, Malaga, Seville and Vitoria) systematically collect data on CD4 count after diagnosis. The clinics are public low-threshold facilities, operating on a free basis, where every effort is made to maximise accessibility for key populations at higher risk. Participation in the EPI-VIH group is voluntary but, to our knowledge, all specialised STI/HCT clinics in Spain belong to this network.

Cases included in this analysis met the European case definition for new HIV diagnosis [19].

Epidemiological variables (age, sex, country of birth, educational level, date of HIV diagnosis, type of sexual partner reported as probable source of infection (casual partner, steady partner, known HIV-infected partner (steady/casual), commercial partner (sex worker/client)), existence of a previous HIV test, date of previous HIV test, and clinical information (CD4 count, AIDS diagnoses, symptoms compatible with an acute retroviral syndrome, availability of health insurance card) were collected by the attending physicians using a standardised questionnaire.

LP was defined as having a CD4 count below 350 cells/µL in the first determination after HIV diagnosis and/or AIDS at diagnosis, following recent European recommendations [8,9]. The analyses were dealt with at the level of 'country/region of birth'; to assign 'region of birth', the World Health Organization Regional Office for Europe's classification was used. Frequency distributions for each variable and prevalence of LP, overall and stratified by different variables, were calculated. To evaluate the association between categorical variables, chi-squared tests were used; the associations between LP and individual explanatory variables were considered statistically significant at a p value <0.05. Trends in LP over time were analysed using a joinpoint regression model. To identify factors associated with

Figure 1

Prevalence of late presentation among men who have sex with men newly diagnosed with HIV, by year of diagnosis, EPI-VIH Network, Spain, 2003–2011 (n=2,499)

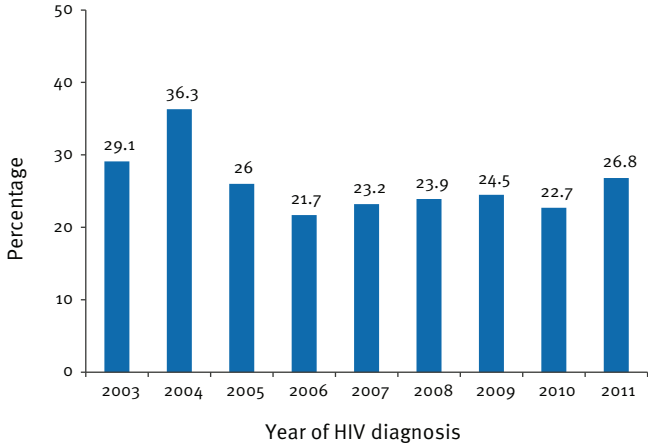


Table 1

Characteristics of men who have sex with men newly diagnosed with HIV, and prevalence of late and not late presentation in different subgroups, EPI-VIH Network, Spain, 2003–2011 (n=2,499)

Variables	Characteristics of MSM newly diagnosed with HIV		Prevalence of late presentation		Prevalence of not-late presentation		p value
	No	%	No	%	No	%	
Age group (years)							
<25	363	14.5	74	20.4	289	79.6	0.00
25–34	1,232	49.3	285	23.1	947	76.9	
35–44	668	26.7	192	28.7	476	71.3	
≥45	208	8.3	75	36.1	133	63.9	
Unknown	28	1.1	5	17.9	23	82.1	
Educational level							
Illiterate/primary education	375	15.0	107	28.5	268	71.5	0.13
Secondary education	1,023	40.9	257	25.1	766	74.9	
University education	912	36.5	212	23.2	700	76.8	
Unknown	189	7.6	55	29.1	134	70.9	
Region of birth							
Spain	1,617	64.7	384	23.7	1,233	76.3	0.02
Western Europe	78	3.1	20	25.6	58	74.4	
Central/Eastern Europe	42	1.7	10	23.8	32	76.2	
Latin America	713	28.5	205	28.8	508	71.2	
Africa	17	0.7	8	47.1	9	52.9	
Unknown	32	1.3	4	12.5	28	87.5	
Source of infection: steady partner							
Yes	938	37.5	243	25.9	695	74.1	0.56
No	1,561	62.5	388	24.9	1,173	75.1	
Source of infection: casual partner							
Yes	1,978	79.2	506	25.6	1,472	74.4	0.46
No	521	20.8	125	24.0	396	76.0	
Source of infection: commercial sexual contact							
Yes	153	6.1	40	26.1	113	73.9	0.79
No	2,346	93.9	591	25.2	1,755	74.8	
Source of infection: known HIV- infected partner							
Yes	263	10.5	50	19.0	213	81.0	0.01
No	2,236	89.5	581	26.0	1,655	74.0	
Acute retroviral syndrome							
Yes	361	14.4	55	15.2	306	84.8	0.00
No	735	29.4	220	29.9	515	70.1	
Unknown	1,403	56.1	356	25.4	1,047	74.6	
Previous HIV-negative test							
No	532	21.3	192	36.1	340	63.9	0.00
Yes, <12 months before HIV diagnosis	611	24.5	87	14.2	524	85.8	
Yes, 12–24 months before HIV diagnosis	557	22.3	114	20.5	443	79.5	
Yes, >24 months before HIV diagnosis	779	31.2	236	30.3	543	69.7	
Yes, but date unknown	20	0.8	2	10.0	18	90.0	
Health insurance card							
Yes	2,271	90.9	568	25.0	1,703	75.0	0.27
No	103	4.1	24	23.3	79	76.7	
Unknown	125	5.0	39	31.2	86	68.8	
Total	**2,499**	**100**	**631**	**25.3**	**1,868**	**74.7**	

MSM: men who have sex with men.

Table 2

Factors associated with late presentation among men who have sex with men newly diagnosed with HIV, univariate/multivariate analysis, EPI-VIH Network, Spain, 2003–2011 (n=2,499)

Variables	Univariate analysis		Multivariate analysis		
	OR	95% CI	aOR	95% CI	p value
Age group (years)					
<25	0.8	0.6–1.1	0.8	0.6–1.0	0.08
35–44	1.3	1.1–1.7	1.3	1.0–1.7	0.02
≥45	1.8	1.4–2.6	1.8	1.3–2.5	0.00
Educational level (university education)[a]					
Illiterate/primary education	1.3	1.0–1.7	n.a.	n.a.	n.a.
Secondary education	1.1	0.9–1.4	n.a.	n.a.	n.a.
Unknown	1.4	0.9–1.9	n.a.	n.a.	n.a.
Region of birth (Spain)[a]					
Western Europe	1.1	0.7–1.9	n.a.	n.a.	n.a.
Central/eastern Europe	1.0	0.5–2.1	n.a.	n.a.	n.a.
Latin America	1.3	1.1–1.6	n.a.	n.a.	n.a.
Africa	2.9	1.1–7.5	n.a.	n.a.	n.a.
Source of infection: steady partner (No)[a]					
Yes	1.1	0.9–1.3	n.a.	n.a.	n.a.
Source of infection: casual partner (No)					
Yes	1.1	0.9–1.4	1.0	0.7–1.3	0.74
Source of infection: commercial sexual contact (No)					
Yes	1.1	0.7–1.5	0.8	0.5–1.2	0.22
Source of infection: known HIV-infected partner (No)					
Yes	0.7	0.5–0.9	0.7	0.5–0.9	0.02
Acute retroviral syndrome (No)					
Yes	0.4	0.3–0.6	0.5	0.4–0.7	0.00
Previous HIV-negative test (Yes, <12 months before HIV diagnosis)					
No	3.4	2.6–4.5	3.1	2.3–4.2	0.00
Yes, 12–24 months before HIV diagnosis	1.6	1.1–2.1	1.4	1.0–2.0	0.03
Yes, >24 months before HIV diagnosis	2.6	2.0–3.4	2.2	1.7–3.0	0.00
Yes, but date unknown	0.7	0.2–3.0	0.6	0.1–3.0	0.54
Health insurance card (No)					
Yes	1.1	0.7–1.8	1.2	0.7–2.1	0.47
Unknown	1.5	0.8–2.7	1.3	0.6–2.5	0.51

aOR: adjusted odds ratio; CI: confidence interval; MSM: men who have sex with men; n.a.: not applicable; OR: odds ratio.
Reference categories in brackets. Model adjusted by clinic of diagnosis.
[a] For convenience, adjusted odds ratio for interactions between these variables are shown in Figure 2.

LP, logistic regression models were fitted using a backward elimination procedure. Associations were measured using the odds ratio (OR) and its 95% confidence interval (CI). Data analyses were performed using the STATA statistical software package Version 13 (Stata Corporation, College Station, TX, US).

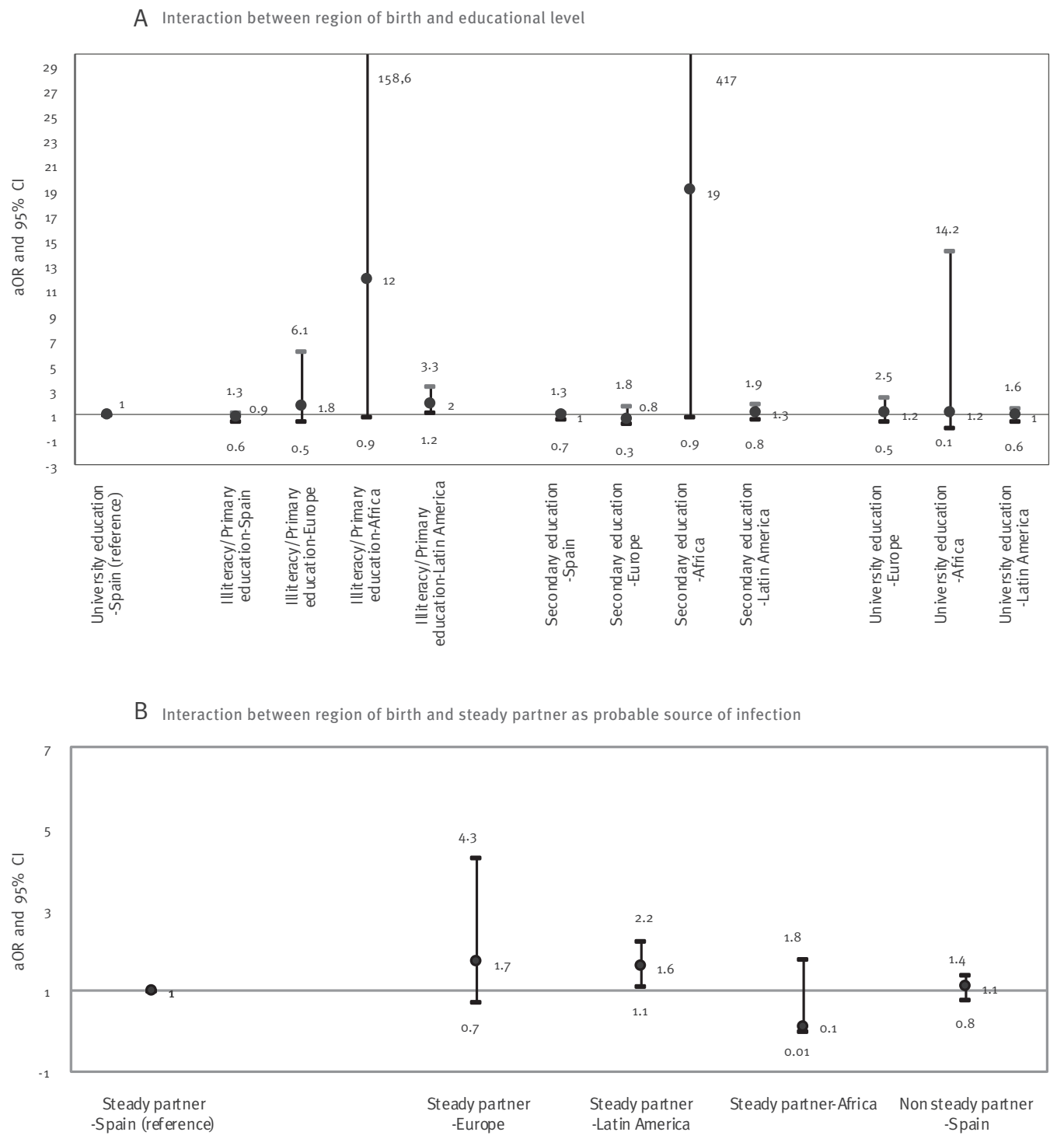
The EPI-VIH Network is an HIV sentinel surveillance system, and the database was registered in the Spanish Data Protection Agency (registry number 2080910068). No personal identifiers were collected.

Results

A total of 3,081 MSM newly diagnosed with HIV were identified during the study period. Of these 2,499 (81.1%) had data on CD4 and/or AIDS diagnosis. The majority were born in Spain (64.7%), were in the 25–34 year age group (49.3%), and had secondary/university education (77.4%). Almost one in six reported symptoms compatible with an acute retroviral syndrome, and 78.7% had been tested for HIV previously (Table 1). Median CD4 at presentation was 497 (interquartile range: 349–690). Overall, 631 MSM (25.3%) met

Figure 2

Interactions of 'region of birth' with 'educational level' (A) and with 'steady partner as probable source of infection' (B), multivariate analysis, EPI-VIH Network, Spain, 2003-2011 (n=2,499)



aOR: adjusted odds ratio; CI: confidence interval.

Bars represent 95% confidence intervals.

Model adjusted by all variables shown in Table 2 plus clinic of diagnosis.

the definition of LP (593 cases had fewer than 350 CD4 cells/µL, 5 presented AIDS at diagnosis and 33 had both). The proportion of LP increased with age, and was higher in men with a low educational level (28.5%), in MSM born in Africa (47.1%) or Latin America (countries of the American continent where Spanish or Portuguese is the main national language) (28.8%), and among those without a previous HIV-negative test (36.1%). Conversely, the prevalence of LP was lower in men attributing their infection to intercourse with a known HIV-infected partner (19%) and those reporting an acute retroviral syndrome (15.2%) (Table 1). No trend was found in the prevalence of LP during the study period (Figure 1).

In the multivariate analysis, factors associated with LP were age over 34 years ((35–44 years: adjusted odds ratio (aOR): 1.3; 95% CI:1.0–1.7; p = 0.02) (>44 years: aOR:1.8; 95% CI:1.3–2.5)), having no history of previous tests (aOR:3.1; 95% CI: 2.3–4.2) or having been tested more than 12 months before the diagnostic test ((12–24 months: aOR:1.4; 95% CI:1.0–2.0) (>24 months: aOR: 2.2; 95% CI: 1.7–3.0)). Factors inversely associated with LP were reporting sexual contact with a known HIV-infected partner as the source of infection (aOR: 0.7; 95% CI: 0.5–0.9) or symptoms compatible with an acute retroviral syndrome (aOR: 0.5; 95% CI:0.4–0.7). Region of birth presented interactions with 'educational level' and with 'probable source of infection: steady partner': MSM born in Africa or Latin America, with low educational level (but not those with high educational level) had higher odds of presenting late, although, for Africans, results were on the edge of significance and confidence intervals were very wide due to the small sample size. Latin-American MSM attributing their infection to their steady partner (but not any other subgroup) were also more likely to present late (Table 2, Figure 2).

Discussion

This paper presents data on LP among MSM newly diagnosed with HIV in the EPI-VIH Network in Spain. Among MSM diagnosed in this network, LP is less common than in those diagnosed elsewhere, but presenting late is not evenly distributed, and the effect of region of birth on LP varies depending on the levels of two other variables.

Reducing diagnostic delay is a policy priority in Spain [20], and HIV testing is free of charge in all public facilities. Since 2009, HIV testing at least once a year has been recommended for MSM, and HIV testing guidelines that reinforce the importance of timely testing in this population have been issued recently [21]. In order to increase HIV testing availability and to facilitate anonymous testing, several regions have implemented testing in pharmacies [22] and others have made available rapid HIV tests in STI clinics and primary health care centres [23,24]. Testing programmes implemented by nongovernmental organisations are also playing an important role [25,26].

The proportion of LP among MSM found in this study (25.3%) is lower than what has been reported in this group in other Spanish settings: in a study performed in Barcelona from 2001 to 2009 the proportion was 47.7% [17], and in another analysis of data from 11 autonomous regions during the period 2007–2011, the figure was 39.1% [18], although in this case the definition of LP did not include AIDS. The prevalence in our study was also lower than the 34% reported in the United Kingdom in 2012 [27]. This finding is not surprising since the main purpose of the clinics belonging to the EPI-VIH Network is to be highly accessible to people with a high perceived risk for HIV, irrespective of their circumstances [15]. Also, MSM attending these clinics are probably very much aware of the importance of frequent testing: almost 80% of the participants in this study reported previous testing, while in the Spanish sample of the European MSM Internet Survey (EMIS-Spain) the proportion of men ever tested was 74% [28]; furthermore, our clinics are located in the main cities, and EMIS-Spain showed that MSM living in big cities were more likely to have been tested for HIV [28].

Participants older than 34 years were found to be more likely to have LP, and the risk increased with increasing age. This finding is frequent in studies analysing LP [16,18,29], and is consistent with results from a study conducted in England, Wales, and Northern Ireland in 2007, where MSM over 50 years of age were almost three times more likely to have a CD4 count of less than 350 cells/µL at HIV diagnosis [30].

Low educational level [2] and migrant status [17,18] have been described as predictors of LP in Spain, and poor education and little knowledge about HIV were also associated with being untested in an online Norwegian sample of MSM [31]. In our study, there was an interaction between education and migrant status, so that Latin-American and African MSM with low educational level (but not those from the same regions with high educational level or men from other regions) were more likely to present late. These results might reflect factors, such as lack of knowledge about HIV infection, lack of access to HIV diagnostics in their country of birth or lack of knowledge about HIV testing policies/facilities in Spain, operating mainly in less educated migrants. In EMIS-Spain, MSM with low to middle educational level or lesser knowledge about HIV/STI, and those who were not confident about accessing HIV testing were more likely never to have been tested for HIV although, surprisingly, Spaniards were less likely than migrants to have been tested [28]; the likely explanation for this finding is that, in this particular study, most participating migrants were Latin-American with better educational level than their Spanish counterparts.

The fact that Latin-American MSM who attribute their HIV infection to their steady partners are at greater risk of LP warrants further investigation and suggests that emotional factors have to be considered

when analysing LP. In any case, Latin-American MSM living in Spain appear to be highly vulnerable to HIV. They are over-represented in new HIV diagnoses [11] and showed higher levels of risky behaviours in EMIS-Spain, despite being highly educated and very knowledgeable about HIV [32].

It seems logical that men experiencing symptoms compatible with an acute retroviral syndrome and those reporting a known HIV-infected partner as their probable source of infection would have sought HIV testing quickly and therefore be less likely to present late. It is less obvious why not having a health card had no effect on LP, but this is not so surprising in our setting because this card is not required to be tested for HIV.
LP was inversely associated with repeat HIV testing, a finding also reported in Danish MSM [33]. Our results even show an upward gradient of risk for LP as the time lag between the previous negative HIV test and the diagnostic test increased, underlining the importance for MSM to follow the recommendation of testing at least yearly.

This study has some limitations. Most importantly, MSM attending the EPI-VIH Network are not representative of the Spanish MSM population, thus our results cannot be extrapolated to all MSM in the country; unfortunately, educational level and probable source of infection are not collected in the regular surveillance system, thus preventing replication of the same analysis with these data. Furthermore, many persons were involved in data collection, thus increasing the probability of introducing mistakes; nevertheless, the EPI-VIH Network has been operating for many years, participating clinicians are very experienced, and a standard questionnaire is used to collect data. Finally, some degree of misclassification might exist if someone newly infected with HIV and presenting a low CD4 count was classified as late presenter.

On the other hand, we believe that results from this study are important to define effective interventions to increase HIV testing in the MSM subgroup that is probably at highest risk of infection. The need to test for HIV at least yearly should be further disseminated among the MSM community, and efforts should be made to increase awareness about symptoms suggestive of an acute antiretroviral syndrome. In addition, measures aiming at improving early diagnosis in poorly educated Latin- American and African migrants are a priority; in these MSM subgroups better knowledge about their situation is also needed to determine the best way to assist them.

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Conflict of interest

The authors declare that they have no conflicts of interest.

Authors' contributions

MD was the main study researcher. She supervised field work and data collection, wrote the statistical analysis plan and the final version of the manuscript. AD performed data collection and management, quality control and statistical analysis, and wrote the first version of the manuscript. JdR, CR, IA JB, FJB, MMC, MLJ, IS, LJV, LG, EM, FG, MCL, IP, JMU, BM, JAV, JT, MAA, and EPI-VIH Study Group: were the clinicians responsible for patient recruitment and follow-up in the participating centres. They all participated in development of the study protocol, collection of epidemiological and clinical data, and critical review of all versions of the manuscript. All authors have seen and approved the final manuscript.

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Assessment of an outreach street-based HIV rapid testing programme as a strategy to promote early diagnosis: a comparison with two surveillance systems in Spain, 2008–2011

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We assess the added value of a multisite, street-based HIV rapid testing programme by comparing its results to pre-existing services and assessing its potential to reduce ongoing transmission. Between 2008 and 2011, 8,923 individuals underwent testing. We compare outcomes with those of a network of 20 sexually transmitted infections (STI)/HIV clinics (EPI-VIH) and the Spanish National HIV Surveillance System (SNHSS); evaluate whether good visibility prompts testing and assess whether it reaches under-tested populations. 89.2% of the new infections were in men who have sex with men (MSM) vs 78.0% in EPI-VIH and 56.0% in SNHSS. 83.6% of the MSM were linked to care and 20.9% had <350 CD4 HIV prevalence was substantially lower than in EPI-VIH. 56.5% of the HIV-positive MSM tested because they happened to see the programme, 18.4% were previously untested and 26.3% had their last test ≥2 years ago. The programme provided linkage to care and early diagnosis mainly to MSM but attendees presented a lower HIV prevalence than EPI-VIH. From a cost perspective it would benefit from being implemented in locations highly frequented by MSM. Conversely, its good visibility led to reduced periods of undiagnosed infection in a high proportion of MSM who were not testing with the recommended frequency.

Introduction

In European countries with HIV epidemics similar to Spain's [1,2], between 20 and 35% of the HIV-infected population remains undiagnosed [3]. Of the new diagnoses reported in Spain in 2012, 47.6% had a CD4 count under 350 cells/µL [4]. Late presenters have both higher morbidity and mortality [5,6] and higher rates of transmission than those who present early [7], therefore, promoting earlier diagnosis is a top priority to fight the epidemic [8].

In Spain, HIV testing is a non-routine procedure and, until recently, has been performed at all levels of the public health system, confidentially and free of charge, when requested by the patient or when considered necessary by the health provider. However, recent regulatory changes limit its access to migrants with illegal administrative status [9]. In some cities, testing is also offered in HIV-sexually transmitted infection (STI) clinics where it is also performed confidentially and free of charge.

Additionally, programmes offering rapid testing in non-clinical settings have proliferated in recent years. They are very heterogeneous in terms of target population, appointment requirement, duration of the counselling provided and type of rapid test used, but most are carried out at the premises of the community-based organisations (CBO) that run them. Despite their expansion in recent years, their effectiveness in terms of seropositivity rates, linkage to care and capacity for promoting early diagnosis have rarely been externally evaluated, and their outcomes have rarely been compared with clinical settings.

Given the fixed nature of these programmes' venues, they reach people who necessarily perceive themselves at risk of being infected or who have interiorised the routine of testing periodically. Conversely, they might miss people with low risk perception, who do not feel the need to be tested. Offering rapid testing in highly visible locations could promote diagnosis in populations that do not actively seek testing in other venues.

Testing is offered free of charge in a wide range of settings in Spain, and this paper aims to appraise the added value of a multi-site outreach programme offering rapid HIV testing in the street. To do this, we first analyse the characteristics of the population tested and the programme's capacity to reach people and link them to care early in the course of HIV infection and compare results against existing services. Second, we determine whether those diagnosed may constitute a population that is either not seeking HIV testing or testing too infrequently, and discuss to what extent the programme reduces time from infection to diagnosis.

Methods

Setting and study period

The programme was run by Madrid Positivo, a non-governmental organisation and it was conducted during three periods: May 2008–December 2008 (season 1, 62 days in total), July 2009–July 2010 (season 2, 65 days) and November 2010–December 2011 (season 3, 35 days). In all three seasons, a mobile unit was located in Chueca, a busy commercial city-centre neighbourhood of Madrid frequented by young people, with a high proportion of gay residents and a high number of gay businesses (hereafter referred to as 'the gay neighbourhood'). It was also deployed in a Madrid neighbourhood with high migrant concentration (hereafter referred to as 'the migrant neighbourhood') (season 3) and in locations outside the city of Madrid with no relation to the gay scene (season 2–3) (additional data available upon request). The programme usually operated in the afternoon, and on certain days throughout the day. The regularity and the days on which the programme was implemented depended on permissions granted by local authorities to deploy the mobile unit in public spaces.

Data collection, rapid test results and linkage to care procedures

Individuals signed an informed consent and entered the mobile unit, where a nurse or doctor completed a brief pre-counselling session, and performed the test (Determine HIV-1/2 test). While waiting for the result, individuals completed an anonymous self-administered paper-based questionnaire code linked to their test (sections used available from authors upon request). The core survey was the same throughout the three seasons and included sociodemographic and behavioural questions (number of sexual partners, condom use, STI history and injecting drug use) and also on HIV-testing history (previous testing experience and time since last test). The questions assessing involvement in gay culture, self-identified sexual orientation, last testing location, main reason for testing today, reason for testing in the programme and future testing intentions were only included during certain periods that will be specified as table footnotes. For those with limited proficiency in Spanish, a form was designed to collect basic socio-demographic, behavioural and HIV-testing history data, in English and French.

In season 1, those with a reactive rapid test were referred to a collaborating STI/HIV diagnostic centre or advised to see their general practitioners. They were asked to give a telephone number in order to obtain their confirmation result and to keep in contact for support during linkage to care. Confirmation results and CD4 count were obtained through direct contact with either the individual or the collaborating diagnostic centre. To shorten the diagnostic process and facilitate linkage to care, from season 2 onwards blood was extracted at the mobile unit and immediately sent to a collaborating STI/HIV diagnostic centre for confirmation. Subjects were then contacted and an appointment set for the result communication and, if positive, the collaborating centres performed a clinical and immunological evaluation for antiretroviral therapy (ART) initiation. We considered as 'linked to care' all the individuals who visited a health centre (mainly the collaborating STI/HIV diagnostic centres) to receive the confirmation result or to ask for a confirmation test. Early diagnosis was defined as having a CD4 count of≥350 cells/µL. Those who revealed during post-test counselling that they had previously tested positive for HIV were excluded from the analysis.

Data analysis

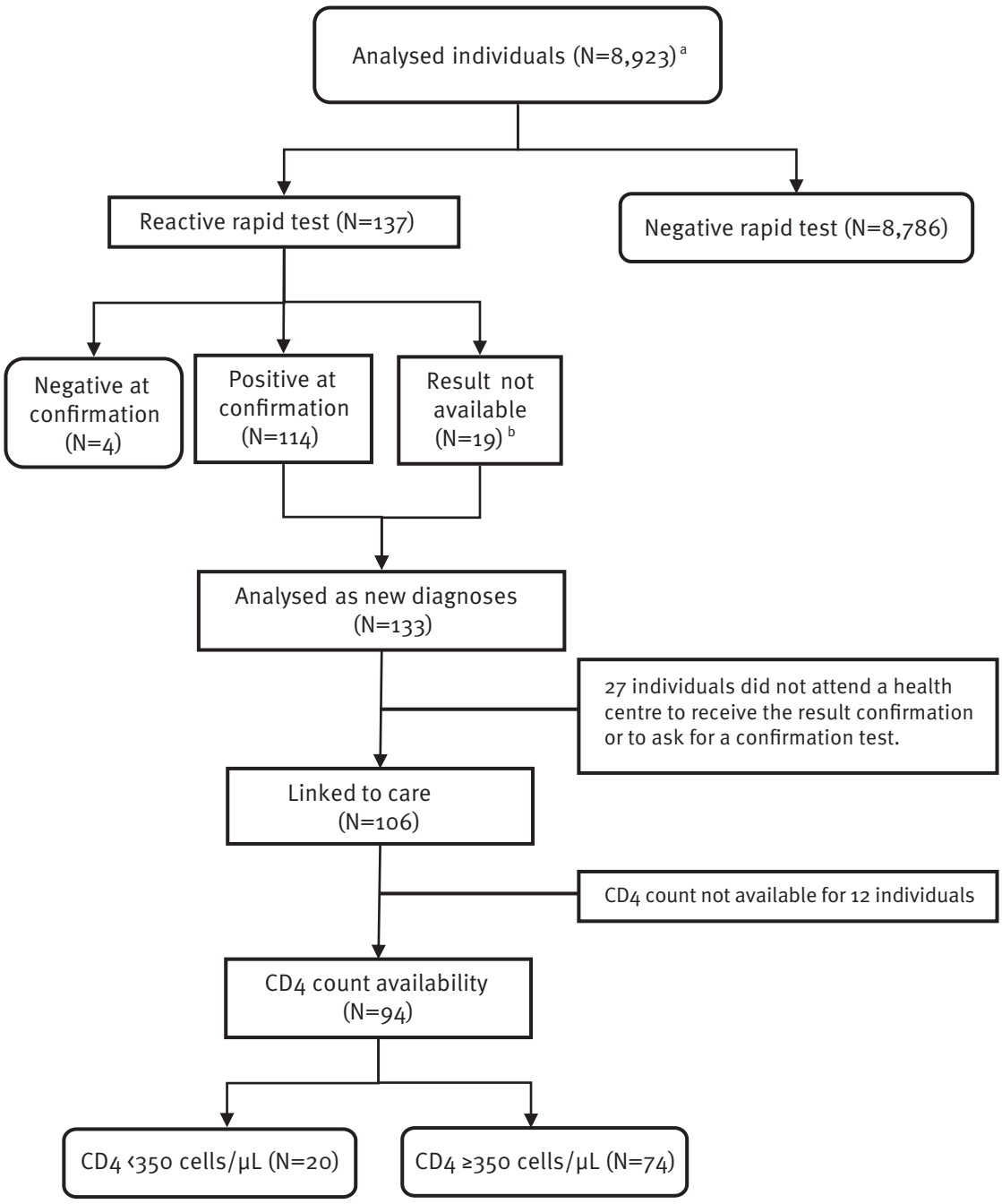
A descriptive analysis was carried out by stratifying the sample into three groups: women, men who have sex exclusively with women (MSW), and men who have sex with men (MSM). Men included in the latter group were those who reported ever having had sex with men. Using the same stratification, we analysed testing history and other testing-related variables. In the MSM group, a further stratification by serostatus was conducted. Differences between the three groups were assessed using the chi-squared test.

In the analysis of HIV positive individuals, we considered new diagnoses (n=133), those rapid test results with a positive confirmation (n=114) and those for which the confirmation result remains unknown (n=19) (Figure 1). To evaluate the programme's capacity to detect previously undiagnosed HIV infections, we present the distribution of persons tested and the prevalence of infection with its 95% confidence interval (CI) by programme location. In each location we performed the same analysis by transmission category and in the MSM by place of birth. Due to limited sample sizes this analysis could not be conducted in heterosexuals or injecting drug users (IDU). We also estimated the prevalence of infection by transmission category (regardless of programme location) and in MSM, by age, country of birth and educational level. Within HIV-positive individuals we estimated the percentage linked to care, and the proportion diagnosed at a late stage of infection, both globally and among MSM.

These outcomes are compared with EPI-VIH-network (EPI-VIH) and the Spanish National HIV Surveillance System (SNHSS). EPI-VIH is a sentinel surveillance system based on 20 STI/HIV clinics located in 19 medium

Figure 1

Rapid test and confirmation results, availability of data on linkage to care and CD4 count for people who underwent testing in a street-based HIV rapid-testing programme, Spain, 2008–2011



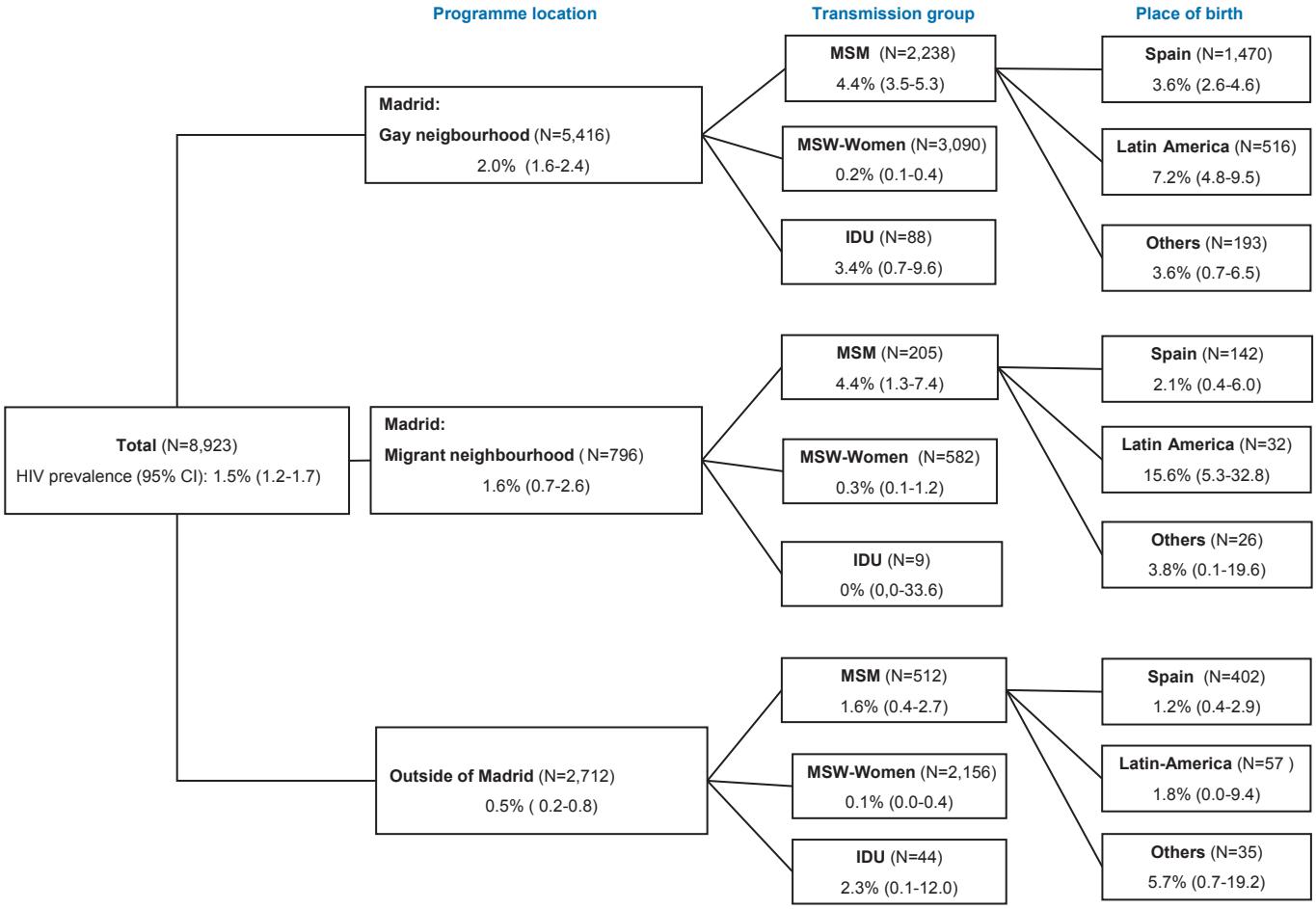
MSM: Men who have sex with men; MSW: Men who have sex with women.

[a] n=70 were not included because they had never had sexual relations or had ever injected drugs ;n=173 men were excluded because they could not be classified as MSM or MSW.

[b] Did not attend a collaborating centre and could not be contacted directly to obtain confirmation results, however they were considered new diagnoses in the analysis.

Figure 2

Number of people tested and prevalence of HIV infection by programme location, transmission group and place of birth, in a street-based HIV rapid-testing programme, Spain, 2008–2011



IDU: injecting drug users; MSM: men who have sex with men; MSW: men who have sex exclusively with women.

and large Spanish cities. They offer voluntary, confidential and free-of-charge HIV testing, and some also offer anonymous testing. No legal documents were required during the study period (2008–2011). This system collects some limited information about people tested including the test result [10]. SNHSS collects new HIV diagnoses data reported by 17 of the 19 Spanish autonomous regions (71% of the Spanish population). It is the best approximation of the characteristics of the national epidemic and its evolution [4]. Both EPI-VIH and SNHSS information is collected using data collection forms completed by a healthcare professional. When comparing our results with those of both surveillance systems, we took into account available data from the years when the programme was implemented: 2008–2010 in the case of EPI-VIH and 2008–2011 in SNHSS. Given the low number of HIV-positive women and MSW in the programme, the characterisation of HIV-infected individuals was restricted to MSM. The capacity of the programme to reduce periods of undiagnosed infections is gauged by i) analysing whether its good visibility prompted testing in individuals who had not though about it and ii) by analysing testing history and future testing intention of HIV-infected participants. Again, due to sample size limitations these analyses were limited to HIV-positive MSM. The study was approved by the Instituto de Salud Carlos III's institutional review board.

Results

Sociodemographic, behavioural characteristics and sexual orientation

Of the 9,166 people tested we excluded from the analysis 70 individuals who had never had sexual relations or injected drugs and 173 men who did not answer the question on sexual behaviour and could not be classified in either of the two subgroups (Figure 1). Of the

Table 1

Sociodemographic, sexual identity, gay community involvement and behavioural risk variables of people receiving rapid HIV testing in a street-based programme, Spain, 2008–2011 (n=8,923)

	Women (n=3,087)		MSW (n=2,832)		MSM (n=3,004)		Total (n=8,923)		p value[a]
	N	%	N	%	N	%	N	%	
Programme location									<0.001
City of Madrid: gay neighbourhood	1,708	55.3	1,429	50.5	2,277	75.8	5,414	60.7	n.a
City of Madrid: migrant neighbourhood	288	9.3	301	10.6	204	6.8	793	8.9	n.a
Outside of the city of Madrid	109	35.3	1,101	38.9	521	17.3	2,712	30.4	n.a
<30 years old	1,816	61.7	1,251	45.9	1,387	47.3	4,451	51.8	<0.001
Place of birth									<0.001
Spain	2,042	68.2	1,793	65.1	2,037	69.7	5,872	67.7	n.a
Latin America	664	22.2	576	20.9	618	21.1	1,858	21.4	n.a
Others	287	9.6	385	14.0	267	9.1	939	10.8	n.a
Completed a university degree	1,517	49.9	1,074	38.6	1,610	54.0	4,201	47.7	<0.001
Sexual identity and gay community involvement									
Sexual orientation[b]									<0.001
Homosexual	84	4.6	11	0.7	1,409	77.8	1,504	28.6	n.a
Bisexual	137	7.5	15	0.9	214	11.8	366	6.9	n.a
Heterosexual	1,599	87.9	1,610	98.4	188	10.4	3,397	64.5	n.a
Relationship with gay culture[c]									
Frequenter of gay scene but not a member of a gay CBO	n.a	n.a	n.a	n.a	1,219	63.0	n.a	n.a	n.a
Not related to gay scene	n.a	n.a	n.a	n.a	499	25.8	n.a	n.a	n.a
Member of a gay CBO	n.a	n.a	n.a	n.a	216	11.2	n.a	n.a	n.a
Behavioural characteristics									
Ever injected drugs	61	2.1	115	4.4	76.0	2.7	252	3.0	<0.001
Diagnosed with an STI (last 12 months)	167	9.5	71	4.9	242	13.5	480	9.6	<0.001
Number of heterosexual partners (last 12 months)									<0.001
0–1	1,135	39.8	675	27.5	2,361	87.7	4,171	52.2	n.a
2	594	20.8	514	21.0	100	3.7	1,208	15.1	n.a
3–4	648	22.7	626	25.6	103	3.8	1,377	17.2	n.a
≥5	473	16.6	635	25.9	130	4.8	1,238	15.5	n.a
Unprotected sex with heterosexual occasional partners (last 12 months)	1,435	50.6	1,230	51.0	212	7.9	2,877	36.3	<0.001
Number of homosexual partners (last 12 months)									
0–1	n.a	n.a	n.a	n.a	570	20.3	n.a	n.a	n.a
2–4	n.a	n.a	n.a	n.a	809	28.8	n.a	n.a	n.a
5–9	n.a	n.a	n.a	n.a	538	19.2	n.a	n.a	n.a
10–19	n.a	n.a	n.a	n.a	442	15.8	n.a	n.a	n.a
≥20	n.a	n.a	n.a	n.a	447	15.9	n.a	n.a	n.a
Unprotected sex with homosexual occasional partners (last 12 months)	n.a	n.a	n.a	n.a	991	36.5	n.a	n.a	n.a

CBO: community-based organisation; MSM: men who have sex with men; MSW: men who have sex exclusively with women; n.a.; not applicable; STI: sexually transmitted infection.

The programme was conducted during three periods: May 2008–December 2008 (season 1, 62 days in total), July 2009–July 2010 (season 2, 65 days) and November 2010–December 2011 (season 3, 35 days).

[a] p value refers to chi-squared test between MSM, Women, MSW.

[b] Included in season 2 onwards.

[c] Included in the first season, but starting October 2008.

8,923 analysed (Table 1), 34.6% were women, 31.7% MSW and 33.7% MSM. Some 60.7% were tested in Madrid´s gay neighbourhood, 8.9% in Madrid´s migrant neighbourhood and 30.4% outside of Madrid (Table 1). The proportion of MSM was notably higher in the gay neighbourhood than in the other two areas (Figure 2). Fifty two percent were under 30 years of age, 21.4% were born in Latin America (defined as people born in countries of the American continent where Spanish or Portuguese is the main national language), 10.8% in other countries and 47.7% had a college degree. During the previous 12 months, 50.6% of the women and 51% of the MSW had had unprotected sex with heterosexual occasional partners. Unprotected sex with homosexual occasional partners was reported by 36.5% of the MSM. Three per cent reported having ever injected drugs (Table 1).

Testing related information

Twenty six per cent of the MSM had never been tested before (18.4% among new diagnoses); this percentage was higher in women (63.8%) and MSW (61.5%). MSM had the shortest time between previous and current testing: 40.2% of MSM had tested in the previous 12 months (although 26.3% of HIV-positive MSM had last been tested two or more years previously). The most common location for most recent test was primary care (26.8%) and having had unprotected sex with occasional partners (34.1%) was the most common reason for testing that day. Testing as a part of a periodical routine was the second most cited reason (12.8%), mainly because 24% of the MSM reported it. This percentage was 4 times lower in the HIV-positive MSM (6.3%) (Table 2). Some 57.5% of all attendees got tested in the programme because they passed by, saw it and decided to take it. Regarding testing intentions, 22.2% said they probably or certainly would not have been tested in the next 12 months if they had not done so that day. This percentage was lower in MSM (10.4%), and even lower in MSM diagnosed with HIV (3.1%) (Table 2).

Analysis of newly diagnosed individuals: comparison with EPI-VIH and SNHSS

The overall HIV prevalence was 1.5%, ranging from 0.5% outside the city of Madrid to 2.0% in Madrid's gay neighbourhood. Prevalence by transmission category was highest in the MSM group (4.4% in Madrid locations) and within the MSM group, in MSMs born in Latin America (prevalence reaching 15.6% in the migrant neighbourhood) (Figure 2).

Positivity rates both overall (1.5%) and in MSM (3.9%) were lower than in EPI-VIH (2.7% and 8% respectively). Regarding the characteristics of the 133 new diagnoses, 89.2% were in MSM compared to 78.0% in EPI-VIH and 56.0% in SNHSS. Our programme showed a greater percentage of new diagnoses in MSM under 30 years of age (49.6%) than EPI-VIH (43.2%) and SNHSS (34.2%). The programme also presented a higher percentage of new HIV diagnoses in Latin Americans (37.7%) than EPI-VIH (21.8%) and SNHSS (27.1%), and a higher educational level (Table 3).

Overall, 79.7% of individuals newly diagnosed with HIV in this programme were linked to care (83.6% in MSM) and CD4 count was known for 70.7% of the newly diagnosed cases (74.1% in the MSM group) (Figure 1). Of those with CD4 count available, 21.3% had <350 CD4 cells/µL (Figure 3), which is 17.8% lower than in EPI-VIH (25.9%), and 61.1% lower than in SNHSS (54.8%). In MSM, delayed diagnosis (20.9%) was 10.4% lower than in EPI-VIH (23.3%), and 46% lower than in SNHSS (38.6%) (Figure 3).

Discussion

The programme described in this paper reached a diverse and under-tested population. However, it diagnosed MSM almost exclusively and presented very low positivity rates when conducted outside of Madrid. We found that the prevalence of infection was half than that of EPI-VIH and that HIV-positive MSM were younger, more frequently from Latin America and had a higher level of education than in EPI-VIH. Compared with SNHSS, MSM diagnosed in the programme were also younger and more frequently from Latin America. The good visibility of the mobile unit led to reduced periods of undiagnosed infection in six out of ten MSM who happened to see it and decided to get tested. The programme was able to reach and diagnose a group of MSM who did not test for HIV with the recommended frequency. Eight out of ten were linked to care and the percentage of late diagnoses was similar to EPI-VIH but half of what was reported in SNHSS.

This study contributes substantially to the scarce body of European literature that analyses community-based testing. It evaluates a programme that is different in terms of its setting and the population it served. Comparing the programme with other healthcare settings puts the results into perspective, which has rarely been done before. Finally, we evaluate how this programme's good visibility could contribute to the control of the epidemic.

Most of the European-based published studies have evaluated programmes where MSM are the target population [11-15]. This is one of the few not specifically focused on them. The good visibility of the programme, and its deployment in settings not related to the gay community may have prompted testing in lower-risk individuals who otherwise would not have thought of it. In fact, two thirds of those who took the test in the mobile unit were either MSW or women, and within these two groups, around six out of 10 had never tested for HIV before. This capacity of the programme to promote HIV testing in populations with no previous testing history has been described elsewhere [16].

The overall prevalence is similar to that found by the handful of studies that evaluate programmes outside clinical settings which do not target vulnerable

Table 2

Testing history, reasons for testing and future testing intentions of people who underwent testing in a street-based HIV rapid-testing programme, Spain, 2008–2011 (n=8,923)

	Total (n=8,923)		Women (n=3,087)		MSW (n=2,832)		MSM (n=3,004)						p value[a]
							Total		HIV-negative (n=2,886)		HIV-positive (n=118)		
	N	%	N	%	N	%	N	%	N	%	N	%	
HIV testing history													<0.001
Never tested previously	3,901	50.6	1,772	63.8	1,449	61.5	680	26.3	661	26.6	19	18.4	
12 months or less	1,718	22.3	316	11.4	363	15.4	1,039	40.2	1,000	40.3	39	37.9	
>1 year and<2	753	9.8	205	7.4	160	6.8	388	15.0	370	14.9	18	17.5	
2 - 3 years	485	6.3	153	5.5	134	5.7	198	7.7	186	7.5	12	11.7	
More than 3 years	859	11.1	330	11.9	249	10.6	280	10.8	265	10.7	15	14.6	
Location of last testing episode[b]													<0.001
Primary care	809	26.8	240	30.0	182	24.9	387	26.0	369	25.9	18	27.7	
Hospital settings	651	21.6	188	23.5	198	27.0	265	17.8	257	18.1	8	12.3	
Community based organisations	571	18.8	128	16.0	136	18.3	307	20.5	297	20.7	10	15.4	
Specific centres: STI/HIV clinics, family planning centres	539	17.9	121	15.1	94	12.8	324	21.8	306	21.5	18	27.7	
Private laboratory	351	11.6	86	10.8	99	13.5	166	11.2	156	11.0	10	15.4	
Others	98	3.3	37	4.6	23	3.4	38	2.7	37	2.7	1	1.5	
Reason for testing today[c]													<0.001
Sex with occasional partner(s) without using a condom	1,744	34.1	701	39.2	517	32.9	526	30.0	504	29.9	22	34.4	
Takes the test periodically	654	12.8	114	6.4	119	7.6	421	24.0	417	24.7	4	6.3	
Sex with a partner that is or could be infected	433	8.5	96	5.4	145	9.2	192	11.0	181	10.7	11	17.2	
Main partner asked to	396	7.7	83	4.6	182	11.6	131	7.5	126	7.5	5	7.8	
Condom failure during sex (breakage/slippage)	372	7.3	130	7.3	102	6.5	140	8.0	135	8.0	5	7.8	
To stop using condom with main partner	304	5.9	107	6.0	113	7.2	84	4.8	82	4.9	2	3.1	
Has health problems that relate to infection	159	3.1	41	2.3	60	3.8	58	3.3	51	3.0	7	10.9	
Knows or thinks that main partner is infected	100	2.0	44	2.5	14	0.9	42	2.4	42	2.5	0	0.0	
Has followed his doctor's advice	60	1.2	28	1.6	25	1.6	7	0.4	6	0.4	1	1.6	
Pregnancy	45	0.9	45	2.5	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	
Others	846	16.5	398	22.3	293	18.8	151	8.6	144	8.5	7	10.9	
Reason for testing in this particular programme[d]													0.001
I knew how it worked and I specifically came to do it here	2,354	39.8	766	37.0	705	40.2	883	42.3	851	42.5	32	37.6	
If I had not passed by I would have never taken the test	3,398	57.5	1,255	60.5	988	56.3	1,155	55.3	1,107	55.3	48	56.5	
Others	162	2.7	52	2.5	61	3.5	49	2.3	44	2.2	5	5.9	
If you hadn't taken the test today, would you have taken it in the next 12 months?[c]													<0.001
Yes, for sure	2,280	45.8	584	33.1	626	41.2	1,070	63.1	1,027	63.0	43	67.2	
Probably yes	877	17.6	322	18.3	260	17.1	295	17.4	278	17.0	17	26.6	
I'm not sure	717	14.4	305	17.3	259	17.0	153	9.0	151	9.3	2	3.1	
Probably not	707	14.2	342	19.4	238	15.7	127	7.5	125	7.7	2	3.1	
Certainly not	396	8.0	209	11.9	137	9.0	50	2.9	50	3.1	0	0.0	

MSW: men who have sex exclusively with women; MSM: men who have sex with men; n.a.: not applicable.

The programme was conducted during three periods: May 2008–December 2008 (season 1, 62 days in total), July 2009–July 2010 (season 2, 65 days) and November 2010–December 2011 (season 3, 35 days).

[a] p value referred to chi-squared test between MSM, women, MSW.

[b] Variable not included in season 3.

[c] Included in season 2 onward.

[d] Included in season 1 and 2. In season 3 it was included starting from June 2011.

Table 3

Comparison of people newly diagnosed with HIV by a street-based HIV rapid-testing programme, Spain, 2008–2011, with those from EPI-VIH (2008–2010) and the Spanish National HIV Surveillance System (2008–2011) (SNHSS)

All	Street-based programme				EPI-VIH network				SNHSS	
	N	%	HIV + prevalence (95% CI)		N	%	HIV + prevalence (95% CI)		N	%
	133	100.0	1.5	(1.2–1.7)	2014	100.0	2.7	(2.6–2.8)	10517	100.0
Injecting drug users	4	3.1	2.8	(0.8–7.0)	104	5.3	10.7	(8.7–12.7)	734	7.7
Heterosexual contact	10	7.7	0.2	(0.1–0.3)	329	16.7	0.6	(0.5–0.7)	3,453	36.3
Heterosexual women	4	3.1	0.1	(0.0–0.3)	154	7.8	0.5	(0.4–0.6)	1,620	17.0
Heterosexual men	6	4.6	0.2	(0.0–0.4)	175	8.9	0.7	(0.6–0.9)	1,833	19.3
Men who have sex with men	116	89.2	3.9	(3.2–4.6)	1,531	78.0	8.0	(7.6–8.4)	5,327	56.0
Men who have sex with men: characterisation										
Age in years										
‹25	31	27.0	4.5	(2.9–6.2)	289	18.2	8.2	(7.2–9.3)	740	13.9
25–29	26	22.6	3.9	(2.3–5.4)	396	25.0	12.3	(10.9–13.7)	1,079	20.3
30–39	43	37.4	4.3	(3.0–5.7)	608	38.3	12.8	(11.6–14.0)	2,045	38.3
≥40	15	13.1	2.8	(1.3–4.2)	291	18.4	12.0	(10.4–13.8)	1,463	27.5
Country of birth										
Spain	61	53.5	3.0	(2.3–3.8)	1,072	67.6	9.2	(8.6–9.9)	3,408	64.0
Latin-America	43	37.7	7.1	(5.0–9.2)	424	26.7	21.8	(19.7–24.0)	1,444	27.1
Others	10	8.8	3.9	(1.3–6.5)	90	5.7	9.7	(7.5–12.3)	475	8.9
Educational level										
Primary/None	6	5.3	8.2	(2.3–4.1)	266	18.3	n.av.	n.av.	n.av.	n.av.
Secondary	57	50.0	4.5	(3.3–5.7)	629	43.3	n.av.	n.av.	n.av.	n.av.
University	51	44.7	3.2	(1.2–15.2)	556	38.3	n.av.	n.av.	n.av.	n.av.

CI: confidence interval; EPI-VIH: network of 20 Spanish STI/HIV diagnostic clinics; n.av.: data not available; SNHSS: Spanish National HIV Surveillance System.

populations [17-20]. It varied by location and was higher in the city of Madrid. The capacity of the programme to reach undiagnosed individuals was substantially lower than in EPI-VIH, which is consistent with the only study comparing a CBO with diagnostic clinics in the past [11]. Almost all of the new diagnoses were in the MSM group which is unsurprising in a country where they are the most vulnerable population for HIV infection. However, their weight among the new diagnoses is much higher than in the national figures represented by SNHSS, and also higher than in EPI-VIH.

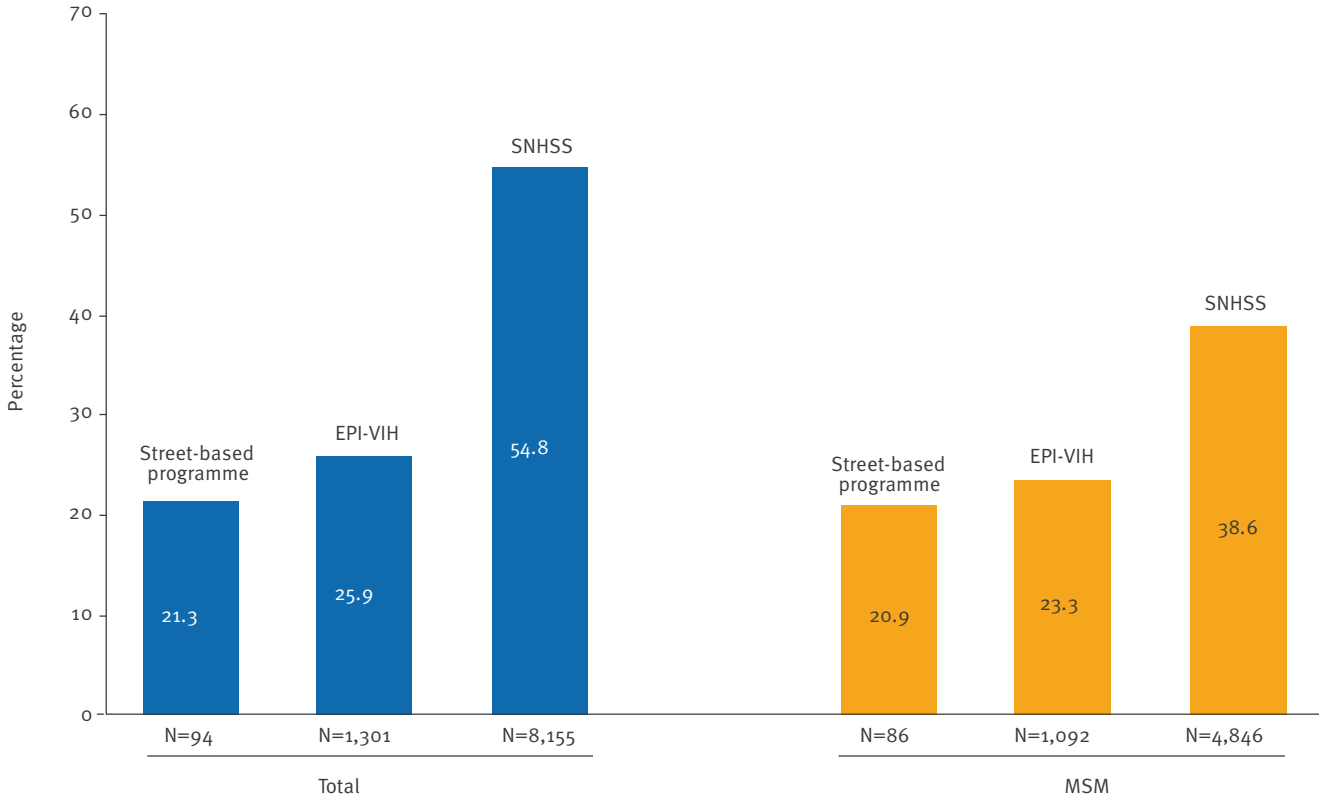
Prevalence in heterosexuals was three times lower than in EPI-VIH and very similar to the prevalence found by another study conducted in primary care in Madrid [21]. This raises the question: is it appropriate to carry out programmes of this nature in locations frequented by lower risk groups? The question is even more pertinent if we consider that, while cost per diagnosis was not assessed, the only example we found concluded that it was considerably higher in outreach settings than in STI/HIV clinics [22].

To evaluate the programme's potential to prevent onward transmission, we must consider factors other than prevalence of infection. Reducing the time an infection remains undiagnosed as a result of the implementation of the programme is a key factor: the sooner an infection is detected, the sooner the community will benefit from viral load reductions and behavioural change. In this sense, good visibility translated into an earlier diagnosis in more than half of the HIV-positive MSM who were not actively seeking to be tested that day: they happened to see the mobile unit and decided to test. According to testing intentions, the time of undiagnosed infection would be reduced by up to one year: almost all of the HIV-infected individuals reported that they would have sought testing in the next 12 months. According to their testing history, however, the gain would be higher: two out of 10 had never tested before and an additional 25% had tested more than two years ago, which is much longer than recommended for this group [8]. It is noteworthy that very few of the HIV-positive MSM reported having tested as a part of a routine check-up. Reaching out to high-risk populations who have not internalised testing as a part of a routine could shorten the time from diagnosis to infection and therefore reduce onward transmission.

The programme also showed a capacity to promote early diagnosis in MSM: only two of 10 had CD4 ‹350 cells/µL, which represents a remarkable improvement when compared with SNHSS. Likewise, programme attendees were also diagnosed earlier than EPI-VIH

Figure 3

Percentage of newly diagnosed HIV infections with CD4 count <350 cells/µL in a street-based HIV rapid-testing programme, Spain (2008–2011) compared with EPI-VIH (2008–2010) and the Spanish National HIV Surveillance System (2008–2011)



EPI-VIH: network of 20 Spanish HIV/STI diagnostic clinics; MSM: Men who have sex with men; SNHSS: Spanish National HIV Surveillance System.

Percentages calculated on those with data available on CD4 count

patients but differences were much smaller. Evidently, as the percentage of delayed diagnosis drops there is less room for improvement. It is also true that HIV-positive MSM were younger and had a higher level of education than in EPI-VIH and SNHSS. The association of delayed diagnosis with increasing age and, in men, with low educational level has been described previously [23-25,26], which means that the programme is reaching subpopulations that are a priori at lower risk of being diagnosed late. On the other hand, in comparison with EPI-VIH and SNHSS, the programme was good at reaching Latin Americans. In Spain, unlike other European countries, they are the largest migrant group, but it is also true that delayed diagnosis in this group is similar to that of the Spanish-born population [4].

Obviously, diagnosis is useless if it is not followed by linkage to the health system for ART eligibility. The linked-to-care percentage was similar to that of the few European studies reporting this outcome [11,12,15] but the definitions used in those studies are not clearly stated and precautions should be taken when comparing results.

The present study has several limitations. First, there is the possibility that some of those with unavailable data on confirmation result did not attend a health centre for this purpose. However, given that access to testing in Spain was universal and performed confidentially in a wide range of settings, we believe that this possibility is minimal. Second, metrics used in 'linkage to care' definitions are heterogeneous. Some are based on clinic visits (as for this study) and some on laboratory monitoring tests. Nevertheless, they always include a time period since diagnosis to either first clinic visit or first laboratory monitoring test [27]. Unfortunately, this parameter was not assessed in the present study and, if included, our 'linkage to care' percentage would probably be lower. Third, when interpreting late diagnosis figures, we should keep in mind that they are calculated by factoring in only those individuals for whom we have a CD4 count. It is not known whether those with no data available are more affected

by late diagnosis. However, the effect of this limitation in the comparison with EPI-VIH is limited, as the proportion of individuals with an unknown CD4 count (33.4%) is similar. Conversely, it might have a greater influence when comparing our study with SNHSS, since the percentage is notably lower (13%). Finally, our data is based on self-reports and could be affected by social desirability bias. However, the use of an anonymous and self-administered questionnaire may have helped to obtain franker answers in the sensitive aspects of the survey.

By giving individuals the chance to rapidly check their serological status, this highly visible programme helped to diagnose a high proportion of individuals who were not actively seeking to get tested. Thus, it diminished the period during which the infection remains undiagnosed and therefore has the potential to reduce onward transmission in a population with high levels of sexual risk behaviours who are not testing with the recommended frequency. All this translated into a substantial contribution to early diagnosis in the MSM group in which late presentation at the population level – despite being lower than in other groups – is still too high. However, the HIV prevalence is notably lower if we compare it with a clinical setting serving at-risk populations. In order to improve its performance from a cost perspective, this programme should concentrate in locations highly transited by MSM.

The Madrid HIV rapid testing group

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Conflicts of interest

None declared

Authors' contributions

MJ Belza and LF designed the study and took overall responsibility of the project, JH, MJ Belza wrote the manuscript, JH, SFB, AD, did the analysis and interpretation of data, AD, MJ Bravo, LF critically revised the manuscript and contributed important intellectual content,
Madrid Rapid HIV testing Group made contributions to the study design, and participated in the acquisition of data.

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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

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To better understand the diversity of practices and behaviours to prevent HIV with casual partners, data from a large convenience sample of men who have sex with men (MSM) in France were categorised into different prevention profiles: no anal intercourse, consistent condom use during anal intercourse, risk-reduction practices (serosorting, seropositioning) and no discernible prevention practice (NDPP). Categories were applied to HIV-positive respondents with controlled (CI; n=672) and uncontrolled infection (UI; n=596), HIV-negative (n=4,734) and untested respondents (n=663). Consistent condom use was reported by 22% (n=148) of HIV-positive-CI respondents, 13% (n=79) of HIV-positives UI, 55% (2,603) of HIV-negatives, and 50% (n=329) of untested (p<0.001). Corresponding figures for NDPP were 45% (n=304), 55% (n=327), 21% (n=984) and 34% (n=227) (p<0.001). Logistic regressions showed that, regardless of respondents' serostatus, NDPP was associated with regularly frequenting dating websites, drug use, exposure to sperm during oral sex, and with HIV diagnosis after 2000 for HIV-positive respondents (CI and UI), with age<30 years for HIV-positive-CI, and with low education for HIV-negatives. Risk-taking remains high, despite implementation of risk-reduction practices. A global health approach should be central to prevention programmes for MSM, to include target behavioural intervention, promotion of condom use, and encouragement of regular HIV testing and early initiation of ART.

Introduction

Sex between men remains the most frequent mode of HIV transmission in men in North America, Australia and western Europe [1]. Newly diagnosed HIV infections among men who have sex with men (MSM) increased in Europe by 33% between 2004 and 2013 [2]. Similar trends have been observed in France, where MSM are increasingly predominant among newly diagnosed cases [3]. Incidence in MSM in France is 200 times higher than in the French heterosexual population [4].

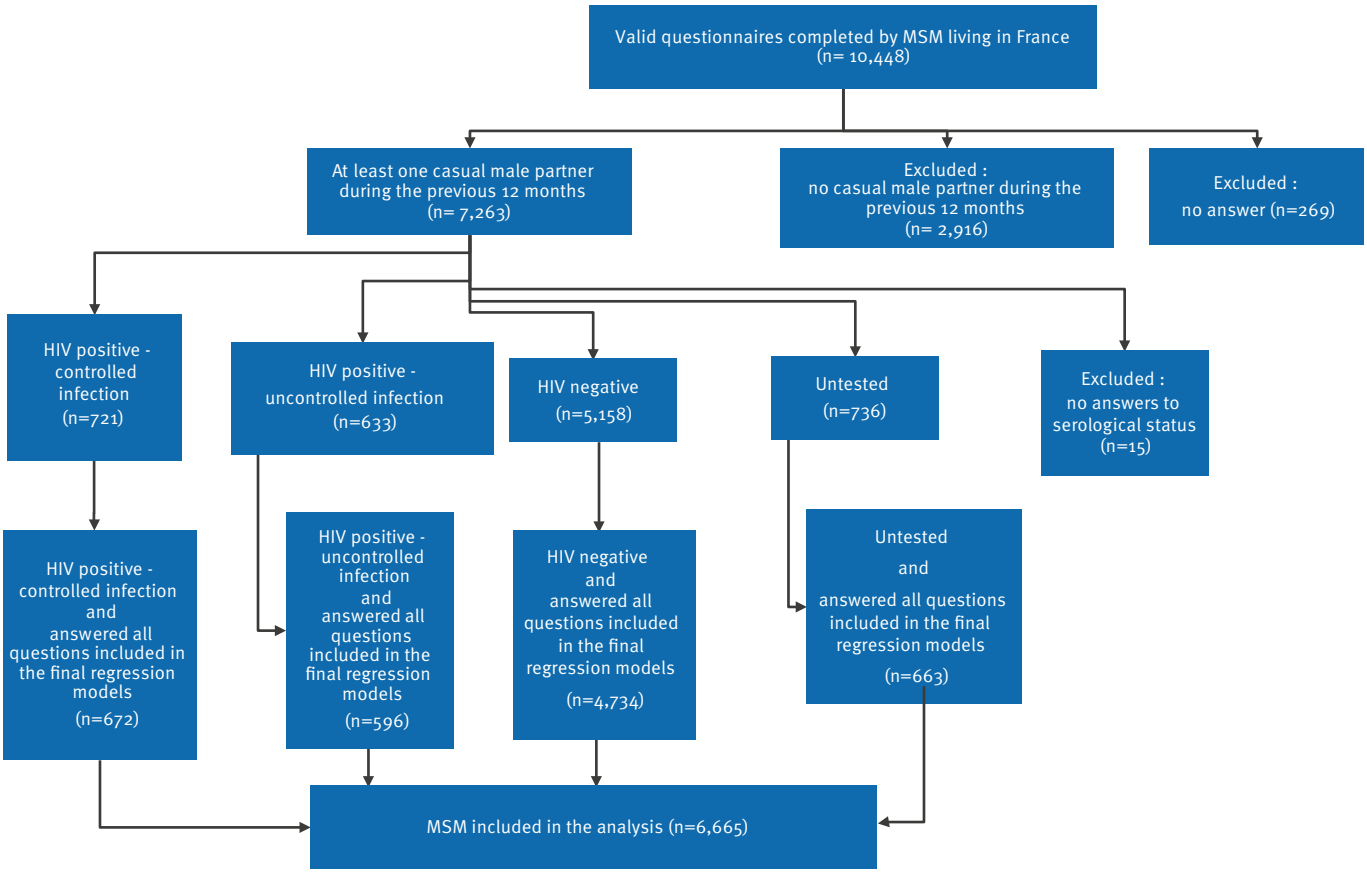
Studies conducted since the epidemic began have shown how MSM have profoundly changed their sexual behaviours by implementing different strategies to manage the risk of HIV transmission. During the second half of the 1980s, MSM reduced their number of partners and began condom use on a widespread basis. During the 1990s, alternative strategies to systematic condom use emerged, such as negotiated safety with a steady partner [5]. Since 2000, condom use has fallen consistently regardless of partner type and HIV serostatus [5]. Simultaneously, alternative risk-reduction strategies have materialised under the umbrella term 'seroadaptation' [6,7]. These strategies include serosorting (engaging in unprotected anal intercourse (UAI) with partners of the same HIV status), seropositioning (HIV-positive men engaging in receptive and HIV-negative men in insertive UAI) and selective avoidance of anal intercourse.

In the meantime, the effectiveness of antiretroviral treatment has contributed to the medicalisation of prevention [8], although more evidence is needed on the efficacy of treatment as prevention among MSM [9]. More frequent testing among sexually active MSM [10] might shorten the delay between contamination and diagnosis [11], so that treatment could start as early as possible [9]. Furthermore, the availability of pre-exposure prophylaxis (PreP) might reduce the risk of transmission in uninfected people [12]. In this context, preventive-behavioural and biomedical approaches need to complement each other [13].

In this article, we first describe the prevalence of sexual preventive behaviours by categorising the different risk-reduction practices according to respondents'

Figure

Flowchart of inclusion of respondents in the analysis, Presse Gays et Lesbiennes survey, France, 2011



MSM: men who have sex with men.

HIV status. Second, we characterise the profiles of respondents with high-risk sexual practices to improve our understanding of the determinants of risk-taking.

Methods

The Presse Gays et Lesbiennes survey (Enquête Presse Gays et Lesbiennes, EPGL) is one of the tools used for behavioural surveillance of HIV and other sexually transmitted infections (STI) among MSM in France [14]. The survey is anonymous, cross-sectional, self-administered and voluntary. The most recent survey questionnaire was inserted in paper format in a monthly gay magazine in June 2011 and posted on the Internet between May and July 2011, accessible through a study-specific website. Participants were recruited through more than 60 information and dating websites for MSM. Web banners, personalised messages and recommendations via Facebook were used to invite MSM Internet users to participate online. There were no inclusion criteria, but the voluntary nature of this study led to the exclusion of some respondents from the analysis. The exclusion rate was higher on the Internet than in the press (9% v. 5%). Of the 10,286 questionnaires completed by men from the Internet, 112 were excluded because respondents reported having had sex exclusively with women, three because respondents reported that they were younger than 14 years-old, and 779 because respondents reported they were not resident in France. Of the 1,110 questionnaires from the press, 54 from men not residing in France were excluded.

The questions asked in the paper and Internet questionnaires were identical. Data were collected on sociodemographic characteristics, social behaviours, sexual and preventive practices. Specifically, respondents were asked to provide, separately for each steady or casual partner in the previous 12 months, information about oral sex, insertive and receptive anal intercourse, condom use, number of UAI episodes, and knowledge of partners' serostatus.

Questions were also asked about HIV testing, both lifetime and during the previous 12 months, and self-reported HIV status at the time of the survey (HIV-negative, HIV-positive). The HIV status indicator is based on the lifetime HIV testing question and self-reported current HIV status.

Table 1

Definitions of four categories of sexual prevention behaviours, Presse Gays et Lesbiennes survey, France, 2011

Category of sexual prevention behaviour	Definition
No anal intercourse	This category comprises respondents who did not report anal intercourse with casual partners in the previous 12 months but who may have had other types of sexual practices (mutual masturbation, oral sex, fisting, etc.).
Consistent condom use	This category comprises respondents who had had anal intercourse with casual partners in the previous 12 months and had systematically used condoms both insertive and receptive intercourse.
Risk-reduction practices	**Exclusive serosorting** Respondents who reported they were HIV-positive or HIV-negative and had at least one episode of unprotected anal intercourse only with casual partners of the same serostatus as themselves in the previous 12 months, were classified in this category. **Exclusive seropositioning** This category comprises respondents who reported they were HIV-positive or HIV-negative and had at least one episode of UAI with casual partners of different or unknown serostatus from themselves in the previous 12 months, and had exclusively insertive anal intercourse for HIV-negative respondents and exclusively receptive anal intercourse for HIV-positive respondents. **Serosorting and seropositioning** Respondents who declared they were HIV-positive or HIV-negative and had at least one episode of UAI with casual partners in the previous 12 months, and who reported serosorting and seropositioning, were classified in this category.
No discernible prevention practice (NDPP)	Respondents who had had UAI with casual partners in the previous 12 months without implementing any of the risk reduction practices (serosorting, seropositioning), regardless of their HIV serostatus, were classified in this category.

Seropositive MSM also answered questions about treatment (if any), viral load, and CD4 count over the past 12 months. They were then classified into two categories — with controlled or uncontrolled infection. In accordance with the Swiss statement recommendations [15], control was defined in relation to both HIV infection and other STIs (urogenital or rectal gonorrhoea, syphilis, hepatitis B, genital herpes, genital warts, chlamydia infection and lymphogranuloma venereum). Thus, regardless of whether they were on treatment, HIV-positive respondents who reported an undetectable viral load and a CD4 count greater than 500 cells/µL in the previous 12 months and no other STI over the same period were considered to have controlled infection. All other HIV-positive respondents were classified with uncontrolled infection.

Reported sexual prevention behaviours with casual partners in the previous 12 months were categorised into four mutually exclusive categories (Table 1): no anal intercourse, consistent condom use, risk-reduction strategies, and no discernible prevention practice (NDPP). These sexual prevention behaviour categories were applied to each serostatus: HIV-positive respondents with controlled infection, HIV-positive respondents with uncontrolled infection, HIV-negative respondents and untested respondents.

Statistical analyses

All statistical analyses were stratified on HIV status. Logistic regressions were performed to investigate bivariate associations between NDPP and sociodemographic and behavioural factors. All factors significantly associated in bivariate analyses with NDPP in at least one HIV status stratum were considered candidate variables for the multivariable analyses. Correlation and multicollinearity between these candidate variables were examined before entering them in multivariable logistic regression models. Interactions were also evaluated. The Hosmer-Lemeshow test was used to evaluate the goodness-of-fit of the final four multivariable models. Statistical analyses were performed with Stata software version 12.0.

Results

Overall, 10,448 men living in France responded to the survey, principally over the Internet (90%; n=9,392). Our analysis was restricted to those who reported sexual intercourse with casual partners during the previous 12 months, self-reported their current HIV status and answered all the questions used in the multivariate analysis (n=6,665) (Figure).

Their median age was 37 years (range: 15–87 years), 72% (n=4,765) had a university degree and 32% (n=2,127) lived in large urban areas (more than 500,000 inhabitants) (Table 2). In the previous 12 months, 49% (n=3,239) had had a steady male partner, and 23% (n=1,532) had regularly frequented sex venues. The median number of sexual partners was 10 (range: 1–100). Among all respondents, 14% (n=938) reported at least one STI in the previous 12 months, and among HIV-positive respondents, 31% (n=388).

Table 2

Sociodemographic and behavioural characteristics of respondents who had a casual partner at least once in the previous 12 months, according to HIV serological status, Presse Gays et Lesbiennes survey, France, 2011 (n=6,665)

Item	HIV-positive: controlled infection (n=672)		HIV-positive: uncontrolled infection (n=596)		HIV-negative (n=4,734)		Untested (n=663)		Total (n=6,665)	
	N	%	N	%	N	%	N	%	N	%
Age (years)										
‹30	29	4.3	71	11.9	1,518	32.1	400	60.3	2,018	30.3
30–44	306	45.5	335	56.2	2,043	43.2	144	21.7	2,828	42.4
45 or more	337	50.1	190	31.9	1,173	24.8	119	17.9	1,819	27.3
Higher education										
No	227	33.8	175	29.4	1,226	25.9	272	41.0	1,900	28.5
Yes	445	66.2	421	70.6	3,508	74.1	391	59.0	4,765	71.5
Activity status										
Student	7	1.0	13	2.2	634	13.4	244	36.8	898	13.5
Employee or self-employed	540	80.4	477	80.0	3,531	74.6	350	52.8	4,898	73.5
Other (retired, unemployed)	125	18.6	106	17.8	569	12.0	69	10.4	869	13.0
Urban area (inhabitants)										
‹20,000	151	22.5	114	19.1	1,302	27.5	244	36.8	1,811	27.2
20,000 to 500,000	252	37.5	200	33.6	1,991	42.1	284	42.8	2,727	40.9
›500,000	269	40.0	282	47.3	1,441	30.4	135	20.4	2,127	31.9
Frequented sex venues regularly during the previous 12 months										
Yes	241	35.9	243	40.8	947	20.0	101	15.2	1,532	23.0
No	431	64.1	353	59.2	3,787	80.0	562	84.8	5,133	77.0
Frequented dating websites regularly during the previous 12 months										
Yes	446	66.4	479	80.4	2,914	61.6	431	65.0	4,270	64.1
No	226	33.6	117	19.6	1,820	38.4	232	35.0	2,395	35.9
Steady partner during the previous 12 months										
No	352	52.4	322	54.0	2,308	48.8	444	67.0	3,426	51.4
Yes	320	47.6	274	46.0	2,426	51.2	219	33.0	3,239	48.6
More than 10 male partners during the previous 12 months										
Yes	427	63.5	441	74.0	1,758	37.1	112	16.9	2,738	41.1
No	245	36.5	155	26.0	2,976	62.9	551	83.1	3,927	58.9
Exposure to semen during oral sex during the previous 12 months (at least once)										
Yes	503	74.9	485	81.4	2,605	55.0	356	53.7	3,949	59.2
No	169	25.1	111	18.6	2,129	45.0	307	46.3	2,716	40.8
Drug use during the previous 12 months (at least once)										
Yes	522	77.7	517	86.7	2,613	55.2	273	41.2	3,925	58.9
No	150	22.3	79	13.3	2,121	44.8	390	58.8	2,740	41.1
HIV test during the previous 12 months										
Yes	215	35.5	222	40.1	3,258	68.8	n.a.	n.a.	3,695	62.7
No	391	64.5	331	59.9	1,476	31.2	n.a.	n.a.	2,198	37.3
HIV diagnosis (year)										
Before 1997	282	42.0	135	22.7	n.a.	n.a.	n.a.	n.a.	417	32.9
1997–2000	90	13.4	70	11.7	n.a.	n.a.	n.a.	n.a.	160	12.6
After 2000	300	44.6	391	65.6	n.a.	n.a.	n.a.	n.a.	691	54.5
At least one STI during the previous 12 months										
Yes	0	0.0	388	65.2	520	11.0	30	4.6	938	14.1
No	672	100.0	207	34.8	4,206	89.0	629	95.4	5,714	85.9

n.a.: not applicable; STI: sexually transmitted infection.

Table 3

Prevalence of sexual preventive behaviour with casual partners during the previous 12 months according to respondent's HIV status, Presse Gays et Lesbiennes survey, France, 2011, (n=6,665)

	HIV-positive: controlled infection[a] (n=672)		HIV-positive: uncontrolled infection[b] (n=596)		HIV-negative (n=4,734)		Untested (n=663)		Total (n=6,665)		p values
	N	%	N	%	N	%	N	%	N	%	
No anal intercourse	20	3.0	13	2.2	393	8.3	107	16.2	533	8.0	p<0.001
Consistent condom use during anal intercourse	148	22.0	79	13.3	2,603	55.0	329	49.6	3,159	47.4	p<0.001
Unprotected anal intercourse											
Risk reduction practices											
• Exclusive serosorting	104	15.5	86	14.4	389	8.2	n.a.	n.a.	579	8.7	p<0.001
• Exclusive seropositioning	82	12.2	80	13.4	260	5.5	n.a.	n.a.	422	6.3	p<0.001
• Serosorting and seropositioning	14	2.1	11	1.8	105	2.2	n.a.	n.a.	130	2.0	p=0.831
No discernible prevention practice	304	45.2	327	54.9	984	20.8	227	34.2	1,842	27.6	p<0.001
Total	672	100.0	596	100.0	4,734	100.0	663	100.0	6,665	100.0	

n.a.: not applicable.

[a] Positive controlled infection: HIV-positive respondents reported that during the previous 12 months they had either antiretroviral treatment, and an undetectable viral load, and no other STI or no treatment but an undetectable viral load and a CD4 count greater than 500 cells/µL, and no other STI.

[b] Positive uncontrolled infection: HIV-positive respondents who did not meet the criteria for controlled infection.

Prevalence of sexual preventive behaviours with casual male partners

The proportion of respondents practicing no anal intercourse with their casual partners in the previous 12 months was low: ranging from 2% (n=13) among HIV-positive respondents with uncontrolled infection to 16% (n=107) among untested respondents (Table 3). Consistent condom use during anal intercourse was more frequent among HIV-negative respondents (55%; n=2,603) and untested (50%; n=329) than HIV-positive respondents (Table 3). HIV-positive respondents with uncontrolled infection reported less consistent condom use than those with controlled infection (13% (n=79) vs 22% (n=148), p<0.001). Risk-reduction practices were reported more often by HIV-positive respondents (30%; n=377), regardless of infection control status, than by HIV-negative respondents (16%; n=754). Exclusive serosorting was practiced more than exclusive seropositioning, regardless of HIV status. No difference was found between HIV-positive respondents with controlled and uncontrolled infection for risk-reduction practices (Table 3). NDPP was reported more frequently by HIV-positive respondents with uncontrolled (55%; n=327) and controlled infection (45%; n=304), than by untested (34%; n=227) or HIV-negative respondents (21%; n=984) (Table 3).

Factors associated with no discernible prevention practice

Univariate analysis (Table 4) showed associations between NDPP and a set of common variables, regardless of serostatus. These variables included age younger than 30 years, no university degree, and each of the following within the previous 12 months: regular frequentation of sex venues and dating websites, a high number of sexual partners, drug use, and exposure to sperm during oral sex. For HIV-positive respondents with controlled or uncontrolled infection, they also included HIV diagnosis after 2000. Multivariate analyses (Table 4) highlighted significant differences in the profiles of NDPP-classified respondents according to their serostatus.

For HIV-positive respondents with controlled infection, NDPP was associated with age younger than 30 years (adjusted odds ratio (aOR) = 2.9, (95% confidence interval (CI): 1.1–8.0)), HIV diagnosis after 2000 (aOR = 2.0, (95% CI: 1.3–3.0)), and each of the following within the previous 12 months: regular frequentation sex venues (aOR = 1.7, (95% CI: 1.2–2.4)), more than 10 partners (aOR = 2.3, (95% CI: 1.6–3.4)), and exposure to sperm during oral sex (aOR = 1.9, (95% CI: 1.3–3.0)) (Table 4).

For HIV-positive respondents with uncontrolled infection, NDPP was associated with unemployment (aOR = 1.8; (95% CI: 1.1–3.0)), residence in a medium-sized urban area (aOR = 1.5; (95% CI: 1.0–2.3)), post-2000 diagnosis (aOR = 1.7; (95% CI: 1.1–2.7)), and each of the following in the previous 12 months: regular frequentation sex venues (aOR = 1.5; (95% CI: 1.0–2.1)), more than 10 partners (aOR = 2.6; (95% CI: 1.7–4.0)) and exposure to sperm during oral sex (aOR = 2.6; (95% CI: 1.6–4.3)) (Table 4).

For HIV-negative respondents, NDPP was associated with age younger than 45 years (<30 years: aOR = 1.4;(95% CI: 1.2–1.8); 30–44 years: aOR = 1.3; (95% CI: 1.0–1.5)), no university degree (aOR = 1.5; (95%

Table 4a

No discernible prevention practice with casual partners of respondents who had a casual partner at least once in the previous 12 months, according to HIV serological status: bivariate and multivariate analysis, Presse Gays et Lesbiennes survey, France, 2011

	HIV-positive: controlled infection (n = 672)				HIV-positive: uncontrolled infection (n = 596)				HIV-negative (n = 4,734)				Untested (n = 663)			
	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI
Age (years)																
<30	2.4	1.1–5.2 [a]	2.9	1.1–8.0 [a]	1.6	0.9–2.8	1.0	0.5–2.0	1.4	1.1–1.6 [b]	1.4	1.2–1.8 [b]	0.9	0.6–1.4	1.0	0.6–1.7
30–44	1.4	1.0–1.9 [a]	1.1	0.8–1.6	1.2	0.9–1.8	1.1	0.7–1.7	1.3	0.9–1.4	1.3	1.0–1.5 [a]	0.6	0.4–1.1	0.7	0.4–1.3
≥45	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Higher education																
No	1.4	1.0–1.9 [a]	1.4	0.9–2.0	1.0	0.7–1.4	0.9	0.6–1.4	1.6	1.4–1.9 [c]	1.5	1.3–1.8 [c]	1.5	1.1–2.1 [a]	1.4	0.9–1.9
Yes	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Activity status																
Student	1.0	1.0–1.0	1.0	1.0–1.0	2.0	0.6–6.5	2.4	0.6–9.9	1.2	0.9–1.5	1.2	0.9–1.5	1.2	0.9–1.7	1.2	0.8–1.9
Employee or self-employed	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Other (retired, unemployed)	0.6	0.4–0.9 [a]	0.7	0.4–1.1	1.3	0.9–2.1	1.8	1.1–3.0 [a]	1.3	1.0–1.6 [a]	1.1	0.9–1.4	1.7	0.9–2.8	1.6	0.9–2.8
Urban [a]rea (inhabitants)																
<20,000	1.2	0.8–1.8	1.2	0.8–2.0	1.2	0.7–1.8	1.6	1.0–2.5	1.3	1.1–1.5 [b]	1.3	1.0–1.5 [a]	1.0	0.7–1.6	1.0	0.6–1.7
20,000 to 500,000	1.1	0.8–1.6	1.2	0.8–1.8	1.3	0.9–1.9	1.5	1.0–2.3 [a]	1.1	0.9–1.2	1.1	0.9–1.3	1.3	0.8–1.9	1.3	0.8–2.0
>500,000	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Frequented sex venues regularly during the previous 12 months																
Yes	2.1	1.5–2.9 [c]	1.7	1.2–2.4 [b]	1.8	1.3–2.5 [c]	1.5	1.0–2.1 [a]	1.8	1.5–2.1 [c]	1.4	1.1–1.6 [c]	1.9	1.3–3.0 [c]	1.5	0.9–2.5
No	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Frequented dating websites regularly during the previous 12 months																
Yes	1.8	1.3–2.5 [c]	1.3	0.9–1.9	1.6	1.1–2.4 [a]	1.3	0.8–2.1	1.6	1.4–1.9 [c]	1.3	1.1–1.5 [b]	1.5	1.1–2.1 [a]	1.5	1.1–2.2 [a]
No	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Steady partner during the previous 12 months																
No	0.8	0.6–1.1	0.8	0.5–1.1	0.9	0.7–1.3	0.8	0.6–1.2	1.5	1.3–1.7 [c]	1.3	1.1–1.5 [c]	Ref	Ref	Ref	Ref
Yes	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	Ref	Ref	Ref	Ref

aOR: adjusted odds ratio; CI: confidence interval;.n.a.: not applicable; OR: odds ratio; Ref: reference category.

Positive controlled infection: HIV-positive respondents reported that during the previous 12 months they had either antiretroviral treatment, and an undetectable viral load, and no other sexually transmitted infection or no treatment but an undetectable viral load and a CD4 count greater than 500 cells/µL, and no other sexually transmitted infection.

Positive uncontrolled infection: HIV-positive respondents who did not meet the criteria for controlled infection.

[a] $p < 0.05$

[b] $p < 0.01$

[c] $p < 0.001$

Table 4b

No discernible prevention practice with casual partners of respondents who had a casual partner at least once in the previous 12 months, according to HIV serological status: bivariate and multivariate analysis, Presse Gays et Lesbiennes survey, France, 2011

	HIV-positive: controlled infection (n=672)				HIV-positive: uncontrolled infection (n=596)				HIV-negative (n=4,734)				Untested (n=663)			
	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI
More than 10 male partners during the previous 12 months																
Yes	3.1	2.2–4.4 [c]	2.3	1.6–3.4 [c]	3.4	2.3–5.0 [c]	2.6	1.7–4.0 [c]	2.2	1.9–2.5 [c]	1.6	1.4–1.9 [c]	1.9	1.3–2.9b	1.3	0.8–2.0
No	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Exposure to semen during oral sex during the previous 12 months (at least once)																
Yes	2.7	1.9–4.0 [c]	1.9	1.3–3.0 [b]	3.3	2.1–5.1 [c]	2.6	1.6–4.3 [c]	3.0	2.5–3.5 [c]	2.3	1.9–2.7 [c]	2.8	2.0–3.9 [c]	2.3	1.6–3.3 [c]
No	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Drug use during the previous 12 months (at least once)																
Yes	1.5	1.0–2.1 [a]	1.1	0.7–1.7	1.6	1.0–2.6 [a]	1.3	0.7–2.1	2.0	1.7–2.3 [c]	1.7	1.5–2.0 [c]	2.2	1.6–3.0 [c]	1.9	1.4–2.7 [c]
No	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
HIV test during the previous 12 months																
Yes	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	1.3	1.1–1.6 [c]	1.1	0.9–1.3	n.a	n.a	n.a	n.a
No	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a	1.0	Ref	1.0	Ref	n.a	n.a	n.a	n.a
HIV diagnosis (year)																
Before 1997	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a
1997–2000	1.7	1.0–2.7 [a]	1.6	0.9–2.8	0.8	0.5–1.5	0.7	0.4–1.3	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a
After 2000	2.2	1.6–3.0 [c]	2.0	1.3–3.0 [c]	1.6	1.1–2.4 [a]	1.7	1.1–2.7 [a]	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a
Hosmer-Lemeshow test (p)	0.1539				0.4052				0.9722				0.6048			

aOR: adjusted odds ratio; CI: confidence interval;.n.a.: not applicable; OR: odds ratio; Ref: reference category.

Positive controlled infection: HIV-positive respondents reported that during the previous 12 months they had either antiretroviral treatment, and an undetectable viral load, and no other sexually transmitted infection or no treatment but an undetectable viral load and a CD4 count greater than 500 cells/µL, and no other sexually transmitted infection.

Positive uncontrolled infection: HIV-positive respondents who did not meet the criteria for controlled infection.

[a] $p<0.05$

[b] $p<0.01$

[c] $p<0.001$

CI: 1.3–1.8)), residence in an urban area of fewer than 20,000 inhabitants (aOR = 1.3; (95% CI: 1.0–1.5)), and each of the following during the previous 12 months: regular frequentation sex venues (aOR = 1.4; (95% CI: 1.1–1.6)), regular frequentation dating websites (aOR = 1.3; (95% CI: 1.1–1.5)), no steady sexual partner (aOR = 1.3; (95% CI: 1.1–1.5)), more than 10 partners (aOR = 1.6; (95% CI: 1.4–1.9)), exposure to sperm during oral sex (aOR = 2.3; (95% CI: 1.9–2.7)) and drug use (aOR = 1.7; (95% CI: 1.5–2.0)) (Table 4).

For untested respondents, NDPP was associated with all of the following activities in the previous 12 months: regular frequenting dating websites (aOR = 1.5; (95% CI: 1.1–2.2)), exposure to sperm during oral sex (aOR = 2.3; 95% CI: 1.6–3.3)) and drug use (aOR = 1.9; (95% CI: 1.4–2.7)) (Table 4).

Discussion

Description of survey

The Presses Gays et Lesbiennes survey is one of the very few surveys in France that describe the sexual behaviours of MSM in detail, based on a large sample of volunteers. Its use of the Internet as its principal mode of recruitment brought forth a wide variety of respondents, in terms of age, place of residence and sociodemographic profile. Because most respondents had had at least one casual partner in the previous 12 months, these data gave us a good understanding of prevention practices used by MSM in such relationships.

Major results

Because our categorisation of sexual prevention behaviours captures the diversity of preventive practices among MSM, we were able to obtain a detailed description of them. Thirty years after the HIV epidemic started, condom use during anal intercourse was not widespread, regardless of HIV status [1]. More detailed information about the determinants of consistent condom use would be interesting, but it seemed to us most useful to describe specific profiles of MSM engaged in high risk-taking in order to implement target prevention programs according to HIV status. Risk-reduction strategies were used to a limited degree by HIV-positive respondents, with no difference according to disease control status, and to a lesser degree by their seronegative counterparts. Nevertheless, a large proportion of respondents had NDPP, a finding consistent with other European studies which used unprotected anal intercourse as the principal indicator of risk-taking [7,16,17]. The factors associated with this lack of protection reflect a number of common characteristics generally associated with risk-taking. These include frequenting Internet meeting sites, using drugs, and exposure to sperm during oral sex [17-19]. In particular, HIV-positive respondents with NDPP most often belonged to the post-AIDS generation and had an adventure-oriented sexuality [20]. HIV-negative respondents with NDPP were characterised by a low education level.

Importance of HIV testing

In this context, HIV testing and knowledge of status are major issues. More than one third of untested respondents and one in five of the HIV-negative respondents engaged in high-risk practices that put them and their sexual partners at risk for HIV infection and other STIs. MSM unaware of their status who engage in these behaviours contribute to driving the hidden epidemic, estimated in France to be more than 9,000 MSM [11]. A seroprevalence study in Paris showed that 20% of undiagnosed HIV-positive respondents reported that they either had never previously been tested or were HIV-negative, but had the same sexual risk behaviours as HIV-positive men aware of their status [17]. It is crucial that untested MSM be encouraged to go for HIV testing and receive counselling on risk-reduction strategies. Accordingly, structural and psychological barriers to testing must be reduced, especially denial about practicing at-risk behaviours and fear of positive HIV test results [21]. It is also essential for HIV-negative respondents to regularly update their HIV status. However, our results did not show any association between NDPP and testing within the previous 12 months. This suggests that these HIV-negative men had not actually recognised that they engaged in risk-behaviours and wrongly believed themselves to be HIV-negative. Encouraging MSM to test for HIV as frequently as possible to confirm their negative status is vital [21].

Risk-reduction practices and their limitations

MSM have taken up serosorting or seropositioning as alternative risk-reduction practices to condom use [7]. Studies have previous associated these practices with positive HIV-status [22,23]. In our study, a substantial proportion of HIV-positive respondents used them, regardless of whether their infection was controlled or not. HIV-negative respondents also engaged in these practices, although at a rate lower than in other studies [22]. Nevertheless, the efficacy of both serosorting and seropositioning has been questioned. Their levels of scientific validation differ, and randomised trials have failed to demonstrate their efficacy. Some studies have shown they have a positive effect on the epidemic's dynamics [6], while others have not [24]. Unlike condom use, these practices do not protect against STIs and are only effective for HIV transmission if both partners have up-to-date knowledge of their serostatus [25]. Moreover, they must discuss the issue, something that cannot always be taken for granted, given the nature of meeting places and the problems of discrimination against seropositive MSM.

Vulnerability of HIV-negative men who have sex with men

HIV-negative respondents displaying NDPP appeared to be more socially vulnerable than other subgroups in our study. Although they were part of the gay community, they had profiles associated with high-risk sexual behaviours: young, with low education levels, and living in non-urban areas. The increase in newly

diagnosed HIV cases among MSM under 30 years old in Europe [2,26], and in France more specifically [3], confirms our findings. Interventions targeting younger MSM are urgently needed to prevent a resurgence of the epidemic.

Moreover, as in our study, a low educational level was found to be associated with risk-taking behaviours in the EMIS network [16] and with an increased risk of HIV seroconversion in European studies [26,27]. These findings must be integrated into prevention campaigns to tailor prevention messages as well as possible to ensure the widest possible participation by this specific population.

Heterogeneity of practices among HIV-positive MSM

Our findings underline the heterogeneity of preventive behaviours among HIV-positive MSM and the need to take this diversity into account to improve therapeutic care. In accordance with the Swiss statement's recommendations [15], in view of the different transmission issues, we categorised HIV-positive MSM according to whether their infection was controlled or uncontrolled and analysed them separately. Randomised trials have shown that treatment, by controlling viral load, reduces the risk of transmission in heterosexual couples [8] and in steady MSM couples [28]. No such result has been observed in MSM for casual relationships [9,29].

Interestingly, in our study, HIV-positive respondents with controlled infection were less likely to show NDPP than those whose infection was uncontrolled. This finding might be due in part to how we constructed the infection control status categories, by considering STI infections as well as viral load over the last 12 months. But this finding is also consistent with a seroprevalence study which showed that HIV-positive MSM in Paris with a low viral load reported a lower proportion of UAI episodes with casual partners of unknown or different HIV status than their counterparts with high viral loads [30].

The association of diagnosis after 2000 with NDPP, regardless of infection control status, demonstrates the generational impact and the effect of treatment on sexual behaviours [31]. A high proportion of the HIV-positive respondents in this study were diagnosed after 2000, at a time when barebacking was emerging and engendering fierce debates and long-term divisions between MSM in France [32]. Some of these men also started their sexual life after the arrival of antiretroviral treatment (ART). Furthermore, the hypothesis of behavioural disinhibition linked to treatment seems be true for this sub-population [33]. These results highlight the urgent need to implement targeted information campaigns for HIV-positive MSM and thus to remind individuals and groups about the importance of treatment adherence, about STI care and about the place of condoms in sexual practices with casual partners.

Study limitations

Our study also has some limitations that must be considered in interpreting our results. First, the methodological limitations must be underlined. As is often the case for surveys related to MSM [14], our study is based on a non-random sample with participant self-selection through the Internet and gay press. Furthermore, the absence of both a sample frame and controls during the inclusion process means that our results cannot be extrapolated to the entire MSM population [1]. We did, however, use websites as varied as possible to invite MSM to participate. MSM recruited through the press have a more established sexual identity and sex life as well as higher educational and economic levels [34]. Those recruited through the Internet are younger and less urban [35]. Furthermore, the serological data based on self-reporting probably underestimated the real proportion of HIV-positive MSM as some respondents were probably unaware that they were HIV-positive. This point has previously been highlighted in studies on seroprevalence in MSM [17,36].

Second, the categorisation we used also has limitations. It was constructed retrospectively, based on the answers to questions about sexual behaviours and self-reported health status. It was not based on questions about a deliberate choice to use serosorting or seropositioning instead of condoms [37,38]. Nevertheless, a comparison of the risk-reduction practices and strategies matched the responses well: 90% of the respondents classified as engaging in serosorting declared they did so to avoid contamination by or transmission of HIV. Another limitation of the categorisation used is that making the risk-reduction categories mutually exclusive is simplistic and inaccurate. It does not take into account the protean reality of different sexual behaviours over time (in this case 12 months) [37] and is the result of a theoretical compromise.

Conclusions

The study captured the diversity of preventive practices among MSM. Our findings highlight the ongoing nature of the normalisation of HIV in this post-AIDS era [39], when HIV has lost the central meaning it had in the lives of gay men in the 1980s and 1990s. Furthermore, the ever-decreasing use of condoms means that HIV testing and treatment are not sufficient to invert the epidemic's trend. Combination prevention is legitimate in the current context where HIV incidence remains very high worldwide. Accordingly, promoting condom use, encouraging regular HIV testing, offering treatment – be it post-exposure (PeP) or pre-exposure (PreP) - to HIV-negative MSM at high risk of exposure, prompt treatment of HIV-positive MSM and, finally, follow-up for STIs are all interventions that belong in prevention programmes for MSM within a global health approach.

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Conflicts of interest

None declared.

Authors' contributions

AV was the principal investigator of the Presse Gays et Lesbiennes survey 2011, carried out the statistical analysis, and conceived and wrote the paper. LS carried out the statistical analysis, commented on the first draft and approved the final version. CSommen carried out the statistical analysis, commented on the first draft and approved the final version, PB carried out the statistical analysis, commented on the first draft of the paper and approved the final version, NB commented on the first draft of the paper and approved the final version, CSemaille commented on the first draft of the paper and approved the final version.

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Incident risk factors as predictors of HIV seroconversion in the Lisbon cohort of men who have sex with men: first results, 2011–2014

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HIV incidence in men who have sex with men (MSM) is increasing in western countries, including Portugal. We aimed to estimate HIV incidence and to assess how individual short-term changes in exposures over time predict seroconversion. We evaluated participants of an open cohort of HIV-negative MSM enrolled after testing at a community-based voluntary HIV counselling and testing centre in Lisbon. At each evaluation a structured questionnaire was completed and HIV status was ascertained using rapid followed by confirmatory testing. Between April 2011 and February 2014, 804 MSM were followed for a total of 893 person-years. Predictors of HIV seroconversion were identified using Poisson generalised linear regression. The overall seroincidence was 2.80/100 person-years (95% confidence interval: 1.89–4.14). Men who seroconverted had a higher mean number of tests per year. Seroconversions were significantly associated with partner disclosure of HIV status during follow-up, newly-adopted unprotected anal intercourse (UAI) with a steady partner and being newly-diagnosed with syphilis during follow-up. Likewise, sexual intercourse with HIV-positive men, having an HIV-positive steady partner at least once during follow-up and persistent UAI with occasional partners were predictors of seroconversion. High HIV incidence in this cohort is likely driven by short-term contextual and behavioural changes during follow-up.

Introduction

A well-established body of potential strategies for the primary prevention of HIV infection stems from increased understanding of disease pathogenesis and transmission [1,2]. Still, there is evidence of growing HIV incidence among men who have sex with men (MSM) in western Europe, North America and Australia [3-8]. These trends are unlikely to be explained by changes in surveillance or testing practices [3], rather reflecting the fact that MSM remain at higher risk in most countries. This is apparent in the burden of newly-diagnosed infections in the European Union and European Economic Area: the largest fraction of HIV diagnoses reported in 2013 was attributable to sex between men (41.9%), followed by heterosexual transmission (32.4%), and finally by unsafe injection practices (5.0%) [9].

This is also the Portuguese pattern: after several years of an HIV epidemic driven by unsafe drug injection, sex between men has gained special relevance as a transmission mode making up 30.3% of all reported cases in 2013 [10]. Two pioneering cross-sectional studies [11,12] targeting MSM living in Portugal collected extensive self-reported information, leading to the first alarming estimates of the point prevalence of infection: 10.9% [13] and 10.3% (personal communication, A Gama, 2013).

Monitoring defined cohorts of MSM provides timely estimates of HIV incidence and predictors beyond the limited information produced by case reporting or cross-sectional surveys. In previous prospective cohorts, the occurrence of new infections has been modelled both as a function of factors that directly increase infection risk (frequency of unprotected anal intercourse (UAI), viral load of the index partner, presence of sexually transmitted infections (STI)), as well as potential markers of exposure, such as number of sex partners, substance use, and adverse childhood circumstances [14-19]. However, how individual exposures change over time and how those changes can predict HIV seroconversion remains to be clarified.

Innovative community-based HIV testing and counselling approaches have been developed that target specific population groups at higher risk and involve

community stakeholders as peer-counsellor and key informants [20]. As such, these are privileged settings for prospective research on the incidence and drivers of the HIV epidemic among MSM, with the ultimate goal of informing realistic preventive strategies.

The objectives of the present study were to estimate the incidence of HIV infection in a cohort of MSM and to assess how individual short-term changes in exposures predict seroconversion.

Methods

Cohort recruitment and follow-up

The Lisbon MSM cohort, established in April 2011, is an observational prospective study conducted at a community-based voluntary HIV counselling and testing centre in Lisbon, Portugal (CheckpointLX). It was designed as an open cohort, and inclusion criteria were: presenting for HIV testing at CheckpointLX, being a man aged 18 or more, reporting having sex with other men and having a negative HIV test result at recruitment. All eligible individuals were invited to enter the cohort by CheckpointLX peer counsellors at their first visit. Follow-up assessments were scheduled at intended intervals of 6 months, although the exact time between visits was adjusted according to the convenience of participants. Since follow-up visits occurred whenever clients decided to appear for testing, this does not strictly constitute an interval cohort and it is likely that a small proportion of MSM had very short or long periods between visits: e.g. in our sample, 6.3% of men had follow-ups shorter than three months. This is problematic for MSM who seroconvert between tests which are close in time (due to possible window period), which is why we opted to exclude five participants with seroconversions that occurred during follow-up periods of less than three months. At each visit a structured questionnaire was administered and a rapid HIV test was performed by a trained CheckpointLX peer counsellor. All participants gave their written informed consent and the study protocol was approved by the ethics committee of Hospital de São João and Medical School, University of Porto (ID 104/12).

Participation and losses to follow-up

Data reported in this study refer to the period from April 2011 to February 2014, during which 3,301 potential eligible individuals presented for testing, 195 (5.9%) of whom had an HIV-reactive test at entry and therefore were not included in the cohort. The remaining 3,106 (94.1%) were eligible to the cohort. Among those, 2,183 (70.3%) were enrolled, of whom 804 (36.8%) had at least one follow-up evaluation (893.37 person-years of observation) and 923 (29.7%) choose not to participate. Those who choose not to participate were less self-identified as homosexual, less frequently born in Portugal, and less educated than those who chose to participate, but had a similar proportion of HIV testing before cohort entry.

Operationally, participants were classified as lost to follow-up if they had chosen to participate but appeared for testing only once (n=707). However, MSM who had been recruited for the cohort recently (12 months or less before the end of the period considered in the present analysis, i.e. from February 2013 to February 2014) were not considered lost to follow-up (n=672). Therefore, we assumed an overall attrition rate of 52%. MSM who were not followed-up were older than those who were (31.2 vs 30.3 years old, p=0.034), but both groups were similar regarding the remaining background characteristics. Also, no significant differences were found between MSM who appeared for follow-up and those who did not regarding such behavioural characteristics as: sexual intercourse with HIV positive men (13.5% vs 12.9%, p = 0.955), having an HIV-positive steady partner (5.8% vs 5.2%, p = 0.528), and condom use with a steady partner (27.7% vs 27.9%, p › 0.999) and with an occasional partner in the previous 12 months (57.1% vs 51.7%, p = 0.069).

Rapid HIV testing

Rapid HIV-1 and HIV-2 testing was performed at each visit. From April 2011 to April 2012 two commercial kits were used, the Retrocheck HIV (QUALPRO DIAGNOSTICS, Goa, India) (manufacturer-described sensitivity = 100.00% and specificity = 99.75%) and Hexagon HIV (Human GmbH, Wiesbaden, Germany) (sensitivity = 100.00% and specificity = 99.50%) and since that time, only the Alere Determine HIV-1/2 (Alere Medical Co., Ltd. Chiba, Japan) (sensitivity = 100.00% and specificity = 99.75%) has been used. In case of a reactive test, an outpatient appointment was scheduled at Santo António dos Capuchos Hospital's HIV/Infectious diseases clinic in Lisbon where a confirmatory test was performed. Pre- and post-test counselling was offered at each visit.

Study instruments and variables

Structured questionnaires were administered at entry and at each follow-up visit collecting data on background and behavioural characteristics, according to European Centre for Disease Prevention and Control (ECDC) [21] and the Joint United Nations Programme on HIV/AIDS (UNAIDS) guidelines [22] for HIV surveillance. For time-varying information the recall period was the previous 12 months (cohort entry questionnaire) or the time since the previous assessment (follow-up visits). Background characteristics included age, sex, country of birth, educational level and sexual identity.

Behavioural indicators included information on the following topics:

- History of previous HIV testing and reasons for index test;
- Age at first anal intercourse, role at anal intercourse, characteristics of sexual partners (bisexual

men, men with different sexual partners, sex workers, HIV-positive men, people who inject drugs, women and trios/group sex), steady (number, sex and HIV status) and occasional partners, having been paid for sex and venues used to meet occasional partners;
- Frequency of condom use for anal intercourse with steady and occasional partners;
- Use of alcohol or recreational drugs (cannabis, lysergic acid diethylamide (LSD), poppers, heroin, ecstasy, amphetamines, mephedrone, gamma-hydroxybutyric acid (GHB), ketamine and cocaine) before or during intercourse;
- Knowledge and use of non-occupational post-exposure prophylaxis for HIV;
- History of other STI and hepatitis.

We were interested in assessing whether intraindividual changes over time in well-documented determinants of HIV incidence were predictive of seroconversion. Even though multiple changes in those determinants throughout follow-up were theoretically possible, we opted to use information collected at two time points for each participant: cohort entry and either the visit of the first HIV positive test (for MSM who seroconverted) or the most recent visit (for the remaining MSM). This choice was based on two main arguments: i) the majority (53.8%) of participants had only two visits, and ii) for participants with three or more visits, using multiple combinations of information from all visits did not change the direction of associations or the main conclusions, i.e. first and last visit were good surrogates for exposure changes during follow-up (data not shown). For this purpose we created new variables for time-varying information that compiled responses from the first and the most recent visit, categorised as 'Yes to No' or 'No to Yes' if the information had changed between those visits, and 'No and No' or 'Yes and Yes' if answers were persistent. In case of 24 participants with more than two visits who preferred not to disclose one or more of the behavioural items at the most recent visit, we used the information obtained in the preceding visit. This option did not alter substantially the magnitude of associations.

Statistical analysis

Characteristics of participants at cohort entry were described using absolute frequencies and proportions in the case of categorical variables. Means and standard deviation (SD) or median and percentiles 25 and 75 (P25-P75) were used, as appropriate, to describe continuous variables. In data analysis, the missing category was excluded from the denominator for each item. In time-varying information related to characteristics of sexual partners, the options 'I do not know' and the 'No' options were collapsed once the incidence rates in both groups were similar. Unprotected anal intercourse (UAI) was defined as not always having used a condom in receptive or insertive anal sex. Incidence rates with 95% confidence intervals (95% CI) were estimated with time at risk defined as the period between recruitment and the most recent follow-up visit. In MSM who seroconverted, half of the period between the last HIV-negative test and the first HIV-positive test was subtracted.

Table 1A

Characteristics at entry of participants followed in the cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

Participants followed-up	804
Background characteristics	
Age (years), mean (SD)	30.3 (8.9)
Missing	0
Sexual identity, n (%)	
Homosexual	692 (86.1)
Bisexual/heterosexual/other	109 (13.6)
Prefer not to answer	3 (0.4)
Missing	0
Country of origin, n (%)	
Portugal	575 (75.0)
Other country	190 (24.7)
Prefer not to answer	2 (0.3)
Missing	37
Educational level (schooling years), n (%)	
Less than higher education (≤12 years of school)	317 (39.5)
Higher education (›12 years of school)	483 (60.1)
Other/Prefer not to answer	3 (0.3)
Missing	1
HIV testing	
Previous HIV testing, n (%)	
No	115 (15.2)
Yes	636 (84.1)
Did not know	5 (0.7)
Missing	48
Number of previous tests[a], median (P25-P75)	4 (2–7)
Missing	16
Reasons for index test, n (%)	
To check health status/routine	602 (77.9)
Perception of HIV exposure more than 3 months before	426 (54.0)
Perception of HIV exposure in the previous 3 months	357 (44.8)
Accident with condom use (rupture/left inside)	65 (8.4)
Partner diagnosed HIV+/Disclosed HIV+ status	59 (7.6)
Possible window period by the time of the last test	55 (7.2)
To stop using condom with my partner	38 (5.0)
My partner asked me to test for HIV	34 (4.4)
Symptoms / Medical indication	20 (2.6)

[a] Among participants who had had a previous HIV test (n=636).
[b] Among participants who had a steady partner in the previous 12 months (n=501).
[c] Among participants who had an occasional partner in the previous 12 months (n=713).
[d] Among participants who had an HIV-positive steady partner (n=46).

Table 1B

Characteristics at entry of participants followed in the cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

Participants followed-up	804
Sexual life and partners	
Age at first anal intercourse, median (P25-P75)	18.0 (16.0–21.0)
Missing	37
Role in anal intercourse, n (%)	
Only insertive	192 (24.1)
Only receptive	72 (9.0)
Versatile	525 (66.0)
Prefer not to answer	7 (0.9)
Missing	8
Sex with at least one of the following in the previous 12 months, n (%)	
Bisexual men	
No	420 (53.1)
Yes	271 (34.3)
Did not know	98 (12.4)
Prefer not to answer	2 (0.2)
Missing	13
Men with different sex partners	
No	148 (18.7)
Yes	588 (74.2)
Did not know	54 (6.8)
Prefer not to answer	2 (0.3)
Missing	12
Sex workers (even if not paid)	
No	707 (89.4)
Yes	51 (6.4)
Did not know	31 (3.9)
Prefer not to answer	2 (0.3)
Missing	13
HIV-positive men	
No	401 (50.7)
Yes	107 (13.5)
Did not know	281 (35.5)
Prefer not to answer	2 (0.3)
Missing	13
People who inject drugs	
No	719 (90.9)
Yes	4 (0.5)
Did not know	65 (8.2)
Prefer not to answer	3 (0.4)
Missing	13
Women	
No	690 (87.2)
Yes	99 (12.5)
Did not know	0
Prefer not to answer	2 (0.3)
Missing	13
Trios/group sex	
No	563 (71.2)
Yes	224 (28.3)

Participants followed-up	804
Sexual life and partners	
Did not know	1 (0.1)
Prefer not to answer	3 (0.4)
Missing	13
Steady partner in the previous 12 months, n (%)	
No	301 (37.4)
One steady partner	449 (55.8)
More than one steady partner	52 (6.5)
Prefer not to answer	2 (0.2)
Missing	0
HIV status of steady partner[b], n (%)	
HIV negative	310 (62.5)
HIV positive	46 (9.3)
Did not know	139 (28.0)
Prefer not to answer	1 (0.2)
Missing	5
Occasional partners in the previous 12 months, n (%)	
No	89 (11.1)
Yes	713 (88.7)
Prefer not to answer	2 (0.2)
Missing	0
Number of occasional partners in the previous 12 months[c], median (P25-P75)	5 (2–10)
Missing	19
Having sex for money or drugs in the previous 12 months[c], n (%)	
No	693 (97.3)
Yes	19 (2.7)
Missing	1
Venues used to meet occasional partners[c], n (%)	
Internet	522 (73.9)
Other venues (discos/gay bars, gym, outdoor cruising venues)	458 (57.6)
Only sexual venues (saunas, dark room, sex clubs)	166 (20.9)

[a] Among participants who had had a previous HIV test (n=636).

[b] Among participants who had a steady partner in the previous 12 months (n=501).

[c] Among participants who had an occasional partner in the previous 12 months (n=713).

[d] Among participants who had an HIV-positive steady partner (n=46).

Table 1C

Characteristics at entry of participants followed in the cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

Participants followed-up	804
Unprotected anal intercourse (UAI), n (%)	
UAI with a steady partner in the previous 12 months[b]	
No	130 (27.4)
Yes	344 (72.4)
Prefer not to answer	1 (0.2)
Missing	26
UAI in the previous 12 months with an HIV-positive steady partner[d]	
No	26 (59.1)
Yes	18 (40.9)
Missing	2
UAI with occasional partners in the previous 12 months[c]	
No	375 (56.1)
Yes	292 (43.7)
Prefer not to answer	1 (0.1)
Missing	45
Recreational drugs, n (%)	
Used recreational drugs before or during sexual intercourse in the previous 12 months	
Never	552 (69.9)
Always/often/occasionally/rarely	238 (30.1)
Missing	14
Post-exposure prophylaxis (PEP), n (%)	
Does not know about PEP	411 (54.7)
Knows but never used	317 (42.2)
Knows and used	23 (3.1)
Missing	53
Sexually transmitted infections, n (%)	
In the previous 12 months:	
Gonorrhea	20 (2.5)
Syphilis	13 (1.6)
Condyloma or genital warts	10 (1.3)
Chlamydia	7 (0.9)
Genital herpes	1 (0.1)
Trichomonas	1 (0.1)
History of hepatitis, n (%)	
Hepatitis B	18 (2.3)
Hepatitis C	3 (0.4)

[a] Among participants who had had a previous HIV test (n=636).

[b] Among participants who had a steady partner in the previous 12 months (n=501).

[c] Among participants who had an occasional partner in the previous 12 months (n=713).

[d] Among participants who had an HIV-positive steady partner (n=46).

Poisson generalised linear regression was used to identify predictors of HIV seroconversion with the default log link and offset in the variable follow-up time (t). To measure the magnitude of associations, crude and adjusted incidence rate ratios (IRR and aIRR) and respective 95% CI were computed. Variables whose regression coefficient through the Wald test had $p<0.10$ in the univariate analyses were further adjusted for UAI with a steady partner and UAI with occasional partners to estimate their direct effects, even though we acknowledge that UAI may be an intermediate step in the causal mechanism. For the multivariate analysis, significance level was set at $p<0.05$. All statistical analyses were computed with Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (SPSS Inc., Chicago, Illinois, US).

Results

Characteristics of participants at cohort entry

Background and behavioural characteristics at entry for the 804 participants who came for a follow-up visit between April 2011 and February 2014 are summarised in Table 1. Briefly, mean (SD) age was 30.3 (8.9) years; 86.1% (692/804) of MSM self-identified as homosexual; 75.0% (575/767) were born in Portugal and 60.1% (483/803) had over 12 years of schooling. HIV testing before cohort entry was reported by 84.1% (636/756) of participants. Slightly less than two thirds (501/804) of participants had at least one steady partner, of whom 9.3% (46/496) were in a serodiscordant couple. UAI with a steady partner in the year before cohort entry was reported by 72.4% (344/475); in particular, 40.9% (18/44) of MSM who had an HIV-positive partner had UAI in the same period; UAI with one or more occasional partners was reported by 43.7% (292/668) in the same period. Almost one third (238/790) of men reported having used recreational drugs before or during sexual intercourse in the previous year. Over 2% (20/804) of MSM had a diagnosis of gonorrhoea during the previous 12 month, in the same period a little less than 2% (13/804) of MSM had a diagnosis of syphilis and 0.4% (3/804) were hepatitis C positive.

HIV incidence

Between April 2011 and February 2014, 804 MSM were followed for a total of 893.37 person-years (ranging from six days to 2.84 years). During follow-up, 25 seroconversions were recorded, yielding an overall incidence of 2.80 per 100 person-years (95% CI: 1.89–4.14). From these 25 newly-identified cases, 19 (76.0%) were effectively linked to care via CheckpointLX. Of the remaining six individuals who did not accept referral, three preferred to use their own means to access health services and three did not provide information on clinical follow-up. Participants who seroconverted had a mean age of 31.2 (9.4) years: not significantly different from those who did not (30.2 (8.9) years, $p=0.598$), and a significantly shorter average follow-up time than those who did not seroconvert (0.79 years vs 1.12 years, $p=0.018$), but approximately the same number of visits, resulting in a higher mean number of tests per year (4.8 vs 3.9, $p=0.012$) (Table 2).

Table 2

Comparison of follow-up time and number of visits between participants who seroconverted and those who did not, cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

	HIV-positive	HIV-negative	p value[a]
N	25	779	
Minimum and maximum of follow-up time	56 days – 1.91 years	6 days – 2.84 years	n.a.
Mean time of follow-up (SD) (years)	0.79 (0.50)	1.12 (0.68)	0.018
Mean number of visits (SD)	2.76 (1.05)	2.85 (1.21)	0.816
Mean number of visits per year (SD)	4.8 (3.0)	3.9 (5.6)	0.012

n.a.: not applicable; SD: standard deviation.

[a] p value for independent samples, Mann-Whitney test

Predictors of HIV infection

Being born before 1970 had a strong point estimate of association, though non-significant, with seroconversion, whereas the remaining background indicators had negligible associations. Variables that were directly associated with HIV incidence even after adjustment for UAI were: reporting partner disclosure of HIV positive status between first and the most recent visit (aIRR=5.25; 95% CI 1.60–17.24; p=0.006); sexual intercourse with HIV-positive men whether only reported at first visit (aIRR=3.79; 95%CI 1.17–12.24; p=0.026), or only at the most recent visit (aIRR=5.99; 95%CI 2.28–15.71; p<0.001); having had an HIV-positive steady partner at least once during follow-up (aIRR=3.28; 95%CI 1.24–8.68; p=0.017); newly-adopted UAI with a steady partner regardless of their HIV status between cohort entry and the most recent visit (aIRR=3.85; 95%CI 1.26–11.78; p=0.018); persistent UAI with occasional partners during follow-up (aIRR=3.63; 95%CI 1.38–9.58; p=0.009) and having been newly diagnosed with syphilis between cohort entry and HIV seroconversion (aIRR=4.71; 95%CI 1.07–20.71; p=0.040).

Even though non-significant, having had sex with sex workers at least once during follow-up (aIRR=2.60; 95%CI 0.92–7.36; p=0.072) and newly adopting UAI with occasional partners between cohort entry and the most recent visit (aIRR=2.79; 95%CI 0.87–8.92; p=0.084) were associated with HIV incidence. Crude associations with more generic markers of exposure (having started to have sex with men four to eight years before cohort entry, reporting recent sexual intercourse with bisexual men or women and persistent use of recreational drugs during follow-up) lost significance after adjustments. Detailed results of HIV predictors are presented in Table 3.

We stratified the analysis of the main determinants of HIV incidence by HIV status of steady partner (Figure). Overall, we observed that MSM who had an HIV-positive steady partner during follow-up had higher incidence rates than MSM who did not have an HIV-positive partner. The greatest increases in HIV incidence were found for MSM reporting newly-adopted UAI with a steady partner (IRR=17.29; 95% CI: 5.00–59.70) and MSM reporting persistent UAI with occasional partners during follow-up (IRR=14.19; 95% CI: 2.75–73.12).

Discussion

The Lisbon Cohort of MSM provides the first quantification of HIV incidence in Portuguese MSM. The overall estimate of 2.80 per 100 person-years is higher than those obtained in other European settings [4,6,8], and shows worrying ongoing transmission of HIV among MSM, consistent with routine surveillance data [23].

In this cohort, having an HIV positive steady partner increased the risk of seroconversion, particularly after newly-adopted UAI with that partner and regardless of UAI with occasional partners. The role of serodiscordant steady relationships in newly acquiring HIV infection is well-recognised [24]. Previous studies suggest that men within a steady relationship are more likely to engage in UAI and have lower rates of HIV testing as a result of lower risk perception and increased confidence of remaining HIV-negative [25]. As for the timing of transmission, among MSM who seroconverted and had an HIV positive steady partner, approximately half reported their disclosure of HIV (whether previously diagnosed or not) during follow-up. This suggests that a substantial fraction of transmission to the index partner might occur during the acute infection stage of the steady partner, when the risk of transmission is highest [26]. Nevertheless, we cannot exclude the contribution of older infections. Indeed, 37.1% of HIV-positive MSM in Portugal presented to care with CD4 count<350/mm3 and, and 39.0% either had detectable or unknown viral load [27].

Persistent UAI with occasional partners was associated with HIV seroconversion, as extensively described [28]. Our study adds that being newly diagnosed with

Table 3a

Predictors of HIV incidence, cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

	HIV cases	PY	HIV incidence	IRR (95% CI)	p value	aIRR [a] (95%CI)	p value
Mean number of tests per year during follow-up							
Less than 2	1	166.74	0.6	1		1	
2	5	367.90	1.4	2.27 (0.26–19.39)	0.455	3.40 (0.40–29.33)	0.266
3	6	215.20	2.8	4.65 (0.56–38.62)	0.155	4.70 (0.51–42.92)	0.170
4	3	83.49	3.6	5.99 (0.62–57.60)	0.121	10.59 (1.09–103.27)	0.042
More than 4	10	60.05	16.7	27.77 (3.56–216.92)	0.002	45.30 (5.62–365.00)	<0.001
Background characteristics							
Birth cohort							
Before 1970	5	109.26	4.6	2.81 (0.76–10.47)	0.123	n.a.	n.a.
1970–1979	4	245.75	1.6	1		n.a.	
1980–1989	12	373.74	3.2	1.97 (0.64–6.12)	0.239	n.a.	n.a.
1990 or after	4	164.63	2.4	1.49 (0.37–5.97)	0.571	n.a.	n.a.
Country of birth							
Portugal	18	648.27	2.8	1		n.a.	
Other	7	211.54	3.3	1.19 (0.50–2.85)	0.694	n.a.	n.a.
Education (schooling years)							
Less than higher education (≤12 years)	11	357.42	3.1	1.17 (0.53–2.58)	0.692	n.a.	n.a.
Higher education (>12 years)	14	533.74	2.6	1		n.a.	
Sexual identity							
Homosexual	22	789.81	2.8	1		n.a.	
Bisexual/heterosexual/other	3	100.31	3.0	1.07 (0.32–3.59)	0.908	n.a.	n.a.
HIV testing							
Number of HIV previous tests at cohort entry							
0	0	120.98	0.0	n.a.		n.a.	n.a.
1 to 5	14	476.42	2.9	1		n.a.	
More than 5	10	234.47	4.3	1.45 (0.65–3.27)	0.368	n.a.	n.a.
Reasons for HIV test during follow-up							
Concerned with exposure to HIV throughout follow-up							
Never	2	163.21	1.2	1		n.a.	
At least once	22	716.67	3.1	2.51 (0.59–10.65)	0.214	n.a.	n.a.
Partner was diagnosed with HIV/disclosed HIV status throughout follow-up							
Persistent No	18	758.15	2.4	1		1	
Changed: Yes to No	2	33.42	6.0	2.52 (0.58–10.86)	0.215	1.91 (0.24–15.01)	0.537
Changed: No to Yes	5	38.48	13.0	5.47 (2.03–14.74)	0.001	5.25 (1.60–17.24)	0.006
Persistent Yes	0	12.22	0.0	n.a.	n.a.	n.a.	n.a.
Sexual life and partners							
Age at first anal intercourse							
More than 15	21	693.42	3.0	1		n.a.	
15 or less	3	136.57	2.2	0.73 (0.22–2.43)	0.603	n.a.	n.a.
Time since the beginning of sexual life with other men							
4 years or less	5	238.32	2.1	1		1	
4 to 8 years	10	185.97	5.4	2.56 (0.88–7.50)	0.086	2.57 (0.77–8.54)	0.123
more than 8 years	9	405.71	2.2	1.06 (0.35–3.16)	0.920	1.09 (0.32–3.70)	0.887
Role in anal sex							
Insertive only	8	213.54	3.7	1		n.a.	
Receptive/both	17	658.75	2.6	0.69 (0.30–1.60)	0.385	n.a.	n.a.

aIRR: adjusted incidence rate ratio; CI: confidence interval; IRR: incidence rate ratio; n.a.: not applicable; PEP: post-exposure prophylaxis; PY: person-years; STI: sexually transmitted infection; UAI: unprotected anal intercourse.

[a] Adjusted for UAI with a steady partner and UAI with occasional partners during follow-up.

Table 3b

Predictors of HIV incidence, cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

	HIV cases	PY	HIV incidence	IRR (95% CI)	p value	aIRR [a] (95%CI)	p value
Sexual life and partners							
Sexual intercourse throughout follow-up with any of the following:							
HIV-positive men							
Persistent No	11	672.50	1.6	1		1	
Changed: Yes to No	5	78.05	6.4	3.92 (1.36–11.27)	0.011	3.79 (1.17–12.24)	0.026
Changed: No to Yes	8	74.57	10.7	6.56 (2.64–16.31)	<0.001	5.99 (2.28–15.71)	<0.001
Persistent Yes	0	33.72	0.0	n.a.		n.a.	
Bisexual men							
Persistent No	10	478.84	2.1	1		1	
Changed: Yes to No	2	152.34	1.3	0.63 (0.14–2.87)	0.549	0.71 (0.15–3.32)	0.660
Changed: No to Yes	3	79.66	3.8	1.80 (0.50–6.55)	0.370	2.23 (0.59–8.42)	0.236
Persistent Yes	8	147.29	5.4	2.60 (1.03–6.59)	0.044	2.12 (0.79–5.66)	0.136
Men with different sexual partners							
Persistent No	3	113.13	2.7	1		n.a.	
Changed: Yes to No	5	194.75	2.6	0.97 (0.23–4.05)	0.965	n.a.	n.a.
Changed: No to Yes	2	85.45	2.3	0.88 (0.15–5.28)	0.891	n.a.	n.a.
Persistent Yes	13	462.90	2.8	1.06 (0.30–3.72)	0.929	n.a.	n.a.
Sex workers (even if not paid)							
Never	18	779.22	2.3	1		1	
At least once	5	78.92	6.3	2.74 (1.02–7.39)	0.046	2.60 (0.92–7.36)	0.072
Women							
Persistent No	18	743.54	2.4	1		1	
Changed: Yes to No	4	64.21	6.2	2.57 (0.87–7.60)	0.087	2.22 (0.74–6.71)	0.156
Changed: No to Yes	0	11.83	0.0	n.a.	n.a.	n.a.	
Persistent Yes	1	38.55	2.6	1.07 (0.14–8.03)	0.946	0.69 (0.09–5.34)	0.723
Trios/group sex							
Persistent No	13	508.19	2.6	1		n.a.	
Changed: Yes to No	0	129.60	0.0	n.a.		n.a.	
Changed: No to Yes	3	84.82	3.5	1.38 (0.39–4.85)	0.613	n.a.	n.a.
Persistent Yes	7	134.39	5.2	2.04 (0.81–5.10)	0.129	n.a.	n.a.
Steady partner during follow-up							
Persistent No	5	180.52	2.8	1		n.a.	
Changed: Yes to No	2	192.56	1.0	0.38 (0.07–1.93)	0.241	n.a.	n.a.
Changed: No to Yes	4	145.44	2.8	0.99 (0.27–3.70)	0.992	n.a.	n.a.
Persistent Yes	13	360.75	3.6	1.30 (0.46–3.65)	0.617	n.a.	n.a.
HIV-positive steady partner during follow-up							
Never	16	777.93	2.1	1		1	
At least once	8	90.14	8.9	4.32 (1.85–10.08)	0.001	3.28 (1.24–8.68)	0.017
Occasional partners during follow-up							
Persistent No	2	40.46	4.9	1		n.a.	
Changed: Yes to No	2	146.52	1.4	0.28 (0.04–1.96)	0.198	n.a.	n.a.
Changed: No to Yes	1	46.70	2.1	0.43 (0.04–4.78)	0.495	n.a.	n.a.
Persistent Yes	18	644.85	2.8	0.56 (0.13–2.43)	0.443	n.a.	n.a.
Number of occasional sexual partners in the previous 12 months at cohort entry							
<=1	3	125.50	2.4	1		n.a.	
2 to 9	12	408.48	2.9	1.30 (0.35–4.36)	0.749	n.a.	n.a.
>=10	6	242.20	2.5	1.03 (0.26–4.14)	0.960	n.a.	n.a.
Having sex for money or drugs during follow-up							
Never	22	854.61	2.6	1		n.a.	
At least once	1	21.84	4.6	1.78 (0.24–13.19)	0.573	n.a.	n.a.

aIRR: adjusted incidence rate ratio; CI: confidence interval; IRR: incidence rate ratio; n.a.: not applicable; PEP: post-exposure prophylaxis; PY: person-years; STI: sexually transmitted infection; UAI: unprotected anal intercourse.

[a] Adjusted for UAI with a steady partner and UAI with occasional partners during follow-up.

Table 3C

Predictors of HIV incidence, cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)

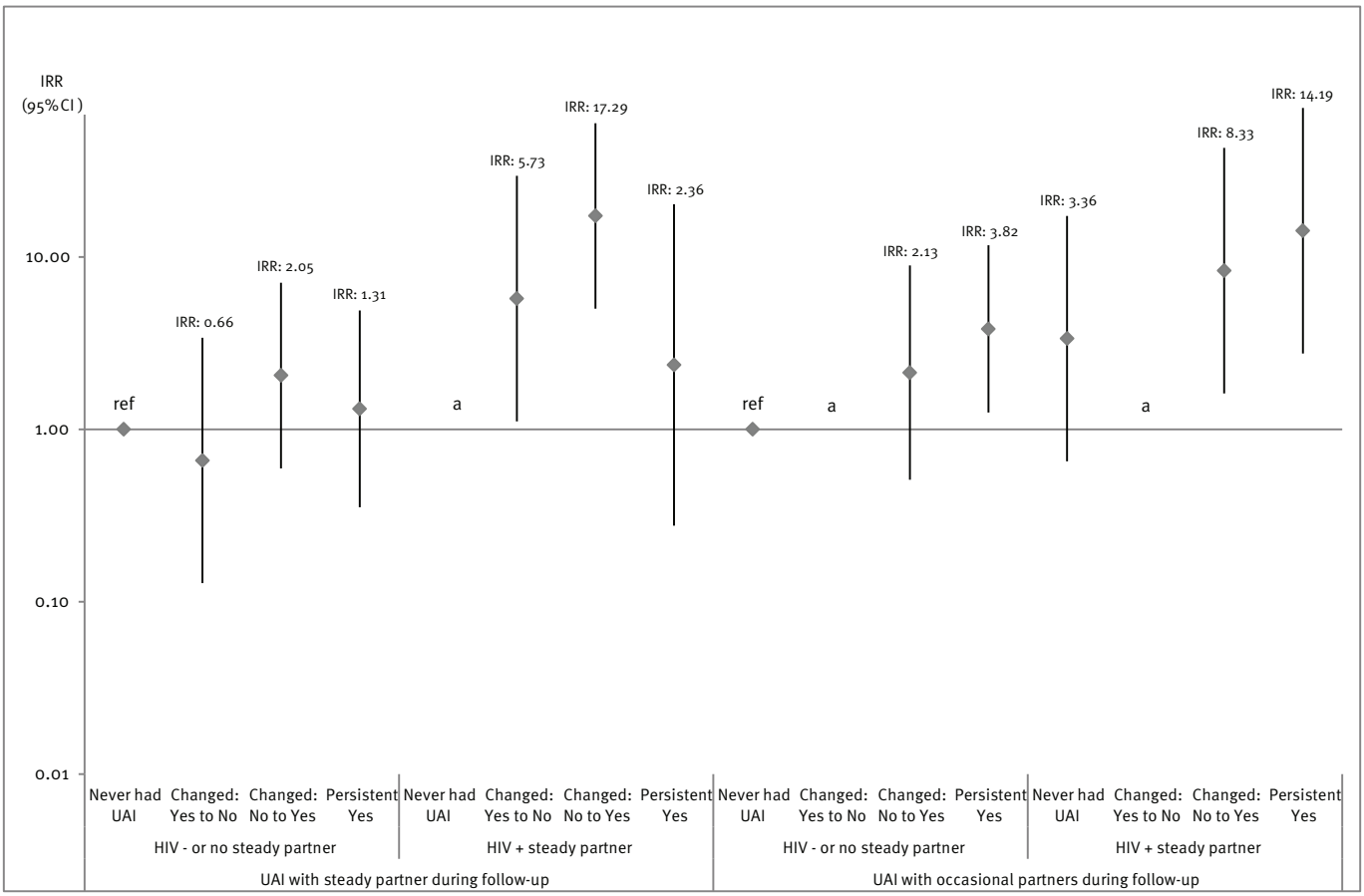
	HIV cases	PY	HIV incidence	IRR (95% CI)	p value	aIRR [a] (95%CI)	p value
UAI during follow-up							
UAI with a steady partner							
Persistent No	5	305.85	1.6	1		1	
Changed: Yes to No	4	191.38	2.1	1.28 (0.34–4.76)	0.714	1.10 (0.29–4.11)	0.892
Changed: No to Yes	10	150.54	6.6	4.06 (1.39–11.89)	0.010	3.85 (1.26–11.78)	0.018
Persistent Yes	5	194.26	2.6	1.57 (0.46–5.44)	0.473	1.83 (0.53–6.38)	0.340
UAI with occasional partners							
Persistent No	7	388.18	1.8	1		1	
Changed: Yes to No	0	148.83	0.0	n.a.		n.a.	
Changed: No to Yes	5	115.29	4.3	2.41 (0.76–7.58)	0.134	2.79 (0.87–8.92)	0.084
Persistent Yes	10	162.34	6.2	3.42 (1.30–8.97)	0.013	3.63 (1.38–9.58)	0.009
Venues used to meet occasional partners at cohort entry							
Only sexual venues (saunas, dark rooms, sex clubs)							
No	19	681.40	2.8	1		n.a.	
Yes	6	195.90	3.1	1.1 (0.44–2.76)	0.841	n.a.	n.a.
Other venues (discos/gay bars, gym and outdoor cruising venues)							
No	10	368.51	2.7	1		n.a.	
Yes	15	513.79	2.9	1.08 (0.48–2.40)	0.858	n.a.	n.a.
Internet							
No	6	313.65	1.9	1		n.a.	
Yes	19	567.72	3.3	1.75 (0.70–4.38)	0.232	n.a.	n.a.
STIs and hepatitis							
Recent history of syphilis during follow-up							
Persistent No	22	858.10	2.6	1		1	
Changed: Yes to No	1	12.16	8.2	3.21 (0.43–23.79)	0.254	3.89 (0.47–31.91)	0.206
Changed: No to Yes	2	21.95	9.1	3.55 (0.84–15.12)	0.086	4.71 (1.07–20.71)	0.040
Persistent Yes	0	0.00	-	-		-	
Recent history of gonorrhoea during follow-up							
Persistent No	24	835.79	2.9	1		n.a.	
Changed: Yes to No	0	25.77	0.0	n.a.		n.a.	n.a.
Changed: No to Yes	1	30.08	3.3	1.16 (0.16–8.56)	0.886	n.a.	n.a.
Persistent Yes	0	0.00	n.a.	n.a.		n.a.	n.a.
Lifetime history of hepatitis C reported at cohort entry							
No/does not know	25	874.81	2.9	1		n.a.	
Yes	0	2.76	0	n.a.		n.a.	
Lifetime history of Hepatitis B reported at cohort entry							
No/does not know	24	862.89	2.8	1		n.a.	
Yes	1	20.64	4.8	1.74 (0.24–12.88)	0.587	n.a.	n.a.
Drug use before or during intercourse							
Use of recreational drugs before or during intercourse during follow-up							
Persistent No	9	507.25	1.8	1		1	
Changed: Yes to No	2	91.08	2.2	1.24 (0.27–5.73)	0.785	0.92 (0.19–4.38)	0.915
Changed: No to Yes	5	117.90	4.2	2.39 (0.80–7.13)	0.118	1.63 (0.42–6.28)	0.477
Persistent Yes	8	155.99	5.1	2.89 (1.12–7.49)	0.029	1.90 (0.70–5.17)	0.209
PEP at cohort entry							
Does not know about	14	437.41	3.2	1		n.a.	
Knows about but never used	10	392.47	2.5	0.80 (0.35–1.79)	0.582	n.a.	n.a.
Knows and used	1	21.15	4.7	1.48 (0.19–11.23)	0.706	n.a.	n.a.

aIRR: adjusted incidence rate ratio; CI: confidence interval; IRR: incidence rate ratio; n.a.: not applicable; PEP: post-exposure prophylaxis; PY: person-years; STI: sexually transmitted infection; UAI: unprotected anal intercourse.

[a] Adjusted for UAI with a steady partner and UAI with occasional partners during follow-up.

Figure

Stratified analysis of the main determinants of HIV incidence by HIV status of steady partner, cohort of men who have sex with men, Lisbon, Portugal, 2011–2014 (n=804)



IRR: incidence rate ratio; 95% CI: 95% confidence interval; UAI: unprotected anal intercourse; ref: reference category.

[a] No seroconversions were observed in the category

syphilis during follow-up was a strong predictor of HIV incidence, independently of self-reported UAI. An additional red flag was the observation that MSM who seroconverted had shorter intervals between follow-up visits and higher mean number of tests per year, which highlights the use of testing as a risk management strategy.

Our findings suggest that, in addition to the pattern of service use itself, incident circumstances (newly-adopted UAI with a steady partner, newly-disclosed HIV-positive partner, and newly-diagnosed syphilis) may be useful markers of the short-term risk of infection. Yet, it is important to note that we cannot assume that any incident circumstance or change in the information provided between visits represents a sustained behavioural change but rather indicates varying behavioural options that may influence seroconversion risk.

Other behavioural factors, such as time since the beginning of sexual life, intercourse with bisexual men or sex workers and persistently using recreational drugs, may be regarded as less specific predictors of incident HIV, even though such effects were probably largely mediated by UAI. The number of sexual partners in the year before cohort entry was not associated with increased HIV incidence. These findings highlight that, rather than extensively characterising the type or number of partners, targeted inquiries about UAI in this context seem to be more accurate for predicting HIV risk.

So far, none of the background variables predicted HIV risk in this cohort of Portuguese MSM. However, higher HIV incidence was found in MSM born before 1970. Older MSM were previously described at higher risk of acquiring HIV from a steady partner [8] and may underestimate vulnerability since they have remained uninfected up to the present [29]. In contrast with previous studies and national and European surveillance data [5,30], younger MSM were not clearly identified as being at higher risk for HIV, but that could be related

to different patterns of use of the CheckpointLX by younger generations.

Methodological options and limitations of this study should be addressed. First, this design option is unlikely to result in a representative sample of the source MSM population, which limits the generalisability of our findings. When compared with data from the 2007 National Health and Sexuality Survey (HSS) [31], MSM in our sample are younger, more self-identified as homosexual (86.1% vs 35.9% of men reporting some kind of sexual contact with men in the HSS) and report more frequently history of HIV testing (84.1% vs 61.0% in HSS). Nevertheless, by setting up a cohort study in a community-based voluntary counselling and testing service we expect to reach MSM on average at higher risk of infection than the general MSM community. Thereby it seems reasonable to admit that we are focusing our attention on a priority subset of the population in terms of HIV risk (even if potentially more aware than those not reached by the service). Additionally, since CheckpointLX promotion strategies remained similar during follow-up, we do not expect that the extent of selection bias will change substantially over time, which is particularly important for estimating secular trends of infection and behaviours in the source population [32-34]. Finally, the fact that the recruitment site is a service which aims to anticipate diagnosis and to provide evidence-based and adapted information may itself modify the risk of acquiring HIV and the consequent incidence estimates. However, we expect that newly-recruited clients reflect the overall incidence of infection in the community.

Another important issue is participation bias: the fact that around 30% of eligible MSM chose not to enter the cohort implies that informative data may be missing on a harder-to-reach subset of the target population. However, the frequency of prior testing was similar between groups, suggesting that both may have similar perceived risk of acquiring HIV [35]. Moreover, the observed attrition means that information about possible seroconversions is missing in half of participants, which is a clear limitation. Follow-ups depend on the frequency of service uptake, which can itself be influenced by perceived risk of infection. Efforts have been made to minimise dropout rates, including active reminders of follow-up visits by peer counsellors. However, we still found differences in mean age between MSM who appeared for follow-up and those who did not, although the absolute difference was small. No differences were found in the frequency of behaviours associated with higher probability of seroconversion. This leads us to hypothesise that our incidence rate might not be substantially affected by losses to follow-up.

Self-reported information is always subject to limitations in validity and reliability. However, we are confident that a relevant strength comes from the involvement of community peer counsellors, since this strategy increases participation and improves validity and completeness of information as well as disclosure of risk, as supported by previous research [34,36].

Despite the high incidence observed, the absolute number of infections is still low, resulting in suboptimal statistical power for some comparisons. In the future, with larger sample size and longer follow-up periods, we expect increased precision of estimates. Nevertheless, these first estimates are important for two main reasons: i) they draw a first picture of HIV incidence and its drivers in Portuguese MSM about whom little was known; ii) they add evidence on the role of changes in individual circumstances in newly acquiring HIV to the existing body of prospective evidence from a variety of settings.

In conclusion, we found high HIV incidence in this cohort of Portuguese MSM likely to be driven by short-term contextual and behavioural changes, namely newly-adopted UAI with a steady partner, newly-disclosed HIV-positive partner and newly-diagnosed syphilis. History of serodiscordant steady relationships and persistently reporting UAI with occasional partners also played a major role in predicting HIV seroconversion.

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Conflict of interest

None declared.

Authors' contributions

PM drafted the manuscript and performed the data analysis. RL participated in the study design, helped draft the manuscript, participated in analysis and interpretation of data, and reviewed the manuscript for important intellectual content. CC reviewed the manuscript for important intellectual content. RF and JB participated in the study design and data collection, and reviewed the manuscript for important intellectual content. MJC conceived the study, participated in the study design and coordination, and reviewed the manuscript for important intellectual content. LM conceived the study, participated in the study design and coordination, and reviewed the manuscript for important intellectual content. HB conceived the study, participated in the study design and coordination, and reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Internet-based recruitment system for HIV and STI screening for men who have sex with men in Estonia, 2013: analysis of preliminary outcomes

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The aim of the current project was to develop an Internet-based recruitment system for HIV and sexually transmitted infection (STI) screening for men who have sex with men (MSM) in Estonia in order to collect biological samples during behavioural studies. In 2013, an Internet-based HIV risk-behaviour survey was conducted among MSM living in Estonia. After completing the questionnaire, all participants were offered anonymous and free-of-charge STI testing. They could either order a urine sample kit by post to screen for chlamydia infections (including lymphogranuloma venereum (LGV)), trichomoniasis, gonorrhoea and *Mycoplasma genitalium* infections, or visit a laboratory for HIV, hepatitis A virus, hepatitis B virus, hepatitis C virus and syphilis screening. Of 301 participants who completed the questionnaire, 265 (88%), reported that they were MSM. Of these 265 MSM, 68 (26%) underwent various types of testing. In the multiple regression analysis, Russian as the first language, previous HIV testing and living in a city or town increased the odds of testing during the study. Linking Internet-based behavioural data collection with biological sample collection is a promising approach. As there are no specific STI services for MSM in Estonia, this system could also be used as an additional option for anonymous and free-of-charge STI screening.

Background

Men who have sex with men (MSM) continue to be one of the groups at highest risk for HIV and sexually transmitted infections (STI) in the European Union. MSM made up the highest proportion of total number of HIV cases in Europe in 2013 (42%), and in 2012 more than a third of reported gonorrhoea cases in Europe were in MSM (38%) [1,2].

In 2013, Estonia had a total population of around 1.3 million, and 24.6 newly diagnosed HIV cases and 1.8 AIDS cases per 100,000 population [3]. It has been estimated that there are about 9,000 MSM in Estonia [4]. Triangulation of data from various studies suggests that HIV prevalence in MSM could be around 2–3% [5]. No data are available on STI prevalence in MSM or the proportion of reported STI cases that are in MSM.

Gathering accurate data on HIV prevalence and risk behaviours in MSM has posed a challenge for researchers in Estonia [6]. For HIV-prevalence estimations, 59 MSM were recruited by using respondent-driven sampling (RDS) [6] and 79 by convenience sampling in gay venues and community-based organisations [7]. These sampling methods did not yield the desired sample size. At the same time, MSM participation in four consecutive Internet studies (2004, 2006, 2007 and 2010) has been relatively high, especially in the European MSM Internet Study (EMIS) [8–11]. Unfortunately, the Internet does not offer the opportunity to gather biological material for testing to estimate HIV/STI prevalence rates.

In other countries, studies of MSM as well as of the general population have shown that Internet-based screening and self-sampled postal testing for STIs is an effective, acceptable and feasible approach [12–16]. Our aim was to develop an Internet-based recruitment system for HIV and STI screening for MSM in order to collect biological samples during behavioural studies.

Methods

We conducted an Internet-based study of MSM to investigate sexual and drug-use behaviours, previous HIV/STI testing, mental health, internalised homonegativity and HIV/STI related knowledge and attitudes among this population group. The eligibility criteria included: self-identifying as male; living in Estonia; age of 18 years or older; and being sexually attracted to men and/or having ever had sex with a man. Taking into account the range of response rates in previous studies, the planned sample size was 300 [8–11].

Questionnaire

The questionnaire was constructed using Internet survey software (http://www.limesurvey.org/). The questionnaire was presented over 63 web pages and included 144 questions. It took around 45 minutes to complete. To minimise completion time, it was tailored with intra-questionnaire filters. For example, specific questions regarding HIV testing and treatment were not shown if the participant had already stated that they had never been tested for HIV or were HIV-negative. The questionnaire was accessible online from April to September 2013. All study materials were available in both Estonian and Russian (25% of the population of Estonia is predominantly Russian-speaking [17]). The questionnaire's design was based on previous Estonian and international experiences [7-11, 18] and included the following domains:

- Sociodemographic data.
- Sexual orientation (homosexual, bisexual, straight, heterosexual, any other term (please specify) or 'I don't usually use a term/define myself'), type of relationship, and sexual behaviour.
- HIV and STI testing and history. To assess HIV testing history, we asked: 'Have you ever been tested for HIV?' and 'What was the result of your last HIV test?' To assess STI testing history, we asked: 'Have you ever been tested for any STI (for example syphilis, gonorrhoea, chlamydia, trichomoniasis, genital herpes)?'; 'Have you ever been diagnosed with any STI (for example syphilis, gonorrhoea, chlamydia, trichomoniasis, genital herpes)?'; and 'Have you ever had anal swabs taken for STI diagnosis?'
- Confidence about HIV and STI testing possibilities was assessed with the following two questions 'How confident are you that you could get an HIV test if you wanted one?' and 'How confident are you that you could get a test for STIs (other than HIV) if you thought you needed it?' [11]. Responses were indicated by using a four-point Likert-type scale (1=very confident, 4=not at all confident).
- Illegal drug use and alcohol use (CAGE questionnaire) [19]. The CAGE questionnaire is widely used to screen patients with alcohol abuse or dependence in the general population as well as in clinical samples. It includes four yes/no items. Subjects who responded affirmatively to two or more questions were classified as CAGE-positive (problem drinkers with high likelihood of the presence of alcoholism).
- Internalised homonegativity. We used a short form of the 'Reactions to Homosexuality' scale [20, 21] that included seven of the original items loading on three factors: personal comfort with a gay identity, social comfort with gay men, and public identification as gay. Responses were indicated by using a seven-point Likert-type scale (0=strongly disagree, 6=strongly agree). All the items were coded at analysis so that a higher score indicated higher internalised homonegativity. The scale was additive, ranging from 0 to 6.
- Contacts with HIV prevention services, HIV/STI knowledge and attitudes to HIV, STIs and related issues.

Recruitment and promotion

The study was promoted through Estonia-based gay online social media, gay community organisations, the national network of anonymous HIV testing sites and youth counselling centres. A special Facebook page was created to promote the study. The English version of the slogan of the study was 'Good health: the pride of every man!' Advertisements directed users to the opening page of the study. The opening page described the study aims and informed potential participants that their data would be anonymous, that no IP addresses were saved, and that the survey software installed no cookies or other trace files on computers. The participants could not pause the process of filling in the questionnaire and sign in later to finish it. Not collecting IP addresses meant that it was possible for one person to submit two or more questionnaires.

Testing for HIV and STIs and reporting of the results

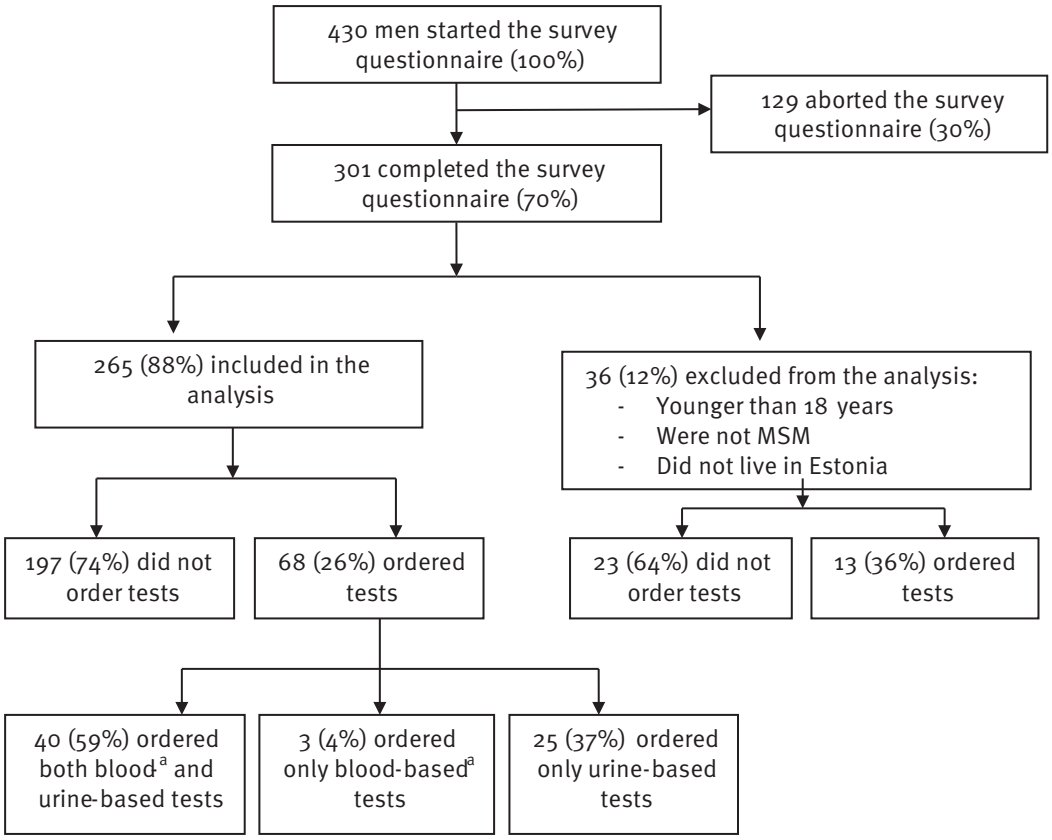
All the participants were offered voluntary, anonymous and free-of-charge HIV and STI testing for HIV, hepatitis C virus (HCV), hepatitis B virus (HBV), hepatitis A virus (HAV) and syphilis markers from blood, and for *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Chlamydia trachomatis* (including lymphogranuloma venereum (LGV) genotyping) and *Mycoplasma genitalia* from urine sample.

After submitting the questionnaire, participants were referred to a landing page where each participant was assigned a unique study participation code (for example, u_aa1234) and detailed information, how to get tested and how the data were protected. For testing we used a special web-based testing service called *Testikodus* ('Test at Home' in English). This is an Internet portal run by Quattromed HTI Laborid OÜ (QM), which is the largest medical laboratory in Estonia. The portal offers anonymous fee-based testing for STIs. For the purposes of our study we created a special pathway for those who had filled in the study questionnaire to order test kits free of charge. There were two options to get tested and receive test results:

1 For blood-based testing (HIV, HCV, HBV, HAV and syphilis) the participants had to visit the QM laboratory in person (six sites in larger cities across Estonia, ranging from the capital city Tallinn (population 406,000, 2013) to Võru (population 12,800, 2013) [17]). The test results were available within five working days and could be received only by visiting the laboratory. Those who went to the laboratory could either return the urine sample kit by post or take the urine sample to the laboratory, depending on their preference.

Figure

Participant flow chart and drop-out in various stages of the project, Internet study of men who have sex with men, Estonia, 2013



MSM: men who have sex with men.

Percentages are calculated on the basis of the previous cell

[a] Required a visit to the laboratory

2 For urine-based testing (gonorrhoea, trichomoniasis, chlamydia, LGV, and mycoplasmosis) the participants could order the urine sample kit to be delivered by SmartPOST courier services. For this they had to create an account in the Testikodus website using their unique study participation code. Participants were asked to give their email address and/or phone number, which were needed for the SmartPOST courier services. Through this account and emails the participants received confirmation once their order was successfully placed and the test results were ready. The test results were available within five working days and could be received through the Testikodus website account.

Testing could be carried out until 31 December 2013 in order to be included in the study.

If a participant tested positive for any of the urine-based tests, he was given information about where to go for treatment. Participants could attend one sexual health clinic in Tallinn anonymously and get treatment free of charge on presentation of the unique study participation code. If a participant tested positive for any of the blood-based tests, it was explained in the laboratory that these were screening tests and that the participant should go to an infectious diseases doctor for further tests to confirm the diagnosis. Due to the anonymous nature of the study we were not able to find out how many participants accessed confirmatory testing.

Laboratory testing

Ten ml of venous blood and/or 20 ml of first void urine were collected from the participants. The following methods were used for infectious marker testing:

- HIV-antibodies and antigen (HIV 1,2 Ab+Ag), HCV-antibodies (HCV Ab), anti-HAV IgM/IgG, HBsAg, and syphilis antibodies: chemiluminescence.
- Chlamydia (*C. trachomatis*, including LGV serovar), gonorrhea (*N. gonorrhoeae*), trichomoniasis (*T. vaginalis*) and mycoplasmosis (*M. genitalium*): PCR.

Data management and statistical analysis

The data from the questionnaire and the unique participation codes (created in the *Testikodus* website and linked to the test results) were stored in different databases. The data were linked manually based on the date and time of day (e.g 10.07.2014 22:34) the participant submitted the questionnaire, and the date and time he reached the landing page (time difference approximately one second). The personal data necessary for ordering test kits (mobile phone numbers, email addresses, etc) were stored only on the *Testikodus* database and never linked to the data from anonymous questionnaires.

The statistical analyses were performed with Stata 11.0 (StataCorp LP, College Station, TX). Descriptive statistics were used to characterise participants. The dependent variable in our analyses was the fact of ordering either blood or urine-based tests. The associations between the participant's characteristics and dependent variables were evaluated using a Wilcoxon rank-sum test, a Fisher's exact test, or a one-way analysis of variance (ANOVA), followed by univariate and multivariable logistic regressions. For multivariable logistic regression, testing during the study was adjusted for age and factors significantly associated in the univariate analysis (at $p<0.05$).

Ethical issues

The study was approved by the Tallinn Medical Research Ethics Committee. Before answering the questions, all participants were required to indicate that they understood the aims and methods of the study and that they consented to take part in it. The opening and landing pages included contact information for the principal investigator in case anybody had any further questions related to the study aims and procedures.

Results

Overall, 430 people began the questionnaire. Of these, 70% of them (n=301) completed the questionnaire and submitted their answers, and 30% (n=129) broke off or did not submit at the end of the questionnaire. Those who completed the questionnaire were compared with those who did not for age, first language (Estonian vs Russian), region (city vs countryside) and satisfaction with their economic situation. The only statistically significant difference was related to region, with more people living in the countryside among those who broke off compared with those who completed the questionnaire (24% vs 13%; p=0.02).

Of the 301 participants who completed the questionnaire, 12% (n=36) did not meet the inclusion criteria (18 did not live in Estonia, 10 were not MSM, and eight were younger than 18 years of age). Thus the total sample size of MSM was 265. As our aim was to develop a testing system and recruit MSM, the analysis of factors related to testing during the study uses data only from those 265 men who were eligible. Participant flowchart and drop-out are presented in the Figure.

Participants

The characteristics of the MSM in the study are presented in Table 1. The median age was 31 years (mean age 33 years; range 18–67 years; 53% were older than 30 years), 90% completed the questionnaire in Estonian, 71% were from the capital city Tallinn and the surrounding area; 85% were working full- or part-time, 43% had higher education; 44% were in a steady relationship with a man or a woman; 76% considered themselves homosexual and 24% bisexual. A total of 98% had ever had sex, 33% were CAGE positive and 23% had used illegal drugs in the last 12 months). The mean internalised homonegativity score was 1.9 (SD 1.2; range 0.2–5.7).

Of the total sample, 70% had ever been tested for HIV, and 36% had been tested in the last 12 months. Self-reported HIV-prevalence was 4%.

Fifty-one per cent of the total sample had ever been tested for STIs, 19% in the last 12 months. 24% had ever been diagnosed with an STI. 8% of those who had ever been tested for STIs reported having had anal swabs taken.

30% of the total sample had received a full-course vaccination against hepatitis B, 3% had ever had hepatitis B. 18% of the MSM had received a full-course vaccination against hepatitis A, and 5% had ever had hepatitis A.

Testing

A total of 81 men were tested during the study (27% of all those who completed the questionnaire): 68 MSM (testing rate among MSM: 26%) and 13 non-eligible participants (testing rate among non-eligible participants: 35%) (Figure). 74 men (91%) were tested within one month of completing the questionnaire, three within two months (4%), and four within four months (5%).

Of the 68 MSM who were tested, 40 were tested for all infections (59%), three (4%) gave only blood and 25 provided only urine samples (37%). Thus a total of 65 provided urine samples (25% of MSM who completed the questionnaire), and 43 provided blood samples (16% of MSM who completed the questionnaire).

The univariate analysis identified several factors associated with testing among MSM during the study (Table 1). The multivariable logistic regression analysis showed that testing during the study was independently associated with Russian as the first language, living in towns/cities and having ever been tested for HIV (Table 1).

Test results

The test results are presented in Table 2. Of the 17 participants positive for HAV antibodies, two had had hepatitis A, five had been vaccinated against HAV, four had not been vaccinated and six did not know their

Table 1A

Participant characteristics, univariate and multivariable analysis of factors associated with biological testing, Internet study of men who have sex with men, Estonia, 2013 (n=265)

	Total n = 265	Testing during the study		Univariate odds ratio (95% CI)	Multiple regression	
		No n = 197	Yes n = 68		Adjusted odds ratio (95% CI)	p value
	N (%)	N (%)	N (%)			
Sociodemographics						
Age						
≤ 30 years	125 (47)	96 (77)	29 (23)	1.00	1.00	-
› 30 years	140 (53)	101 (72)	39 (28)	1.29 (0.73–2.23)	1.26 (0.67–2.27)	-
First language						
Estonian	238 (90)	185 (78)	53 (22)	1.00	1.00	-
Russian	27 (10)	12 (44.4)	15 (55.6)	4.36 (1.93–9.89)a	3.82 (1.61–9.08)	0.002
County[b]						
Tallinn/Harjumaa	186 (70)	129 (69)	57 (31)	1.00	-	-
Other	78 (29)	67 (86)	11 (14)	0.29 (0.14–0.59)a	-	-
Region						
Town	231 (87)	165 (71)	66 (29)	1.00	1.00	-
Countryside	34 (13)	32 (94)	2 (6)	0.16 (0.04–0.67)c	0.37 (0.18–0.76)	0.007
Education						
Primary/secondary	151 (57)	113 (75)	38 (25)	1.00	-	-
Higher	114 (43)	84 (74)	30 (26)	1.06 (0.61–1.85)	-	-
Occupation						
Working full- or part time	225 (85)	165 (73)	60 (27)	1.00	-	-
Other (retired, student, long-term sick leave, etc.)	40 (15)	32 (80.0)	8 (20)	0.69 (0.30–1.58)	-	-
Relationship type						
No regular partner	146 (55)	107 (73)	39 (27)	1.00	-	-
Male regular partner	92 (35)	69 (75)	23 (25)	0.91 (0.50–1.66)	-	-
Female regular partner	21 (8)	15 (71)	6 (29)	1.10 (0.40–3.03)	-	-
Sexual behaviour						
Condom use at last anal sex with a man (k29)						
No	112 (47)	79 (71)	33 (29)	1.00	-	-
Yes	126 (53)	95 (75)	31 (25)	0.78 (0.44–1.39)	-	-
Condom use last anal sex with a male casual partner (k45)						
No	64 (30)	41 (64)	23 (35.9)	1.00	-	-
Yes	151 (70)	111 (73)	40 (26.5)	0.64 (0.34–1.20)	-	-
Casual sex with a man in the last 12 months						
No	65 (28)	50 (77)	15 (23)	1.00	-	-
Yes	170 (72)	120 (71)	50 (29)	1.39 (0.71–2.70)	-	-
Unprotected anal sex with a man in the last 12 months						
No	83 (35)	65 (78)	18 (22)	1.00	-	-
Yes	155 (65)	109 (70)	46 (30)	1.52 (0.82–2.85)	-	-
Sex abroad ever						
No	116 (46.2)	89 (77)	27 (23)	1.00	-	-
Yes	135 (53.8)	96 (71)	39 (29)	1.34 (0.76–2.37)	-	-
Anal sex in a club ever						
No	140 (54)	108 (77)	32 (23)	1.00	-	-
Yes	118 (46)	82 (69)	36 (31)	1.48 (0.85–2.58)	-	-

CI: confidence intervals; SD: standard deviation; STI: sexually transmitted infection.

[a] p<0.001

[b] Was not included in multivariable regression analysis because it was highly correlated to region of living (which included both town and countryside)

[c] p<0.01

[d] Includes those who have never drunk alcoholic beverages (n=11; 4.2% of the participants)

[e] p<0.05

Table 1B

Participant characteristics, univariate and multivariable analysis of factors associated with biological testing, Internet study of men who have sex with men, Estonia, 2013 (n=265)

	Total n = 265	Testing during the study		Univariate odds ratio (95% CI)	Multiple regression	
		No n = 197	Yes n = 68			
	N (%)	N (%)	N (%)		Adjusted odds ratio (95% CI)	p value
Sexual behaviour						
Sex with a woman ever						
No	119 (46)	84 (71)	35 (29)	1.00	-	-
Yes	140 (54)	107 (76)	33 (24)	0.74 (0.43–1.29)	-	-
Sexual orientation						
Homosexual	192 (76)	139 (72)	53 (28)	1.00	-	-
Bisexual	61 (24)	49 (80)	12 (20)	0.64 (0.32–1.30)	-	-
Internalised homonegativity (mean, SD)	1.9 (SD 1.2; 95% CI 1.8–2.1)	1.9 (SD 1.2; 95% CI 1.7–2.1)	2.1 (SD 1.2; 95% CI 1.7–2.3)		-	-
Drug and alcohol use						
Illegal drug use in the last 12 months						
No	204 (77)	152 (75)	52 (25)	1.00	-	-
Yes	61 (23)	45 (74)	16 (26)	1.04 (0.54–1.99)	-	-
CAGE score [17]						
Negative (0–2)d	178 (67)	131 (74)	47 (26)	1.00	-	-
Positive (3–4)	87 (33)	66 (76)	21 (24)	0.89 (0.49–1.61)	-	-
HIV and STI testing and history						
Responses to 'How confident are you that you could get a test for HIV if you wanted one?'						
Not so confident	93 (35)	71 (76)	22 (24)	1.00	-	-
Very confident	172 (65)	126 (73)	46 (27)	1.18 (0.66–2.12)	-	-
Responses to 'How confident are you that you could get a test for STIs (other than HIV) if you wanted one?						
Not so confident	130 (50)	97 (75)	33 (25)	1.00	-	-
Very confident	135 (51)	100 (74)	35 (26)	1.03 (0.59–1.79)	-	-
STI test ever						
No	126 (49)	100 (79)	26 (21)	1.00	-	-
Yes	132 (51)	93 (71)	39 (30)	1.61 (0.91–2.85)	-	-
STI test in last 12 months						
No	216 (82)	166 (7)	50 (23)	1.00	-	-
Yes	49 (18)	31 (63)	18 (37)	1.93 (0.99–3.73)	-	-
STI ever						
No	202 (76)	153 (76)	49 (24)	1.00	-	-
Yes	63 (24)	44 (70)	19 (30)	1.35 (0.72–2.52)	-	-
HIV test ever						
No	79 (30)	67 (85)	12 (15)	1.00	1.00	-
Yes	185 (70)	129 (70)	56 (30)	2.4 (1.22–4.83)e	2.38 (1.15–4.94)	0.02
HIV test in last 12 months						
No	168 (63)	130 (77)	38 (23)	1.00	-	-
Yes	97 (37)	67 (69)	30 (31)	1.53 (0.87–2.69)	-	-

CI: confidence intervals; SD: standard deviation; STI: sexually transmitted infection.

[a] p<0.001

[b] Was not included in multivariable regression analysis because it was highly correlated to region of living (which included both town and countryside)

[c] p<0.01

[d] Includes those who have never drunk alcoholic beverages (n=11; 4.2% of the participants)

[e] p<0.05

Table 2

Results of biological testing, Internet study of men who have sex with men, Estonia, 2013 (n=265)

	Positive		Negative		Total number of tests
	N	%	N	%	N
Chlamydia trachomatis LGV	-	-	65	100	65
C. trachomatis	1	2	64	98	65
Mycoplasma genitalium	-	-	65	100	65
Neisseria gonorrhoeae	1	2	64	98	65
Trichomonas vaginalis	-	-	65	100	65
Treponema pallidum (antibodies)	2	5	41	95	43
HAV antibodies	17	40	26	60	43
HBsAg	-	-	43	100	43
HCV antibodies	2	5	41	95	43
HIV 1/2 antigen + antibodies	3	7	40	93	43

LGV: lymphogranuloma venereum; HAV: hepatitis A virus; HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus.

vaccination status. HAV antibody prevalence among non-vaccinated men was 32% (11/34). Neither of the two participants who tested positive for HCV antibodies had been aware of their status; one had had blood transfusion before 1994 and one had injected drugs in the past. Three people were HIV-positive, two of whom were already aware of their status. The third man had considered himself HIV-negative, and had last been tested for HIV less than a year previously. As he was willing to provide his personal data for the laboratory (which was not mandatory), his test result was confirmed and he was linked to HIV care in Tallinn.

Discussion

This was the first attempt in Estonia to collect biological samples for blood-borne and STI marker detection from MSM participating in an Internet-based behavioural study. We recruited 265 MSM, of whom 26% underwent various types of testing. We detected 4 STI cases, and one new HIV case.

Of the people who began the questionnaire, 30% broke off before the end. We presume this was most likely due to the length of the questionnaire. To improve this in the future, we will shorten the questionnaire considerably. Those who broke off the questionnaire were more likely to be living in the countryside. One reason may have been perceived difficulties in accessing the testing offered during the study. People living in smaller communities may also have been more worried about confidentiality when ordering the test kits by post.

The overall sample size was smaller compared with EMIS 2010, but more or less comparable to the earlier Internet studies [8-11]. Table 3 presents the main sociodemographic and HIV-testing-related data from the previous studies. Our sample appears to be less diverse compared with previous Internet studies, which recruited a larger proportion of MSM who were bisexual, non-Estonian and lived outside the capital city Tallinn and the surrounding Harju county. The mean age of the participants in different studies has increased somewhat as well as the proportion ever tested for HIV (which may be related to vigorous HIV testing campaigns targeting MSM in recent years).

According to Statistics Estonia, 79% of households in Estonia had access to the Internet at home in 2013 (82% of those living in towns and 73% of those living in the countryside). This has improved considerably since 2005 when the respective percentage was 37% (32% living in towns and 24% living in the countryside) [17]. We do not have specific data about Internet access among MSM, but we assume it is at least as good as among the general population. Thus the reason for lower sample size is not related to the decreased access to the Internet.

The way in which the survey was promoted may be one of the reasons for the smaller and less diverse sample. With EMIS 2010, for example, the largest recruiters were not national websites but pan-European websites that sent instant messages (IMs) to their members, and 24% of the Estonian participants in EMIS were recruited through IMs sent by PlanetRomeo [11], which we did not use this time. In 2010, 12 national websites were used for promotion, but this time only 11 were used, only one of which was primarily Russian-language. In the future, participation rates could be improved by better promotion.

Twenty-six per cent of participants were tested for STIs or bloodborne infections. In a population-based survey conducted in Estonia to estimate the prevalence of

Table 3

Comparison of sample size, and selected sociodemographic, HIV testing, and HIV prevalence data from studies of men who have sex with men in Estonia, 2004–2013

Study type	2004 [7]	2006 [8]	2007 [9]	2007 [16]	2008 [6]	2010 [10]	2013
	Internet	Internet	Internet	RDS	Venue-based	Internet	Combination
Number of participants who completed the questionnaire	358	331	399	NA	NA	629	301
Final eligible sample size, n (%)	312 (87%)	232 (70%)	361 (90%)	59	79	594 (94%)	265 (88%)
Mean age of the participants, years	28	27	31	27	30[a]	32	33
Percentage homosexual	59	66	67	68	55	65	76
Percentage with higher education	38	43	40	54	51	45	43
Percentage of Estonians	76	60	79	53	71	85	90
Percentage living in Tallinn and Harju county	62	59	66	100	100	60	71
Percentage HIV-tested ever during lifetime (%)	41	47	50	71	68	60	70
Self-reported HIV-prevalence, n (%)	NA	NA	NA	NA	1 (1.3%)[b]	10 (1.7%)[b]	8 (3.0%)[b]
HIV-prevalence during the study, n (%)	NA	NA	NA	1 (1.7%)[b]	2 (2.5%)[b]	NA	3/43 (7.0%)

RDS: respondent-driven sampling; NA: not available.

[a] Median age

[b] Among all participants eligible for the study

C. trachomatis infection (tests were collected by participants and returned by post) the overall response rate for men was 32% [22]. In a systematic review of strategies for home-based chlamydia and gonorrhoea screening, the median specimen return rate for postal test kits requested through the Internet or telephone was 32% (27–47%) for the general population [15].

STI testing was used more than blood-borne infections (HIV and hepatitis) testing. It may have been more convenient (a sampling kit could be ordered and returned by post and there was no need to visit a laboratory in person), and more attractive as there have been several HIV testing campaigns for MSM in Estonia, but there are no free-of-charge and anonymous STI testing opportunities [5]. The participants concerned about confidentiality may have considered it also more anonymous.

Testing during the study period was independently associated with Russian as the first language, living in towns/cities and having ever been tested for HIV. No other sociodemographic and behavioural indicators (including recent sexual risk behaviours) were related to testing. Men who had ever been tested for HIV were more likely to test during this study. This may indicate a habit for testing or personal attitudes and values which support testing and/or participation in research projects. Our dependent variable was 'testing during the study'. We did conduct separate analysis for those who were tested only for STIs or for blood-borne infections and also for those who were tested for both, but no other associations were found. One reason could be the very small sample size.

Despite the Internet-based questionnaire and testing sites in six larger cities in Estonia, the vast majority of participants were still from larger cities: the capital city, Tallinn, and surrounding Harju county (population 430,000) and the second largest city, Tartu (population size 99,500), as in previous studies [8-11]. Also, most of the MSM tested were from Tallinn (n=57; 84%), eight men were from Tartu and three from other regions. It may be related to the fear of being identified as gay or testing for STIs in general in smaller communities. The proportion of gay people in smaller communities may be very low, as many gay people may choose to move to the capital city, where they can be more anonymous and also experience less stigma.

The sample size for testing (n=68) was comparable with the previous studies [7,18]. As time and resources are at a premium in case of limited resources for active surveillance, we consider that one of the advantages of our approach lay in using the existing laboratory network. Thus we avoided the costs related to setting up special study sites and engaging personnel (as was the case with RDS and venue-based studies). The self-collection of urine samples worked well: all samples sent to the laboratory were suitable for processing. We received no complaints from the participants. The vast majority (91%) were tested within one month of answering the questionnaire.

We detected one case each of gonorrhoea and chlamydia (not LGV). No LGV cases have yet been reported in Estonia [3]. The limitation of our project was STI testing only from urine samples, so possible rectal and pharyngeal STI cases were missed.

HAV antibody prevalence among non-vaccinated men was 32%. This prevalence rate is in accordance with the previous studies. According to Tefanova and colleagues [23], the prevalence of hepatitis A among 20–29 year olds in Estonia was 41%. According to the World Health Organization, the proportion of people in eastern Europe who are immune to hepatitis A by the age of 40 years is 75% [24].

Self-reported HIV prevalence was 4%, and 7% of the men who were tested for HIV during the study were found to be positive. Both rates are somewhat higher than in previous studies [6,18]. Unfortunately, our sample size was too small for us to make definite conclusions about HIV trends among MSM in Estonia. However, the data on self-reported sexual behaviours show that many participants take risks, and so there is a possibility for further spread of HIV and other STIs among MSM.

MSM are not a priority group for HIV prevention in Estonia. The Internet, which provides a useful venue for delivering HIV/STI prevention and safer sex messages to MSM, could be better used, especially since gay-oriented bars, clubs and saunas (where condoms and lubricants are provided for free) only reach MSM in Tallinn and those MSM who are most likely to be open about being gay [5]. Considering that there are no gay-friendly sexual health services in Estonia, the system we have developed may be exploited in the future as an alternative venue for anonymous and free-of-charge STI and blood-borne infection testing among MSM. It could be further expanded by including sample kits for rectal and pharyngeal swabs, and also HIV home-test kits (currently not available in Estonia).

Limitations

One limitation of this study is that it was cross-sectional and we used a non-random sample. People who may have been more likely to participate include those with better-than-average access to the Internet, those who were more comfortable with technology, and those who were interested in free testing. The data were self-reported, and social desirability as well as recall bias may have been involved. In order to secure the anonymity of our participants we did not collect IP addresses, and so it was possible for one person to submit two or more questionnaires.

Conclusions

Linking Internet-based behavioural data collection with biological sample collection is a promising approach for studying hard-to-reach populations and merits further development. Further research is needed to determine the characteristics of people who opt to test in such studies and thereby the representativeness of the prevalence data. Considering the high prevalence of risk behaviours and low testing rates, higher priority to MSM sexual health should be given when planning HIV/STI prevention strategies.

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Conflict of interest

None declared.

Authors' contributions

KR, LL and JJ designed the study. KR supervised the data collection. KR and LL designed the data analysis and LL conducted the statistical analysis. KR wrote the first draft of the manuscript. All of the authors contributed to the final version of the manuscript. All of the authors read and approved the final manuscript.

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Anal human papillomavirus and HIV: A cross-sectional study among men who have sex with men in Moscow, Russia, 2012–2013

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Anal human papillomavirus (HPV) is prevalent among men who have sex with men (MSM), but has not been studied in the Russian Federation. A cross-sectional survey and HPV genotyping were conducted among HIV seropositive (n=58) and seronegative MSM (n=65) in Moscow. Multivariable logistic regression was performed to identify correlates of infection with oncogenic HPV genotypes 16 and/or 18 (HPV 16/18). Forty per cent (49/124) of all MSM were infected with at least one anal HPV genotype, 31.5% (39/124) had HPV16/18, and 11.5% (14/121) had high-grade squamous intraepithelial lesions (HSIL). HPV 16/18 was more prevalent in HIV seropositive than seronegative men (24/58, 41.4% vs 15/65, 23.1%; p=0.03). HIV infection was independently associated with HPV 16/18 (adjusted odds ratio (AOR): 5.08; 95% confidence intervals (CI): 1.49–17.34, p=0.01), as was having 2–4 steady male sex partners in the last year (vs ≤ 1 partner; AOR: 6.99; 95%CI: 1.94–25.24, p<0.01). History of prison/detention, migration to/within Russia and use of incompatible lubricants were marginally associated with HPV 16/18 (p<0.10). Comprehensive prevention options are needed to address HIV and HPV infection among MSM in Russia and may benefit from inclusion of young men in piloted HPV vaccination programmes.

Introduction

Globally, men who have sex with men (MSM) have the highest prevalence of human papillomavirus (HPV), high-grade anal dysplasia (pre-cancer) and anal squamous cell cancer (ASSC), compared with other risk groups [1]. The presence of high-risk (HR) HPV (types 16 and 18) in particular is closely associated with the progression from low-grade squamous intraepithelial lesions (LSIL) to high-grade SIL (HSIL) and also with ASSC [2–4]. This prevalence and incidence is more common in MSM infected with HIV [2,5]. In particular, there is an increased prevalence of HPV infections among MSM living with HIV, with a 35.4% pooled HPV 16 prevalence and anal cancer incidence of 45.9 per 100,000 HIV-infected men, as estimated by a recent meta-analysis [4]. Comparatively, in that same meta-analysis, HPV 16 prevalence was estimated to be 12.5% in HIV-uninfected men, with an anal cancer incidence of 5.1 per 100,000 men [4]. Evidence also suggests increased risk for HIV acquisition during infection with oncogenic HPV and persistent HPV infection is more common among men living with HIV compared with uninfected men [6].

Most epidemiological data on HPV in MSM is from North America, western Europe, and Oceania [4]. While recent epidemiological investigations have demonstrated high-risk sexual behaviours and up to 15% HIV prevalence among Moscow-based MSM, substantially higher than the 1% prevalence in the general adult population, HPV infection has not been a focus of research or public health surveillance among MSM in the Russian Federation [7–11]. Currently, estimates of the proportion of anal cancers that may be attributable to HPV in eastern Europe and central Asia are currently unavailable. Other modelling estimates from the Statistical Office of the European Union (Eurostat), however, suggest that of 72,694 new cancer cases each year among European men, 17,403 of these could be attributable to HPV and 15,497 attributable to high-risk HPV genotypes [12]. Approximately 30% of all new annual European cancer cases attributable to HPV16/18 are estimated to occur in men [12].

In light of the lack of information on anal HPV infection among MSM and potential co-infection among those living with HIV in the Russian Federation, this study aimed to explore the existence of anal HPV infection among HIV seronegative and seropositive MSM as well as correlates of infection with oncogenic HPV genotypes 16 and/or 18. Nested within a large epidemiological study of HIV among MSM in Moscow, circulating anal HPV genotypes, anal dysplasia, and other sexually transmitted infections (STIs) among HIV seropositive and seronegative MSM were evaluated.

Methods

Study population and site

Between January 2012 and January 2013, HIV seropositive and seronegative men (n=124) were enrolled from a pool of participants enrolled in a larger cross-sectional study of homosexual, bisexual and other MSM based in Moscow. This parent study also sought to compare the efficiencies of respondent-driven sampling (RDS) and Internet-based sampling (IBS) methods for recruiting MSM for HIV testing and counselling. Eligibility criteria for the parent study included adult men (age › 18 years) who reported anal sex with another man in the last 12 months.

Parent study participants were sampled via RDS and IBS, surveyed, and completed rapid HIV and syphilis testing. Briefly, RDS is a chain recruitment method often used to achieve representative samples of hard-to-reach populations [13]. Recruitment began with three purposively-selected 'seeds' who were each provided with four study-specific coupons with which to recruit peer MSM from their social network into the study. Seeds were recruited from the pool of MSM who were involved in local HIV prevention programmes or had participated in prior formative research and were selected to represent a range of individual characteristics. Individuals who were recruited by seeds were assessed for eligibility, consented, and enrolled in the study. At completion of study activities, participants were then provided with three study coupons for further recruitment of peers, constituting a new wave of recruitment. This process continued and 31 waves of participants were ultimately enrolled. A full description of traditional RDS methodology can be found elsewhere [14]. RDS was conducted in Moscow between October 2010 and April 2013 while IBS recruitment took place from late October 2010 to November 2012. IBS recruitment was conducted through banner ads posted on dating websites for MSM, including *Qguys*, *Parniplus*, and *Bluesystems.ru*. When clicked, banner ads linked interested viewers to an online consent form and a brief 10-item online quiz to obtain information on sociodemographic characteristics, sexual identity, and sexual practices. No personal identifiers or IP addresses were obtained from participants. Participants who were preliminarily deemed eligible for the full study, based on online quiz responses, were then directed to a study information page. Participants from both IBS and RDS were provided with the study telephone number via webpage or coupon, respectively, and advised to call to schedule an appointment. All procedures from the appointment onward were the same for RDS and IBS participants.

Participants who completed parent study activities, which included an interviewer-administered survey and HIV and syphilis rapid and confirmatory testing, were assessed for eligibility to participate in a nested HPV sub-study. Because the of the small sample size and the primary interest of identifying circulating HPV genotypes, eligibility for the sub-study was limited to those who self-reported inconsistent condom use during receptive anal sex (last 12 months) to ensure that men who are at risk of HPV infection were included in the sub-study. The HPV sub-study targeted enrolment to relatively equal samples of participants by HIV serostatus. Research activities were conducted in a private health clinic that is known to be accepting of MSM and activities were implemented by a local non-governmental organisation, AIDS Infoshare, which has a history of HIV research with key populations. All activities were conducted in the Russian language and all data collection and testing was anonymous. Remuneration for participation in the sub-study was RUB 2,000 (approximately EUR 50).

Survey measures

As part of the parent study, all participants were asked to complete an anonymous, interviewer-administered, structured survey to capture information on demographics, history of HIV and STI prevention and service use; sexual behaviours with men and women, including anal/oral/vaginal sex; number of sexual partners and partner characteristics; transactional sex (purchased or sold); and substance use. Sexual behaviour measures were adapted from the United States Centers for Disease Control and Prevention (CDC)'s National Health Behavior Survey [15]. Participants who reported past diagnosis of HIV infection were asked additional questions about HIV care and treatment. Additional sexual behaviour questions were asked of HPV sub-study participants to determine if any items had been placed in the anal canal within the last 24 hours, such as douching, use of sex toys, and anal sex, that might impair tests or result in indeterminate results. Computer-based surveys were administered by trained AIDS Infoshare interviewers and time for survey completion ranged from 60 to 90 minutes.

Biological sampling and testing

MSM were tested for HIV and syphilis infection within the parent study; these procedures have been described elsewhere [7]. Briefly, syphilis infection was measured with Lues rapid plasma reaction (RPR) (Nearmedic Plus, Moscow, Russia) and those samples testing positive for syphilis were confirmed with Lues RPGA test (Nearmedic Plus, Moscow, Russia). HIV testing used Determine HIV-1/2 test (Abbott Laboratories, Abbott Park, IL, US) rapid tests. Samples from those

Table 1

Demographic characteristics of Moscow-based men who have sex with men, stratified by HIV serostatus, cross-sectional study, Moscow, Russia, January 2012–January 2013 (n=123)

	HIV seronegative (n=65)		HIV seropositive (n=58)		p value	Total	
	n	Col %	n	Col %		n	Col %
Age (years)					0.03		
‹25	24	36.9	10	17.2		34	27.6
25 to 29	20	30.8	17	29.3		37	30.1
30 to 35	10	15.4	20	34.5		30	24.4
›35	11	16.9	11	19.0		22	17.9
Place of birth					0.60		
Russia	56	86.2	48	82.8		104	84.6
Outside Russia	9	13.8	10	17.2		19	15.4
Moved to or within Russian Federation for work (n=122)					0.42		
No	41	64.1	33	56.9		74	60.7
Yes	23	35.9	25	43.1		48	39.3
Sexual identity					0.65		
Homosexual	44	67.7	37	63.8		81	65.9
Bisexual	21	32.3	21	36.2		42	34.1
Ever married to a woman					0.29		
Never	59	90.8	49	84.5		108	87.8
Past/current marriage	6	9.2	9	15.5		15	12.2
Number of dependents					0.17		
1	43	66.2	38	65.5		81	65.9
2 to 3	22	33.8	17	29.3		39	31.7
≥4	0	0.0	3	5.2		3	2.4
Education (level completed)					0.99		
Primary education	1	1.5	1	1.7		2	1.6
Secondary education	17	26.2	13	22.4		30	24.4
Specialised secondary education (diploma)	21	32.3	18	31.0		39	31.7
Undergraduate education	6	9.2	6	10.3		12	9.8
Higher education	20	30.8	20	34.5		40	32.5
Employment categories (n=121)					0.50		
Full-time	31	49.2	26	44.8		57	47.1
Part-time	26	41.3	22	37.9		48	39.7
Student only	3	4.8	2	3.4		5	4.1
Other, including retired, disabled	0	0.0	1	1.7		1	0.8
Unemployed	3	4.8	7	12.1		10	8.3
Income level					0.22		
Poverty	2	3.1	5	8.6		7	5.7
Low	37	56.9	25	43.1		62	50.4
Middle	25	38.5	28	48.3		53	43.1
High	1	1.5	0	0.0		1	0.8
Usual healthcare provider (n=117)					0.73		
Private only	18	29.0	12	21.8		30	25.6
Public and private/other	11	17.7	9	16.4		20	17.1
Public only	32	51.6	32	58.2		64	54.7
Other only	1	1.6	2	3.6		3	2.6

Col: column.

Table 2

HPV and anal cytology results among MSM in Moscow, Russia, stratified by HIV serostatus (n=123)

	HIV seronegative (n=65)		HIV seropositive (n=58)		p value	Total	
	n	Col %	n	Col %		n	Col %
Anal cytology results (n=120)					0.81		
Normal	57	87.7	49	89.1		106	88.3
HSIL	8	12.3	6	10.9		14	11.7
Infection with HPV genotype							
6[a] (ref: no)	7	10.8	13	22.4	0.08	20	16.3
11 (ref: no)	4	6.2	4	6.9	0.87	8	6.5
16 (ref: no)	9	13.8	11	19.0	0.44	20	16.3
18[b] (ref: no)	4	6.2	12	20.7	0.02	16	13.0
31 (ref: no)	8	12.3	9	15.5	0.61	17	13.8
33 (ref: no)	7	10.8	5	8.6	0.69	12	9.8
Any HPV genotype[b] (ref: no)	20	30.3	29	50.9	0.04	49	39.8
HPV16/18a (ref: no)	15	23.1	24	41.4	0.03	39	31.7

Col: column; HSIL: high-grade squamous intraepithelial lesions; HPV: human papilloma virus; Ref: reference category not displayed

[a] p-value<0.10;
[b] p-value<0.05

testing positive were sent to the local reference laboratory for confirmatory testing. The clinic staff physician provided pre- and post-test HIV counselling and followed all federal protocols [16]. For the purposes of the HPV study, participants are defined as HIV seropositive or seronegative, based on confirmatory study results.

Participants of the HPV sub-study provided additional biological specimens for testing for urethral, oral, and rectal gonorrhoea and chlamydia, as well as for anal cytology and anal HPV genotyping. All specimens for the sub-study were collected by the same study physician and transferred daily for laboratory analysis by a local reference laboratory (Lages Laboratory, Moscow, Russia).

Anorectal specimens were first collected for anal cytology (Papanicolaou (Pap) test) to detect HPV-associated anal dysplasia and followed by anorectal specimen collection for HPV genotyping. Both specimens were collected by inserting a saline-moistened polyester swab into the anal canal into the rectum to ensure sampling of the anorectal transition zone. The swab was rotated slowly during withdraw to capture cells. HPV testing of swabbed cellular material was conducted at the reference laboratory using PCR for amplification of a fragment of the L1 gene to detect the following HPV genotypes: 6, 11, 16, 18, 31, and 33.

Rectal specimens to test for gonococcal and chlamydial infection were then collected by polyester swab inserted at least 2 inches beyond the anal margin and withdrawn in a rotating motion. Participants had the option to provide urethral swabs or urine specimen collection to test for urethral gonococcal and chlamydial infection. The local reference laboratory analysed swabs and urine specimens for gonococcal and chlamydial infection using nucleic acid amplification tests (DiaGen, Moscow, Russia).

All tests, except those for HPV, were performed within 2–3 days of collection, so that participants could be informed of their test results and provided with treatment according to national treatment standards for genital warts, gonorrhoea, syphilis, and chlamydia. Treatment was provided by the study clinic. Participants who screened positive for anal dysplasia by cytology were provided with referrals to the Institute of Proctology in Moscow, where the participant could receive specialised care. Participants with HPV infection, with exception of those with HPV-related genital warts, were not informed of HPV test results as testing was conducted in batches and no treatment was available for men.

Statistical analysis

Descriptive analyses were conducted to estimate the distribution of HPV genotypes, STIs, behavioural characteristics, sexual health history, and use of antiretroviral therapy (ART). Bivariate analysis was used to compare distributions of HPV genotypes among participants with and without HIV infection as well as to compare distributions of characteristics of participants with and without HPV 16/18 infection. HPV 16 and 18 were the focus of this analysis due to the attribution of HPV 16 or 18 to most anal cancers and the inclusion of these genotypes in the quadrivalent vaccine. Chi-squared tests were used to evaluate statistical significance in bivariate analysis. HIV status, known confounders (such as age), and variables that test at least

Table 3A

Distribution of demographic and sexual behaviour characteristics among men who have sex with men in Moscow, Russia, by oncogenic human papilloma virus infection (n=124)

	No HPV 16/18 infection (n=95)		HPV 16/18 infection (n=29)		p value	Total	
	n	Col %	n	Col %		n	Col %
Demographics					0.81		
Age, years					0.14		
‹25	30	31.6	4	13.8		34	27.4
25–29	25	26.3	12	41.4		37	29.8
30–35	21	22.1	9	31.0		30	24.2
›35	19	20.0	4	13.8		23	18.5
Born in Russia (ref: born outside of Russia)	82	86.3	23	79.3	0.36	105	84.7
Homosexual identity (ref: bisexual)	61	64.2	21	72.4	0.41	82	66.1
Ever married to a woman (ref: never)	12	12.6	3	10.3	0.74	15	12.1
Moved to or within Russian Federation for work (n=123; ref: no)[a]	32	33.7	16	57.1	0.03	48	39.0
Usual healthcare provider (n=118)[b]					0.07		
Private only	24	26.7	6	21.4		30	25.4
Public and private/other	12	13.3	8	28.6		20	16.9
Public only	53	58.9	12	42.9		65	55.1
Other only	1	1.1	2	7.1		3	2.5
Lifetime history of prison/detention (ref: no)[a]	5	5.3	7	24.1	0.01	12	9.8
Sexual behaviours							
Ever disclosed sexual identity/ behaviour to others (n=121; ref: no)	70	75.3	25	89.3	0.11	95	78.5
Age of first sex (n=122)					0.73		
‹=18	61	64.9	16	57.1		77	63.1
19–25	31	33.0	11	39.3		42	34.4
›25 yrs.	2	2.1	1	3.6		3	2.5
No. of male sexual partners (last 12 months)					0.58		
One or less	16	16.8	4	13.8		20	16.1
2 to 4	20	21.1	4	13.8		24	19.4
5 or more	59	62.1	21	72.4		80	64.5
No. of steady male partners (last 12 months) [a,c]					0.02		
One or less	60	64.5	13	48.1		73	60.8
2 to 4	20	21.5	13	48.1		33	27.5
5 or more	13	14.0	1	3.7		14	11.7
Received money/goods for sex (last 12 months; n=118; ref: no)	36	39.1	8	30.8	0.44	44	37.3
Paid money/goods for sex (last 12 months; n=118; ref: no)[a]	24	26.7	2	7.1	0.03	26	22.0
Use alcohol or drugs before sex (last 12 months; n=120)					0.27		
Alcohol only	59	63.4	18	66.7		77	64.2
Drugs only (including poppers)	1	1.1	2	7.4		3	2.5
Both alcohol and drugs (including poppers)	19	20.4	4	14.8		23	19.2
Neither	14	15.1	3	11.1		17	14.2
Incompatible lubricant used during sex (n=121; ref: Compatible)[b]	36	38.7	16	57.1	0.08	52	43.0

ART: antiretroviral therapy; *C. trachomatis*: *Chlamydia trachomatis*; Col: column; HPV: human papilloma virus; HSIL: high-grade squamous intraepithelial lesions; *N. gonorrhoeae*: *Neisseria gonorrhoeae*; Ref: reference category not displayed.

[a] p-value‹0.05

[b] p-value‹0.10

[c] Steady partner was defined as 'another man whom you consider to be your boyfriend or partner and to whom you are most committed.'

Table 3B

Distribution of demographic and sexual behaviour characteristics among men who have sex with men in Moscow, Russia, by oncogenic human papilloma virus infection (n=124)

	No HPV 16/18 infection (n=95)		HPV 16/18 infection (n=29)		p value	Total	
	n	Col %	n	Col %		n	Col %
Sexually transmitted infections, HIV serostatus and treatment							
HSIL (n=121; ref: normal)[a]	7	7.6	7	24.1	0.02	14	11.6
Positive rectal *N. gonorrhoeae* results (n=124; ref: negative)	4	4.2	3	10.3	0.21	7	5.6
Positive urine/urethral *N. gonorrhoeae* results (n=123; ref: Negative)	1	1.1	0	0.0	0.58	1	0.8
Positive rectal *C. trachomatis* results[a] (n=124; ref: negative)	6	6.3	6	20.7	0.02	12	9.7
Positive urine/urethral *C. trachomatis* results (n=122; ref: Negative)	5	5.3	2	7.1	0.72	7	5.7
Positive syphilis results (n=123; ref: negative)	13	13.7	7	24.1	0.36	20	16.1
HIV seropositive (n=123; ref: negative)[a]	39	41.5	19	65.5	0.02	58	47.2
Last CD4 count (among 7 HIV seropositive men who had ever had a CD4 test)					0.65		
>500 cells/µL	1	25.0	1	33.3		2	28.6
200 –500 cells/µL	2	50.0	2	66.7		4	57.1
<200 cells/µL	1	25.0	0	0.0		1	14.3
Currently on ART (n=11; ref: no)	2	33.3	2	40.0	0.82	4	36.4

ART: antiretroviral therapy; *C. trachomatis*: *Chlamydia trachomatis*; Col: column; HPV: human papilloma virus; HSIL: high-grade squamous intraepithelial lesions; *N. gonorrhoeae*: *Neisseria gonorrhoeae*; Ref: reference category not displayed.

[a] p-value<0.05

[b] p-value<0.10

[c] Steady partner was defined as 'another man whom you consider to be your boyfriend or partner and to whom you are most committed.'

marginally significant in bivariate analysis (p<0.10) were used to construct a multivariable logistic regression model to identify independent factors associated with infection with HPV 16/18. Statistical significance was set at p<0.05 and marginal significance at p<0.10. Sensitivity analyses were conducted to evaluate the associations with HPV 16/18 when the comparison group comprised only those with no HPV infection of any kind. Data were not weighted for RDS network size during modelling, given that participants of this sub-study were selected on the basis of HIV status and using both RDS and IBS sampling methods. All statistical analyses were conducted using Stata version 12 (StataCorp, College Station, TX, USA).

Research ethics

The study was conducted in partnership with a local non-governmental organisation, AIDS Infoshare, and approved by both the Ethics Committee of the State Medical University, IP Pavlov, Saint Petersburg, Russia and the Johns Hopkins Bloomberg School of Public Health Institutional Review Board, Baltimore, Maryland, USA.

Results

Final enrolment of HPV sub-study participants included 124 MSM, of whom 58 were HIV-seropositive, and 65 HIV seronegative, based on confirmatory testing, and one with indeterminate HIV test results. Four participants who reported a past diagnosis of HIV, tested positive by rapid test, and declined further confirmatory testing were included among the sample of HIV-seropositive participants. One participant provided only a rapid test, which was negative, but had reported a past diagnosis of HIV infection. This participant's HPV and behavioural data were included in the analysis, but HIV status was considered indeterminate for this analysis. No indeterminate HPV results were returned for any of the 124 sub-study participants. Three participants had indeterminate anal cytology results, yielding a final anal cytology sample of 121.

Table 1 presents demographics and select sexual practices of participants in the sub-study, stratified by HIV serostatus. Overall, participants had a median age of 29 years (range: 19–50 years) though HIV-seropositive participants tended to be slightly older, compared with seronegative participants (p=0.03). No other differences across HIV serostatus existed among collected demographic characteristics.

All evaluated HPV types were present among study participants and 39.5% (49/124) were diagnosed with infection by at least one HPV genotype. Table 2 presents HPV diagnoses among MSM participants, stratified by HIV serostatus. Infection with any HPV genotype was higher among HIV seropositive men (29/58; 50.0%) compared with seronegative men (20/66, 30.3%; p=0.04). Some 41.4% (24/58) of seropositive men were identified with HPV 16/18 compared with 23.1% among seronegative men (15/65; p=0.03).

Table 4*

Crude and adjusted associations of demographic and sexual behaviour characteristics with human papilloma virus 16/18 infection among men who have sex with men in Moscow, Russia (n=124)

	Crude analysis				Adjusted analysis[a]			
	OR	95% CI		p value	AOR	95% CI		p value
Demographics								
Moved to or within Russian Federation for work (n=123)[b,c]								
No	Ref				Ref			
Yes	2.63	1.11	6.21	0.03	3.18	1.00	10.09	0.05
Usual healthcare provider (n=118)[d]								
Private only	Ref							
Public and private/other	2.67	0.75	9.45	0.13				
Public only	0.91	0.30	2.70	0.86				
Other only	8.00	0.62	103.67	0.11				
History of prison/detention[b,e]								
No	Ref				Ref			
Yes	5.66	1.64	19.55	0.01	6.53	0.85	50.42	0.07
Sexual behaviours								
No. of steady male partners (last 12 months) [b,c,f]								
One or less	Ref				Ref			
2 to 4	3.00	1.20	7.53	0.02	6.99	1.94	25.24	P<0.01
5 or more	0.36	0.04	2.96	0.34	0.14	0.01	2.09	0.16
Purchased sex (last 12 months; n=118)[b,e]								
No	Ref				Ref			
Yes	0.21	0.05	0.96	0.04	0.23	0.04	1.26	0.09
Type of lubricant used during sex (n=121)[d,e]								
Condom compatible	Ref				Ref			
Incompatible	2.11	0.90	4.97	0.09	2.84	0.86	9.44	0.09
Sexually transmitted infections								
Rectal *C. trachomatis* results[b]								
Negative	Ref				Ref			
Positive	3.87	1.14	13.12	0.03	3.17	0.67	14.90	0.15
HIV diagnosis (n=123)[b,c]								
Seronegative	Ref				Ref			
Seropositive	2.68	1.12	6.39	0.03	5.08	1.49	17.34	0.01

AOR: adjusted odds ratio; *C. trachomatis: Chlamydia trachomatis*; CI: confidence intervals; OR: odds ratio.

[a] The final model included HIV status, rectal Chlamydia infection, migration to/within Russia, lifetime history of detention in prison, number of steady male sex partners, type of lubricant typically used during anal sex with men (condom compatible v. incompatible), and age (continuous); Dependent variable reference group is no HPV 16/18 infection;

[b] Crude analysis p-value for total variable<0.05;

[c] Adjusted analysis p-value for total variable<0.05;

[d] Crude analysis p-value for total variable <0.10;

[e] Adjusted analysis p-value for total variable <0.10;

[f] Steady partner was defined as 'another man whom you consider to be your boyfriend or partner, to whom you are most committed.'

HPV genotypes among HIV seropositive MSM demonstrated slightly different patterns and prevalence compared with HIV seronegative men. Among the total sample, prevalence of HSIL was 11.7%, with no difference by HIV serostatus (p=0.81).

Table 3 presents the distribution of sexual and health behaviours among participants with and without HPV 16/18 infection. Participants were similar across most demographic characteristics. Among those with HPV 16/18, over 57.1% (16/28) had moved within or into Russia for work, compared with 33.7% of those without HPV 16/18 (32/95; p=0.05). Likewise, 24.1% (7/29) of those with HPV 16/18 infection had a lifetime history of detention or prison, compared with 5.3% of those without HPV 16/18 (5/94; p=0.01). Differences were observed across some sexual behaviours. Higher proportions of MSM with HPV 16/18 tended to report greater numbers of steady male sexual partners than those without HPV 16/18 infection (p=0.02), although the total numbers of male sexual partners in the last 12 months did not differ by HPV infection. Over half of

MSM with HPV 16/18 infection (57.1%; 16/28) reported the use of a condom-incompatible lubricant or no lubricant (incompatible lubricants are those which are not water- or silicon-based, including oils and lotions), which was marginally higher than those without infection (36/93; 38.7%; p=0.08). HSIL (p=0.02) and rectal infection with *Chlamydia trachomatis* (p=0.02) were associated with HPV 16/18 infection HSIL was present among 24.1% (7/29) of participants with HPV 16/18 infection, compared with 7.6% of those without HPV16/18 (7/92; p=0.02). In the sensitivity analysis (data not shown) with a comparison group of those without any HPV infection, patterns of association were similar to those in Table 3.

Table 4 presents crude and adjusted associations with HPV 16/18 infection. HIV infection was independently associated with HPV 16/18 infection (adjusted odds ratio (AOR): 5.08; 95% confidence intervals (CI): 1.49–17.34; p=0.01), as was having 2–4 steady male sex partners in the last year (vs ≤ 1; AOR: 6.99; 95% CI: 1.94–25.24; p<0.01). History of prison or detention (AOR: 6.53; 95% CI: 0.85–50.42; p=0.07), use of incompatible lubricants (AOR: 2.84; 95% CI: 0.86–9.44; p=0.07), and migration to/within Russia (AOR: 3.18; 95% CI: 1.00–10.09; p=0.05) were marginally associated with HPV 16/18. Rectal infection with C. trachomatis was no longer associated with HPV 16/18 after adjustment for other variables, though the magnitude of the odds ratio suggests potential association. In the sensitivity analysis (data not shown) for the crude and adjusted logistic regression, HIV infection, rectal *C. trachomatis* infection, history of moving to/within the Russian Federation, having 2–4 steady male partners were independently associated with HPV16/18.

Discussion

HPV, particularly its oncogenic genotypes, is prevalent among this sample of Moscow-based MSM and more common among those living with HIV infection. All tested genotypes were detected among the total sample, with 41.2% infected with at least one HPV genotype, the majority of which were comprised of HPV 16 or 18 genotypes. To a lesser degree, HSIL was also identified among this sample. HPV 16/18 infection was significantly or marginally associated with structural factors, sexual behaviours, and individual biological factors. In this context, HIV infection may act as a biological factor for HPV infection, as well as serving as a marker for sexual risk. While rectal *C. trachomatis* infection was not significant after inclusion in the full model, the magnitude of the odds ratios suggests that such infections may be related to HPV 16/18, which is consistent with studies in other settings [17]. These data represent the first data on HPV and anal dysplasia in MSM from the Russian Federation, as well as the wider EECA Region.

Consistent with other research of HPV in MSM, HPV 16/18 was associated with individual sexual behaviours [3,18]. In this study, HPV was specifically associated with higher numbers of steady male sexual partners in the last 12 months. While there was no difference across the total numbers of sex partners within the last 12 months, the association with the number of steady partners may actually reflect the sexual relationships where condoms are most inconsistently used, given that condoms tend to be used more consistently during relationships with new partners [9,19]. Additionally, increased numbers of steady partners among MSM with HPV 16/18 infection may reflect more transient relationships and greater risk behaviour among this subgroup. HPV 16/18 was also associated with regular use of lubricants that are incompatible with latex condoms. Oil-based lubricants or other methods of lubrication (such as body lotion) have been shown to degrade latex condoms during use, potentially facilitating exposure to HPV infection during anal intercourse [20]. Simple interventions that improve condom use with all sexual partners and increase use of condom-compatible lubricants may reduce HPV transmission, as well as HIV and other STIs.

Several structural factors were marginally associated with HPV 16/18. These factors included history of detention in prison and migration to or within the Russian Federation. These may be markers of exposures to new networks in which HPV and/or HIV may be prevalent (e.g. among MSM networks in prison or in a new city) or may reflect low access to prevention methods for HIV/STI [9,21]. In the absence of data on HPV in Russia or EECA, understanding of HPV transmission related to these structural factors may be derived from research on HIV and other STI. An Internet survey conducted among MSM in 38 European countries in 2010 found that around 65% of Russian men had received information about how STIs can be transmitted during same-sex practices and only 50% had accessed HIV prevention programmes. These indicators for information and access to HIV prevention were below the median estimates for their European counterparts [22]. For those detained in prison/detention or who are new migrants, access to information and prevention methods may be even more limited [23]. Condoms and other HIV prevention methods are not available within prisons or detention facilities in Russia, despite evidence of exposure opportunities and transmission within prisons in Russia and wider EECA countries [24,25]. During detention, HIV, HPV and other STI transmission may occur through consensual same sex behaviours, rape or other non-consensual practices, and HIV exposure through shared syringes among those who inject drugs [24]. Outside of prison or detention, access to public healthcare is limited by the propiska-like system that requires individuals to be registered and hold documentation for their city of residence. For migrant populations, including internal migrants, this limits access basic HIV and STI prevention [23,26]. In other European countries, migration status has been associated with increased prevalence of HIV and STI infection [27].

Findings should be viewed in light of several limitations. First, this was a small, cross-sectional study to explore circulating HPV and oncogenic HPV genotypes among MSM in Moscow, Russia; thus, this small sample size limits statistical power and broader inferences. Selection on the basis of HIV status and self-reported inconsistent condom use may bias the estimates of HPV prevalence. Consistent with other socio-behavioural surveys, additional bias may be introduced with the length of the survey and/or selection bias associated with presenting to the study clinic for participation and participant incentives. As such, these data are not intended to provide prevalence estimates for the country or Moscow city, but provide insight into anal HPV infection among Moscow-based MSM and circulating genotypes. Findings from the multivariable analysis are informative for future research, but the generalisability may be limited by the small sample and non-random sampling method and should be interpreted with caution. Studies with larger samples and prospective analyses are needed to fully understand correlates or predictors of HPV infection among Russian MSM. Data were not collected on smoking duration or dose, which is a known risk factor for progression to HSIL and is relevant in Russia where smoking remains very common [3]. As this was a cross-sectional study, longitudinal data on anal clearance rate of the different HPV types or persistence of infection were not collected and further research is warranted, as persistence has been significantly greater for persons living with HIV, compared with those who are uninfected [6,18].

Interventions to reduce HPV transmission among MSM in the Russian Federation are warranted. Both the quadrivalent and bivalent vaccines have demonstrated efficacy against oncogenic HPV-vaccine-type infections in MSM and other men [28]. Modelling estimates have taken such findings further and estimated an 86% reduction in HPV 16/18-related carcinomas among men in Europe with implementation of vaccination of girls and boys vs screening alone [29]. Relative to a female-only programme, vaccination of both genders has demonstrated a greater reduction in male and female HPV-related carcinomas [29]. The quadrivalent HPV vaccine has been licensed for use in Russia and is being tested in school-based, pilot programmes for adolescent girls in four Russian cities, including Moscow, though regional experts have recommended inclusion of boys in vaccination campaigns [30,31]. While HIV prevention programmes for MSM in the Russian Federation are limited by stigmatization and laws ban 'homosexual propaganda', equitable HPV vaccination programmes for young men and women in the country may impart benefit without requiring disclosure of sexual preferences [32, 33]. Research from North American settings also support the use of anal Pap screening among MSM as an acceptable means of secondary prevention, though cost-effectiveness analyses have yielded mixed results [34,35].

Prevention of HPV infection among MSM in the Russian Federation — and ultimately prevention of HSIL — may rely on basic tenets of HIV prevention: condom distribution and ART treatment for those living with HIV. Enabling access to and encouraging use of appropriate condoms and compatible lubricants with all partners during anal intercourse provides protective barriers against HPV acquisition in the absence of other HPV prevention methods. Given that ART has also demonstrated protective benefits against oncogenic HPV, in addition to preventing onward transmission of HIV, HIV testing and access to ART care for MSM who are living with HIV remain critical [36,37]. As resources for HIV prevention among key populations in the Russian Federation become limited, programmes that are comprehensive and address multiple STIs, including HIV and HPV, and facilitate engagement with HIV care, may be most efficient and promising for protecting health of Russian MSM.

* Erratum:

The title of Table 4 was corrected on 28 April 2015.

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Conflict of interest

None declared.

Authors' contributions

CB, AW, CZ, NG, VM, AP, and CL collaborated in the design and oversight of the overall study. RC, IM, and AD provided additional expertise into the design and analysis of the HPV sub-study. IK and PD coordinated local study implementation and conducted data collection. AW wrote the initial drafts of this manuscript. AW conducted the statistical analysis and composed the initial draft of the paper. All authors had full access to the data, reviewed and edited the manuscript, and all take responsibility for its integrity as well as the accuracy of the analysis.

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A systematic review of evidence to inform HIV prevention interventions among men who have sex with men in Europe

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An estimated 42% of all newly diagnosed HIV cases in Europe in 2013 were transmitted during sex between men. This review was performed to identify and describe studies evaluating the efficacy and effectiveness of HIV prevention interventions among men who have sex with men (MSM), in relation to implementation data from European settings. A systematic search was performed individually for 24 interventions. Data were extracted from studies including efficacy or implementation data from European settings, appraised for efficacy, implementation and plausibility, and assigned a grade (1-4) according to the Highest Attainable Standard of Evidence (HASTE) framework. Four interventions (condom use, peer outreach, peer-led groups, and using universal coverage of antiretroviral treatment and treatment as prevention) were assigned the highest HASTE grade, 1. Another four interventions were assigned 2a for probable recommendation, including voluntary counselling and testing for HIV, using condom-compatible lubricant, using post-exposure prophylaxis, and individual counselling for MSM living with HIV. In addition, seven interventions were assigned a grade of 2b, for possible recommendation. Encouragingly, 15 interventions were graded to be strongly, probably or possibly recommended. In the relatively resource-rich European setting, there is an opportunity to provide global leadership with regard to the regional scale-up of comprehensive HIV prevention interventions for MSM.

Introduction

In 2012 the global burden of HIV was estimated to include 35.3 million people living with the virus (people living with HIV, PLWH). Among adults between the ages of 15–49 years old HIV prevalence was estimated at 0.8% [1]. Globally there is a declining trend in new infections, morbidity and mortality due to HIV/AIDS [2]. Improved treatment regimens and access to treatment are important factors behind these trends [2].

Gay, bisexual and other men who have sex with men (MSM) are disproportionately affected by HIV in every setting where data are available [3]. HIV rates reported among MSM show an increasing trend, in contrast to the declining trends reported in the general population [4]. A 2013 systematic review of HIV epidemiology in 33 high-income countries where data were available estimated a total of 2.3 million PLWH [5] and a male–female median case ratio of 2.5: 1 [5,6], indicating male-predominant epidemics. High-income countries where antiretroviral treatment (ART) and prevention services are available show increasing trends in HIV prevalence among MSM [5,7].

Of the 29,157 persons diagnosed with HIV and reported in the European Union/European Economic area (EU/EEA) in 2013, 42% of cases were estimated to be due to sex between men [8]. Since 2006, MSM represent the only key population where an increase in HIV diagnoses has been observed, with a 33% increase between 2004 and 2013 in the EU/EEA overall and with increases of more than 100% observed in some EU countries during the past decade, including Bulgaria, Cyprus, Czech Republic, Hungary, Romania, and Slovakia [9]. HIV prevalence among MSM was estimated to be at or above 5% in 14 of the 26 EU/EEA countries reporting national data in 2012 [10].

In accounting for the relatively higher rates of HIV among MSM compared with the general population, recent epidemic modelling highlights the importance of the higher transmissibility of HIV during unprotected anal intercourse (as opposed to vaginal) and the importance of insertive/receptive sexual role versatility among MSM [4,11]. Clusters of HIV transmission

indicative of outbreaks within sexual networks of MSM may also play an important role in the higher transmission probability reported [12-14].

The current picture of the HIV epidemic among MSM in Europe highlights significant variation between countries. Biological and behavioural surveillance systems vary across European countries, as do the extent of sexual health needs assessment, collaborative service planning and the availability of acceptable and accessible sexual health services [15]. Prevalence data for MSM, a population of unknown size, can be estimated in diverse ways and therefore prevalence rates may not be fully comparable between countries. Most European countries report the number of newly diagnosed cases annually [10].

Community, research, medical and public health efforts to prevent HIV have existed in Europe for over three decades, with European gay community organisations at the forefront of peer-led HIV prevention globally. However, overall national responses have been inadequate to contain HIV epidemics among MSM, with continuing high and in some countries increasing HIV incidence among MSM [5,16].

HIV prevention interventions for MSM are purposeful activities intended to increase the uptake of HIV precautionary behaviours or to reduce HIV risk behaviours. Intervention activities can target MSM directly, they can be directed to intermediaries who deliver activities to MSM, or they can influence the policy and service environment. The effectiveness of HIV prevention interventions among MSM has been assessed previously, most recently by the World Health Organization Global Guidelines process in 2010–11 [17]. In order to capture more recent data in the rapidly evolving field of HIV prevention and to ensure context-specific relevance, there was a need to update and extend the previous reviews and catalogue the evidence in order to inform MSM prevention interventions in Europe [18,19].

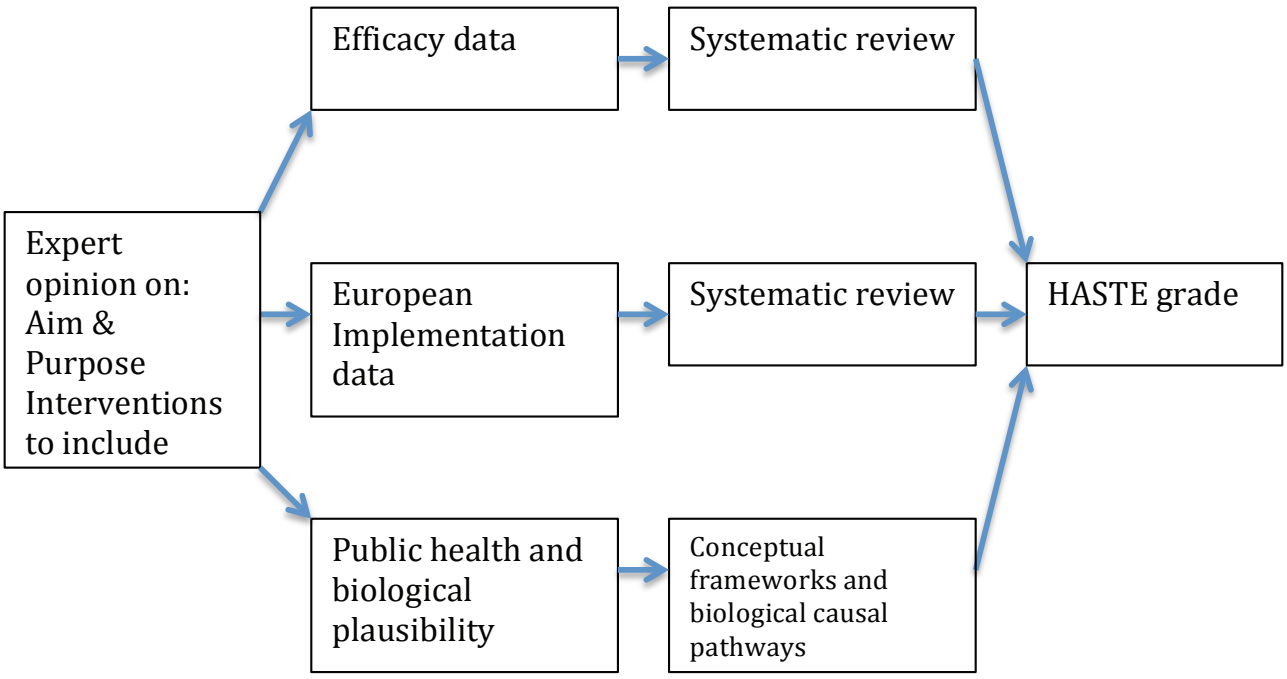
The objectives of this review were to identify and describe studies evaluating the efficacy, and effectiveness of HIV prevention interventions among MSM in relation to implementation data from the European setting, and to further appraise the evidence according to the Highest Attainable Standard of Evidence (HASTE) framework [20]. The review of evidence was performed in order to inform the development of guidance by the European Centre for Disease Control and Prevention (ECDC) to Member States on the commissioning and delivery of HIV prevention interventions to MSM in the EU/EEA [21].

Methods

In this review the term 'men who have sex with men' (MSM) refers to the population of men engaged in same-sex sexual behaviour, inclusive of sexual identities (e.g. gay, bisexual, straight, experimenting, etc.)

Figure

Work process for systematic review of HIV prevention interventions among men who have sex with men within the European setting, searches performed December 2012–February 2013



HASTE: Highest Attainable Standard of Evidence

Table 1

Highest Attainable Standard of Evidence (HASTE) system for HIV interventions[a]

Grade level		Strength of recommendation	Explanation
Grade 1		Strong	• High plausibility • Efficacy is consistent • Large body of consistent implementation data
Grade 2	Grade 2a	Conditional: probable	• Plausibility • Limited efficacy data • Consistently effective from implementation data
	Grade 2b	Conditional: possible	• Plausibility • Limited or inconsistent efficacy data • Limited or paucity of implementation data[b]
	Grade 2c	Conditional: pending	• Plausibility • Ongoing efficacy trials
Grade 3		Insufficient	• Undefined plausibility • Inconsistent data • Inconsistent or paucity of implementation data
Grade 4		Inappropriate	• Consistent data demonstrating lack of efficacy • Consensus from implementation data of inappropriate intervention

[a] Modified from [21]

[b] A modification has been made, adding paucity of implementation data to grade 2b.

and sexual desire. The term MSM includes people who identify as men, and therefore includes transgender men who have sex with men. Transgender women might share some biological risks with MSM such as receptive anal intercourse, but recent data shows a higher HIV burden in this group, indicating a different epidemic scenario [22], and therefore transgender women are not included as a sub-group of MSM in this review. We use the term MSM in this review recognising the diversity and heterogeneity of this group but also the limitations of this term.

First, we made a comprehensive list of known interventions that address primary HIV transmission among MSM, inclusive of biomedical, psychosocial, and programmatic interventions. The list was developed, discussed and agreed by an expert review group and included medical, social science and policy experts, programme implementers from non-governmental organisations and government representatives. The group was convened by the ECDC for the development of European guidelines on HIV prevention in MSM. A systematic review was performed for each intervention included (Figure 1).

Existing evidence from randomised controlled trials (RCTs) evaluating public health interventions with biological endpoints for MSM populations are limited, which highlights the need for strategies additional to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system when performing a review such as this [18-19,23]. The HASTE system builds on the GRADE system and was developed specifically to evaluate evidence regarding HIV/sexually transmitted infection (STI) interventions among most at-risk populations, in particular MSM [19]. HASTE takes into account three categories that are given equal weight: efficacy data, implementation science data and biological and public health plausibility (Table 1) [19]. Hill's criteria for causality remain the most relevant set of determinants of whether an intervention causes prevention and/or mitigation of disease in the HASTE grading system [24].

Implementation data were defined as data reporting on availability, acceptability, uptake, feasibility of implementation, implementation costs, and effectiveness of the intervention among MSM in the European setting.

Public health plausibility was defined as the intervention having a likely pathway leading to a decrease in HIV incidence. For example, HIV testing itself might not lead directly to lower HIV incidence, but it has a crucial role because it is on the pathway to uptake of ART for people living with HIV, which does decrease HIV onward transmission and HIV-related morbidity and mortality.

Search strategies

The Population, Intervention, Comparison, Outcome (PICO) model was used to develop inclusion criteria and search terms per intervention [25]. The population for the intervention was MSM. All types of comparison and no comparison were included. Outcomes included were biological markers (prevalence and incidence of HIV/STIs), self-reported diagnoses of HIV infection and self-reported behavioural outcomes on condom use or unprotected anal intercourse (UAI). Studies reporting on implementation data were only included if performed in Europe. Systematic reviews previously performed on these topics were included. Non-peer-reviewed literature was not used as a source of original

Table 2

Number of articles found through search strategies, screened and included according to inclusion criteria for HIV prevention interventions among men who have sex with men in Europe

Interventions	Articles identified through searches	Number of articles included addressing efficacy	Number of articles included addressing implementation
Condom use	130	1	3
Universal coverage of antiretroviral treatment and treatment as prevention	9	1	4
Peer-led group interventions	326	2	0
Peer outreach	326	2	0
Voluntary HIV counselling and testing	717	2	8
Condom-compatible lubricant use (when using condoms)	130	5	2
Post-exposure prophylaxis	28	3	2
Individual counselling for MSM living with HIV	327	4	2
Peer-led group interventions targeting MSM living with HIV	326	1	2
Sex venue-based interventions	25	1	8
Social marketing interventions	476	3	7
Individual counselling for MSM	327	2	1
Internet-based HIV prevention messages	40	6	4
Training for healthcare providers to provide comprehensive care for MSM	225	0	1
MSM friendly clinics	234	0	1
Voluntary anonymous partner notification	126	0	7
Voluntary medical male circumcision	49	3	2
Pre-exposure prophylaxis	4	1	0
Campaigns for lesbian, gay, bisexual and trans equality	3	0	1
Female condom use	4	3	1
Serosorting	9	3	4
Avoid ejaculation of semen orally	226	3	0
Avoiding poppers during anal intercourse	5	0	0
Reducing alcohol binge drinking among MSM	119	1	0
Total number of articles[a]	**3,865**	**47**	**60**

MSM: Men who have sex with men.

Searches were performed between 10 December 2012 and 8 February 2013.

[a] Search strategies captured the same articles to some extent.

data, but these documents did guide further searches for literature. Studies published in English, French, and Spanish were included. Studies not fitting these criteria were excluded from the review.

Electronic searches were performed in PubMed, Embase, Medline, Cinahl, PsycINFO, the Cochrane Library and the World Health Organization publication database. The search included medical subject headings (MeSH) terms for HIV or AIDS, and terms associated with MSM and the specific interventions reviewed (Annex I). Searches were particularly designed to be broad and comprehensive initially and were performed between 10 December 2012 and 8 February 2013. We reviewed the search strategies performed between 8 June 2010 and 17 March 2011 to guide the WHO's 2011 recommendations for 'Prevention and treatment of HIV and other sexually transmitted infections among MSM and transgender people', and where relevant these were updated up to 8 February 2013 [17].

Screening and data extraction

After the removal of duplicates, titles were screened independently by two researchers (SS, MS) to exclude those that did not fit the inclusion criteria. When a title was judged to be relevant, the abstract was reviewed and included if the inclusion criteria were met. When it was not clear whether the abstract met the inclusion criteria, the full article was reviewed.

For all selected articles, data were extracted by two researchers (SS, MS) using a pre-designed data extraction form that included details on individual study design, methods of recruitment, sampling frame,

sample size, location, response rate, analysis performed, results, confounders, reported HIV prevalence/incidence and self-reported sexual behaviour, HIV prevalence/incidence and self-reported sexual behaviour in comparison groups (if provided).

Analysis

First, a critical appraisal of the quality of each individual efficacy study was performed by two researchers (SS, MS) using a checklist approach to assess the methodological components [26]. In the next step a compilation was done, including all relevant studies or reviews for each intervention. The data compilations were then reviewed by SS and MS, together with a senior researcher (AT), in order to check for consistency. Implementation studies were appraised for availability, acceptability, uptake, feasibility of implementation, implementation costs, and (when available) effectiveness of the intervention among MSM in the European setting.

A paucity of implementation data was found in the EU/EEA setting. Therefore the HASTE grading framework was adjusted slightly regarding grade 2b. Interventions with limited efficacy data, defined as being plausible but lacking European implementation data were assigned a grade 2b. Interventions without established efficacy were assigned a grade 2c in order to differentiate interventions with (grade 2b) and without (grade 2c) established efficacy.

The evidence gathered for each intervention was reviewed using the HASTE grading framework [20]. The grading was performed independently by two researchers (SS and MS) and showed high agreement (90%). All grades were reviewed by a senior scientist (AT) and discrepancies were discussed initially in the smaller group, and following that in a conference with the co-authors (SS, MS, AP, FH, SB, AT) where remaining discrepancies and questions were resolved. Biological and public health plausibility was determined through a process of discussions within the team of co-authors.

Results

Twenty-four HIV prevention interventions for MSM were included and reviewed. Table 2 presents the intervention topics as well as the number of articles found through search strategies, screened and included per intervention.

Interventions assigned a strong recommendation (HASTE grade 1)

Four interventions were assigned a HASTE grade 1: condom use, universal coverage of antiretroviral treatment and treatment as prevention, peer-led group interventions and peer outreach within the MSM community.

Condom use

Consistent efficacy data showed that condom use during anal intercourse prevents HIV transmission. A systematic review including five cohort studies (n=8,825) reported that condom use reduced HIV transmission (relative risk (RR): 0.36; 95% confidence interval (CI) 0.20–0.67) [27-32]. Implementation data supported acceptability and feasibility of condom use among MSM and the feasibility of condom distribution programmes in Europe [33-35]. Thirteen per cent of MSM in European countries reported they had UAI in the last 12 months solely because they did not have a condom available, which points towards an unmet need of condoms among some MSM [36]. Plausibility was determined as condoms are a barrier method, thereby preventing the transmission of HIV. No serious potential risk with using condoms was identified.

Universal coverage of antiretroviral treatment and treatment as prevention

A randomised, double-blinded controlled trial with 1,763 serodiscordant heterosexual couples and 37 serodiscordant male MSM couples, reported a relative reduction of 96% in the number of linked HIV-1 transmissions cases resulting from the early initiation of antiretroviral therapy, as compared with delayed therapy. Since only 37 MSM couples were included, the size of the relative reduction reported may not accurately reflect the protective effect on sexual transmission between MSM. Implementation data reports that ART programmes are available in all EU/EEA countries. However, national treatment guidelines show diversity regarding when to start treatment (at diagnosis or at CD4 count threshold level) [10]. Plausibility was deemed high as ART decreases the replication of HIV-1 and has been shown to reduce the amount of HIV-1 in genital secretions [37], which is likely to be the mechanism by which antiretroviral treatment reduces sexual transmission of the virus among MSM. However, the effectiveness of this intervention is dependent on comprehensive HIV testing programmes among MSM, and effective linkage to and retention in high-quality HIV treatment and care.

Peer-led group interventions

Peer-led group interventions, defined as interactive group activities where a trained peer facilitates promotion of precautionary behaviours for HIV, were found to cause a significant reduction in UAI by a systematic review including 21 studies (n=5,197 and one study of unknown sample size) [38]. The size of the reduction ranged from 13% to 33% [38-40]. Implementation data show high uptake of peer-led group interventions among MSM in Europe [38,41]. The intervention was judged plausible as the effect of peer-led group interventions may decrease high-risk behaviours for HIV through a combination of increased knowledge, social learning, influence of peers and normative group behaviour [38].

Peer-outreach

A review of systematic reviews that included 4 reviews (in total including 11 studies with n›7,890) found that peer outreach interventions, where a trained peer approaches MSM in community settings providing

Table 3a

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/inconsistent/NA	Available/NA from European setting	Biological plausibility /Public health plausibity	HASTE grade 1–4
Condom use	HIV incidence	Efficacy data are consistent. A systematic review from 2010 including five cohort studies (n=8,825) reports that the overall effect of condom use on HIV transmission was RR: 0.36; 95% CI 0.20–0.67, consistent condom use was found to reduce HIV transmission by 64% [27-32].	Available. Distribution of condoms is feasible. High acceptability and feasibility of condom use has been reported among MSM [33-35]	The intervention has biological plausibility. The condom acts as barrier, thereby preventing the transmission of HIV. No serious potential risk with using condoms has been identified. Operations research emphasises the importance of condom-compatible lubricant use at condom use during anal sex [120].	Strong, grade 1
Universal coverage of antiretroviral treatment and treatment as prevention	HIV incidence	Efficacy is consistent [37, 121-124]. A randomised, double-blinded controlled trial with 1,763 serodiscordant heterosexual couples and 37 serodiscordant male MSM couples, reported a relative reduction of 96% in the number of linked HIV-1 transmission cases resulting from the early initiation of ART, as compared with delayed therapy [37].	Available. Implementation data reports that ART programmes are available in all EU/EEA countries. However, national treatment guidelines show diversity regarding when to start treatment (at diagnosis/CD4 count threshold level) [10, 121-124].	The intervention has biological plausibility. ART decreases the replication of human immunodeficiency virus type 1 and has been shown to reduce the amount of HIV-1 in genital secretions [37], the likely mechanism for how ART reduces sexual transmission of the virus among MSM. A consideration is the reported low rates (43–84%) of ever having tested for HIV among European MSM, limiting the effect of serostatus-dependent prevention interventions [125].	Strong, grade 1
Peer-led group interventions	UAI	Efficacy data are consistent. A systematic review including 21 studies (n=5,197 and one study on unknown sample size) found a significant reduction in UAI. The size of the reduction ranged from 13% to 33% [38-40].	Available. Implementation data are consistent and show high uptake of peer-led group interventions [33, 38].	Peer-led group interventions for MSM have public health plausibility. Acceptability and uptake might be improved by the involvement of peers creating enabling and safe environments for MSM to provide information and counselling.	Strong, grade 1
Peer outreach	UAI	Efficacy data are consistent. A systematic review including 11 studies (n>7,890) reports that peer-led outreach interventions are effective in reducing UAI. Three meta-analysis reports significant reduction in UAI (OR: 0.7; 95% CI 0.49–0.99; OR: 0.65; 95% CI 0.48–0.89), RR: 0.70; 95% CI 0.55–0.91) in comparison with no HIV prevention [38].	Available. Peer outreach is common and generally well-received among MSM in Europe [10].	Peer outreach has public health plausibility through that peers can serve as a first point of interaction to create an enabling environment were persons who may not seek prevention interventions can be reached and introduced to such interventions.	Strong, grade 1
Voluntary testing and counselling for HIV	Condom use	Efficacy data are limited. A systematic review including 11 studies (n=4,416, of which 418 MSM), where six studies compared PLWH aware of their status with PLWH unaware of their status and five studies compared individuals before and after seroconverting. The data concluded that high-risk sexual behaviour for HIV is reduced after becoming aware of living with HIV, reduction in UAI ranged from 25% to 65%. No reduction was seen among those testing negative. Among MSM living with HIV, studies report increased condom use and decrease in number of sexual partners following HIV diagnosis [42-45].	Available. Acceptability for testing was found to be high, EMIS reports that the national proportion of MSM reporting having had an HIV-test during the past 12 months ranged from 20% to 47%, with a median of 37% [35, 46-48].	The intervention has biological plausibility, VCT may influence behaviour change through a process involving acquisition of HIV/AIDS knowledge and learning one's HIV serostatus [26]. Knowledge of HIV status enables access to treatment and prevention efforts dependent on HIV serostatus.	Probable, grade 2a

ART: antiretroviral therapy; CI: confidence interval; EEA: European Economic Area; EMIS: European MSM Internet survey; EU: European Union; FTC–TDF: emtricitabine and tenofovir ; LGBTI: lesbian, gay, bisexual, transgender and intersex; MSM: men who have sex with men; NA: not available; OR: odds ratio; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; PLWH: people living with HIV; RCT: randomised controlled trial; RR: relative risk; UAI: unprotected anal intercourse; US: United States; VCT: voluntary testing and counselling.

Table 3b

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/inconsistent/NA	Available/NA from European setting	Biological plausibility /Public health plausibity	HASTE grade 1–4
Condom-compatible lubricant use	Condom failure	Efficacy data are limited. Lack of additional lubricants during anal intercourse has been associated with condom failure [49-52]. A study investigating usage of 915 condoms at anal intercourse reported a reduction in slippage and breakage when using lubricants [53]. Oil-based lubricants (not condom-compatible) have been shown to decrease tensile strength and increase permeability in latex condom and thereby increase breakage rates [50,51].	Available. Studies have showed that use of lubricants among MSM is common. Distribution of condom compatible lubricants is feasible [54-55].	The intervention has biological plausibility, decreasing the amount of condom failure as well as the amount of micro-tears in rectum of the receptive partner by using condom-compatible lubricants at anal sex might provide a protective effect for HIV transmission [54-56].	Probable, grade 2a
Post-exposure prophylaxis	HIV incidence	Efficacy data are limited. Two retrospective cohort studies of patients receiving PEP in Denmark (n=374) and Amsterdam (n=189) have been performed, each study reported one seroconversion [57-58]. No adherence data was found.	Available. Implementation data reports a low demand for PEP in some European settings, the national proportion of MSM who have ever taken PEP ranged from 0% to 3.4% with a country median of 1.3% [36,57-58].	The intervention has a high biological plausibility. ART is highly effective in preventing the HIV-1 virus to replicate, thereby removing any virus before it can establish an infection. However, a low demand has been noticed in some European settings, which might decrease the public health plausibility, and information and availability might need to be strengthened.	Probable, grade 2a
Individual counselling for MSM living with HIV	UAI	Efficacy data are limited. A cohort study with one intervention (n=146 MSM) and one control arm (n=180) reported a significant decrease in UAI among MSM with ≥2 sex partners. A study comparing counselling vs standard of care in a primary-care setting found no difference regarding UAI at six-month follow-up. A RCT of peer-led individual counselling intervention reported a decline in HIV transmission at 6- and 12-month follow-up (n=249) [59-61].	Available. Implementation data report that acceptability and uptake of individual counselling is high [60-61].	Counselling for MSM living with HIV has biological plausibility, through a process where increased knowledge may lead to behaviour change reducing the risk of HIV transmission and risk of acquiring STIs, which might increase viral load and accelerate disease progression [62]. The benefit of episodic or one-time intervention was subject to decay over time and it would need boosters to maintain its effect.	Probable, grade 2a
Individual counselling for MSM	UAI	Efficacy data are inconsistent. A systematic review found inconsistent evidence regarding the effectiveness of counselling interventions in reducing UAI among MSM (n=11,636) [38]. Two meta-analysis report that HIV counselling (from studies with a comparison group receiving standard of care) was significantly associated with a reduction in UAI (OR: 0.59; 95% CI 0.36–0.97 n=2339; OR: 0.57; 95% CI 0.37–0.87 n=4689) [39,40]. Another meta-analysis found the absolute effects (from studies with a wait list control group) to show a non-significant reduction in UAI (RR: 0.80; 95% CI 0.60–1.06) [63].	Available. HIV counselling interventions are reported to be acceptable and feasible among MSM in Europe [36].	Interventions to increase knowledge of HIV and prevention measures have public health plausibility as they can influence behaviour change [126].	Possible, grade 2b

ART: antiretroviral therapy; CI: confidence interval; EEA: European Economic Area; EMIS: European MSM Internet survey; EU: European Union; FTC–TDF: emtricitabine and tenofovir ; LGBTI: lesbian, gay, bisexual, transgender and intersex; MSM: men who have sex with men; NA: not available; OR: odds ratio; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; PLWH: people living with HIV; RCT: randomised controlled trial; RR: relative risk; UAI: unprotected anal intercourse; US: United States; VCT: voluntary testing and counselling.

Table 3c

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/inconsistent/NA	Available/NA from European setting	Biological plausibility /Public health plausibity	HASTE grade 1–4
Peer-led group interventions targeting MSM living with HIV	UAI	Efficacy data are limited. A study comparing a five-session group intervention focusing on promoting safe sex (n=97) with a five-session standard of care support group (n=77) reports a decrease in UAI among participants [64]	NA	Public health plausibility was determined. The effect of peer-led group interventions may improve uptake of intervention and promote safe sex behaviour through a combination of increased knowledge, social learning, influence of peers and normative group behaviour [38].	Possible, grade 2b
Internet-based HIV prevention messages	UAI	Efficacy data are inconsistent. An RCT of a persuasive computing interactive intervention has shown a reduction of UAI at three months but could not maintain the effect at 12-month follow-up [65]. An RCT that evaluated the short-term efficacy (60 days) of a low intensity digital media intervention found significant reductions in UAI among men exposed to videos or to a website [57]. Two RCT report no differences in UAI between intervention and control groups [67-68].	NA	Interventions that increase knowledge on HIV and prevention measures have biological plausibility. Internet is one of the largest venues where MSM meet sexual partners [69,70]. Thereby messaging on the Internet would potentially reach a large number of MSM. In addition, safe-sex messaging on the venue where MSM meet sex partners could influence normative behaviour around safe sex.	Possible, grade 2b
Interventions in sex-on-premises venues	UAI and uptake of HIV testing	Efficacy data are limited. A study performing a VCT intervention at a bathhouse tested 133 men, of whom 48% had not been tested in the previous 12 months. A decrease in UAI was reported three months after the intervention [73-75].	NA	Sex venue-based interventions have public health plausibility through creating easy access to prevention interventions at the location where men meet sex partners, possibly reaching MSM who do not visit service sites [76,77]. Programmes may create social norms that can impact how MSM negotiate around sexual behaviour at sex venues [127,128] [47].	Possible, grade 2b
Social marketing interventions	Uptake of HIV-testing	Efficacy data are limited. A systematic review including three studies of cross-sectional design before and after the intervention reports a significant increase in HIV-testing uptake (OR: 1.58; 95% CI 1.40–1.77) [78].	NA	Social marketing interventions have public health plausibility through increasing knowledge on HIV and prevention measures and services. Awareness campaigns can also spark discussions and strengthen awareness, which can create a change in social norms.	Possible, grade 2b
Pre-exposure prophylaxis[a]	HIV incidence	Efficacy data are limited. One multicentre RCT, iPrEx, shows a 44% reduction in the incidence of HIV (95% CI 15–63; p=0.005) during a 3,324 person-years follow-up period among MSM. Detectable FTC–TDF blood levels strongly correlated with the prophylactic effect, emphasising the importance of adherence to PrEP [83].	NA	The intervention has biological plausibility. See section for PEP. Little is known about potential long-term side effects, adherence and drug resistance.	Possible, grade 2b

ART: antiretroviral therapy; CI: confidence interval; EEA: European Economic Area; EMIS: European MSM Internet survey; EU: European Union; FTC–TDF: emtricitabine and tenofovir ; LGBTI: lesbian, gay, bisexual, transgender and intersex; MSM: men who have sex with men; NA: not available; OR: odds ratio; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; PLWH: people living with HIV; RCT: randomised controlled trial; RR: relative risk; UAI: unprotected anal intercourse; US: United States; VCT: voluntary testing and counselling.

[a] New data have been published during 2015 providing implementation data for PrEP [115, 116].

[b] Assigned possible, grade 2b, for MSM who are only or mostly insertive during intercourse.

Table 3D

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/ inconsistent/NA	Available/NA from European setting	Biological plausibility / Public health plausibity	HASTE grade 1–4
Voluntary medical male circumcision[b]	HIV incidence	Efficacy data are consistent among men primarily or exclusively being insertive at anal sex. A Cochrane comprehensive review of 21 observational studies with a total of 71,693 participants found insufficient evidence that male circumcision prevents acquisition of HIV among MSM. Among men having primarily or exclusively insertive anal sex, a significant decrease in HIV infection was found (OR:0.27; 95% CI 0.17–0.44) [84]. A longitudinal study reports a reduced risk of HIV acquisition by 69% among MSM who reported ≥60% of acts as insertive with their last three sex partners) [85].	NA	The intervention has a biological plausibility among MSM who are only or mostly insertive during anal intercourse [85,130-133].	Possible, grade 2b
Training for healthcare providers to offer comprehensive care for MSM	NA	NA	NA. Many published and online resources are available to train health providers about issues facing MSM [7].	Training for providers to offer comprehensive care for MSM has public health plausibility. With adequate education and training, healthcare providers can provide appropriate routine care for MSM patients and help patients to avoid internalising stigma associated with homosexuality, prevent HIV acquisition, reduce unsafe sex, and lead more satisfying and healthy lives [7].	Pending, grade 2c
MSM-competent clinics	NA	NA	Available. MSM clinics that offer comprehensive services to MSM are available in many European metropolitan areas and have demonstrated high uptake of their services [86].	MSM-friendly clinics that offer comprehensive services have biological plausibility through removing barriers that stop MSM from seeking care or from disclosing relevant personal information once in care [87].	Pending, grade 2c
Voluntary anonymous partner notification	HIV incidence	NA	Available. Acceptability, defined as willingness of index patients to notify their sex partners, has been shown to be high among MSM in Europe [88,89].	Contract tracing has biological plausibility by enabling early diagnosis, treatment and care, which benefits the individual person as well as likely interrupting the transmission chain, thereby reducing incidence.	Pending, grade 2c
Campaigns for lesbian, gay, bisexual, transgender and intersex equality	Self-reported stigma towards LGBTI	No studies have fully evaluated structural interventions for MSM. Education programmes focusing on changing straight-identified persons' perceptions and challenging gender norms have been shown to be successful in decreasing stigma [90,91].	NA	Anti-stigma and LGBTI rights promotion has public health plausibility by removing structural barriers and providing a climate where MSM can access preventive service without fear of stigma [134].	Pending, grade 2c

ART: antiretroviral therapy; CI: confidence interval; EEA: European Economic Area; EMIS: European MSM Internet survey; EU: European Union; FTC–TDF: emtricitabine and tenofovir ; LGBTI: lesbian, gay, bisexual, transgender and intersex; MSM: men who have sex with men; NA: not available; OR: odds ratio; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; PLWH: people living with HIV; RCT: randomised controlled trial; RR: relative risk; UAI: unprotected anal intercourse; US: United States; VCT: voluntary testing and counselling.

[a] New data have been published during 2015 providing implementation data for PrEP [115, 116].

[b] Assigned possible, grade 2b, for MSM who are only or mostly insertive during intercourse.

Table 3e

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/ inconsistent/NA	Available/NA from European setting	Biological plausibility /Public health plausibity	HASTE grade 1–4
Female condom use at anal sex	Condom failure	Further evidence is needed to establish efficacy. One study reports no significant difference regarding condom breakage at anal sex compared with male condoms, but a higher rate of condom slippage OR: 2.7; 95% CI 1.2–5.8) (n=76) in comparison to male condoms [92].	NA	The intervention has biological plausibility as a barrier method. Female condoms potentially offer a protection method controlled by the receptive partner at anal sex. Higher rates of slippage, pain and discomfort when using the female condom at anal sex has been reported compared with using male latex condoms which is a potential risk/harm with female condom use at anal sex [92]. There is a need for safety and efficacy studies of a female condom designed for anal sex.	Pending, grade 2c
Serosorting	HIV incidence	Efficacy data are inconsistent. A systematic review included three observational studies found that serosorting increased HIV transmission by 79% compared with condom use [27]. However, compared with no condom use serosorting reduced HIV transmission by 53% [27,93]. The Explore trial performed among MSM in six US cities found that serosorting was associated with a modest reduction in HIV acquisition for HIV-negative MSM (OR: 0.88; 95% CI 0.81–0.95) [94].	NA. European men have reported in studies that they use serosorting as a risk management approach [95,96].	Serosorting may not have an effect due to low testing rates and the low possibility of detecting primary HIV infection. Public health plausibility is undefined, There is a risk that individuals may rely on a negative HIV-testing result that is not accurate.	Insufficient, grade 3
Avoiding semen in the mouth/ unprotected oral sex	HIV incidence	Efficacy data are inconsistent. One prospective cohort study including 2,189 high risk MSM in the US between 1992 and 1994 (2,633 person-years) reports a 0.06% risk of HIV at receptive oral sex with a sexual partner living with HIV and a 0.04% (95% CI 0.01–0.17) risk with a sexual partner. A cross-sectional study including 239 MSM reporting only having oral sex over the past six months (1999–2001) detected no cases of HIV. Observational studies from several high-income country settings have reported cases of self-reported oral transmission of HIV [102, 135-137].	NA	There is biological plausibility that not taking semen in the mouth and thereby limiting the contact between semen with possible HIV virus content and the oral mucosa could potentially remove this opportunity for transmission. However, transmission rates reported are between 0% and 0.04%, which is lower than estimated per contact risk of HIV at receptive anal intercourse with a condom (0.18%; 95% CI 0.10–0.28%). The low risk of HIV transmission implies that the avoidance of taking semen in the mouth would not have any significant effect.	Insufficient, grade 3

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Table 3f

Highest Attainable Standard of Evidence (HASTE) evaluation per HIV prevention intervention in men who have sex with men in Europe

Intervention	Outcome	Efficacy data	Implementation data	Plausibility	Grading
		Consistent/limited/ inconsistent/NA	Available/NA from European setting	Biological plausibility /Public health plausibity	HASTE grade 1–4
Avoiding nitrite inhalants/poppers at UAI	NA	NA	NA. Consistent high usage of poppers across European settings was self-reported in the EMIS 2010 study [35].	The pathway by which nitrite inhalants could lead to transmission of HIV is unclear. Nitrites inhalants cause peripheral vasodilatation and are believed to decrease anal sphincter tone, potentially leading to more traumatic sexual intercourse or more direct exposure to HIV target cells [98]. There are limited animal and human data suggesting that nitrite inhalants may cause transient immunosuppression or alter cytokine profiles, which could enhance transmission of HIV across mucosal barriers [99, 100]. Nitrite inhalants have been reported to be associated with high-risk sexual behaviour for STI/HIV including higher number of partners [101-103]. Frequent use of sex drugs may imply a high-risk marker of behavioural disinhibition that includes receptive UAI with multiple partners [98,104]. Limited evidence supporting biological plausibility was found.	Insufficient, grade 3
Interventions to reduce alcohol binge drinking	UAI	Efficacy data are inconsistent. A RCT study evaluated a combined intervention among MSM living with HIV promoting two target behaviours, abstinence from/ reduction in alcohol use and safe sex practices, compared with an unexposed control group reports no effect on UAI (n=253) [105].	NA	There is plausibility that alcohol binge drinking through disinhibition can lead to increased sexual risk behaviour [138]. Thus, behavioural interventions that decrease alcohol consumption might lead to decrease in UAI.	Insufficient, grade 3

ART: antiretroviral therapy; CI: confidence interval; EEA: European Economic Area; EMIS: European MSM Internet survey; EU: European Union; FTC–TDF: emtricitabine and tenofovir ; LGBTI: lesbian, gay, bisexual, transgender and intersex; MSM: men who have sex with men; NA: not available; OR: odds ratio; PEP: post-exposure prophylaxis; PrEP: pre-exposure prophylaxis; PLWH: people living with HIV; RCT: randomised controlled trial; RR: relative risk; UAI: unprotected anal intercourse; US: United States; VCT: voluntary testing and counselling.

information and peer support, are associated with a 30% reduction in UAI compared with minimal or no HIV prevention [38]. Peer outreach is common and generally well-received among MSM in Europe [10]. The intervention was judged plausible as peers can serve as a first point of interaction to create an enabling environment were persons who may not seek prevention interventions can be reached and introduced to interventions such as counselling, HIV/STI testing and treatment.

Interventions assigned a probable recommendation (HASTE grade 2a)

HASTE grade 2a was assigned to four interventions: Voluntary counselling and testing for HIV, condom-compatible lubricant, post-exposure prophylaxis (PEP), and individual counselling for MSM living with HIV.

Voluntary testing and counselling for HIV

A systematic review performed in 2005 including 11 studies (n=4,416, of which 418 MSM), where six studies compared PLWH aware of their status with PLWH unaware of their status, and five studies compared individuals before and after seroconverting. The data concluded that high-risk sexual behaviour for HIV is reduced after becoming aware of living with HIV, reduction in UAI ranged from 25% to 65%, but no reduction was seen among those testing negative. Among MSM living with HIV, studies report increased condom use and decrease in number of sexual partners following HIV diagnosis and counselling [42-45].

Acceptability for testing was found to be high, EMIS reports that the national proportion of MSM reporting having had an HIV-test during the past 12 months ranged from 20% to 47%, with a country median of

37%. However, the proportion that were 'quite' or 'very' confident they could access an HIV test if they wanted one ranged from 73% to 96% with a median of 91% [35,46-48]. Plausibility was determined as VCT may influence behaviour through a process involving acquisition of HIV/AIDS knowledge and learning one's HIV serostatus [45]. In addition, knowledge of HIV status enables access to ART and care, reducing onward transmission.

Condom-compatible lubricant use

Lack of additional lubricants during anal intercourse has been associated with condom failure [49-52]. A study investigating usage of 915 condoms at anal intercourse reported a reduction in slippage and breakage when using lubricants [53]. However, oil-based lubricants (not condom-compatible) have been shown to decrease tensile strength and increase permeability in latex condom and increase breakage rates [50,51]. Implementation data reports that lubricant use among MSM is high [36]. The intervention was judged plausible by the decrease in condom failure as well as that the amount of micro-tears in rectum of the receptive partner may be diminished by using condom-compatible lubricants [54-56].

Post-exposure prophylaxis

PEP, defined as the administration of ART starting within 72 hours post exposure and prolonged for 28 days, was evaluated by two retrospective cohort studies of patients receiving PEP in Denmark (n=374) and Amsterdam (n=189), each study reported one seroconversion [57,58]. No adherence data were found. Implementation data reports a low demand for PEP in some European settings, although it is considered the standard of care. The national proportion of MSM who have ever taken PEP ranged from 0% to 3.4% with a country median of 1.3% [36]. Low demand and uptake limit the public health impact of PEP. Information about and availability of PEP might need to be strengthened [57,58]. Plausibility is determined by the effect of ART post-exposure (within 72 hours) that diminishes the HIV-virus before an infection can be established.

Individual counselling for men who have sex with men living with HIV

A cohort study comparing an intervention group receiving individual counselling on risk reduction for HIV by a trained counsellor (n=146) and one control group (n=180) reported a significant decrease in UAI among MSM living with HIV with more than two sexual partners. Another RCT of peer-led individual counselling intervention reported a decline in sexual risk behaviour for HIV at 6 and 12 months follow-up (n=249) [59-61]. Implementation data report that acceptability and uptake of individual counselling are high [60,61]. Plausibility is determined through a process where increased knowledge may lead to behaviour change reducing the risk of HIV transmission and risk of acquiring STIs that might increase viral load and accelerate disease progression [62].

Interventions assigned a possible recommendation (HASTE grade 2b)

An additional seven interventions were graded HASTE grade 2b including: individual counselling for MSM, peer-led group interventions targeting MSM living with HIV, Internet-based HIV prevention messages, interventions in sex-on-premises venues, social marketing interventions, pre-exposure prophylaxis (PrEP) and voluntary medical male circumcision.

Individual counselling for men who have sex with men

Two meta-analyses examining individual counselling on HIV risk reduction with a comparison group receiving standard care found significant 41% and 43% reductions in UAI (OR: 0.59; 95% CI 0.36–0.97, n=2,339; OR: 0.57; 95% CI 0.37–0.87, n=4,689) [39,40]. A recent systematic review which included both these studies reports inconsistent evidence regarding the effectiveness of individual counselling in reducing UAI among MSM (n=11,636) [38]. This is due to the inclusion of another meta-analysis that found individual counselling clients (compared with waiting list control group) to report a non-significant 20% reduction in UAI (RR: 0.80; 95% CI 0.60–1.06) [63]. HIV counselling interventions are reported to be acceptable and feasible among MSM in Europe [36]. Plausibility is defined as interventions that increase knowledge of HIV and prevention measures can influence behaviour change.

Peer-led group interventions targeting men who have sex with men living with HIV

Peer-led group interventions among MSM living with HIV are defined as interactive group activities facilitated by a trained peer. A study comparing a five-session group intervention focusing on promoting safe sex (n=97) with a five-session standard of care support group (n=77) reports a decrease in UAI among participants [64]. Implementation data were not available. Plausibility was determined as the effect of peer-led group interventions may improve uptake by creating enabling and safe environments for MSM and promote safe sex behaviour through a combination of increased knowledge, social learning, influence of peers and normative group behaviour [38].

Internet-based HIV prevention messages

The Internet is a special venue in the sense that apart from being another potential meeting-dating venue, it may also be a venue for private and anonymous access to sexual health and well-being, at your own choice of time and physical place. Since specific longitudinal online interventions exist that are exclusively for use on the Internet, it was deemed important to review Internet-based interventions separately from other sex-venue based interventions.

An RCT of a persuasive computing interactive HIV messaging intervention has shown a reduction of UAI at three-month follow-up, but could not maintain the effect at 12-month follow-up [65]. An RCT that evaluated the short-term efficacy (60 days) of a low-intensity

digital media HIV messaging intervention found significant reductions in UAI among men exposed to videos or to a website [66]. Two RCTs report no differences in UAI between an intervention group receiving Internet-based messaging and non-exposed control groups [67,68]. The Internet is a common setting for MSM to meet sexual partners [69-72]. Messaging on the Internet would potentially reach a large number of MSM. The intervention was judged plausible as safe sex messaging on the online venue where MSM meet sex partners could influence normative behaviour around safer sex practices.

Interventions in sex-on-premises venues

Interventions in sex-on-premises venues are defined as prevention activities such as information, counselling and VCT at venues where MSM gather and seek sexual partners. A VCT intervention at a bathhouse tested 133 men of whom 48% had not been tested in the previous 12 months. A decrease in UAI was reported 3 months after the intervention, which highlights the prevention effect of HIV testing among those never tested before [73-75]. Implementation data were not available. Sex venue-based interventions have public health plausibility through creating easy access to prevention interventions at a location where MSM gather and meet sex partners, possibly reaching MSM who do not visit service sites [76,77].

Social marketing interventions

A systematic review of social marketing strategies promoting HIV testing (including three intervention evaluations of cross-sectional before-and-after design) reports a significant increase in HIV-testing uptake (OR: 1.58; 95% CI 1.40–1.77) [78]. Social marketing interventions include media messaging (any form of media) grounded in social marketing theory [79-82]. Implementation data were not available. Public health plausibility is achieved through increasing knowledge of HIV and prevention measures and services, through manipulation of perceptions of the desirability of precautions (and the undesirability of risks) and through the promotion of social norms for precaution.

Pre-exposure prophylaxis

One multicentre RCT, iPrEx, evaluated the efficacy of once-daily oral emtricitabine and tenofovir (FTC–TDF, Truvada) among men and transgender women who have sex with men (n=1,251) compared with placebo (n=1,224) for the prevention of HIV acquisition. One hundred people became infected during the follow-up period of 1.8 years (median, 1.2 years; maximum, 2.8 years, total of 3,324 person-years). Thirty six in the FTC–TDF group and 64 in the placebo group became infected, which indicates a 44% reduction in the incidence of HIV (95% CI 15–63; p=0.005). In the FTC–TDF group, the study drug was detected in 22 of 43 of seronegative subjects (51%) and in 3 of 34 HIV-infected subjects (9%) (p<0.001) [83]. Detectable FTC–TDF blood levels strongly correlated with the prophylactic effect, emphasising the importance of adherence to PreP. Little is known about potential long-term side effects, adherence, impact on other risk behaviour and drug resistance. Biological plausibility is determined; ART is highly effective in preventing replication of the HIV-1 virus, and so its presence could remove any virus before an infection can be established.

Voluntary medical male circumcision

A Cochrane comprehensive review of 21 observational studies with a total of 71,693 participants found insufficient evidence that male circumcision prevents acquisition of HIV among MSM [84]. However, among men having primarily or exclusively insertive anal sex, there was a significant decrease in HIV infection (OR: 0.27; 95% CI 0.17–0.44) [84]. The longitudinal study suggested that it reduced risk of HIV acquisition by 69% among MSM who reported ≥60% of acts as insertive with their last three partners [85]. Programmatic issues such as safety of male circumcision, sexual behaviour following male circumcision, and sexual satisfaction and function have not been addressed specifically among MSM. No implementation data were found. The effect is plausible among MSM who are only or mostly insertive during anal intercourse, which would comprise a limited group of MSM. Therefore, the intervention receives a grade of 2b for MSM who are only or mostly insertive during anal intercourse.

Interventions assigned a pending recommendation (HASTE grade 2c)

A HASTE grade 2c was assigned to five interventions: training for healthcare providers to offer comprehensive care for MSM, MSM-competent health clinics, voluntary anonymous partner notification, campaigns for lesbian, gay, bisexual, transgender and intersex equality (LGBTI), and female condom use for anal intercourse.

Training for healthcare providers to offer comprehensive care for men who have sex with men

Published and online resources are available to train health providers about issues facing MSM, but no evaluation study was found [7]. Implementation data were not available. Plausibility was deemed strong because training providers can offer comprehensive care for MSM, including appropriate routine care for MSM patients, and help patients to avoid internalising stigma associated with homosexuality, prevent HIV and other STI acquisition, and lead more satisfying and healthy lives [7].

MSM-competent health clinics

MSM-competent health clinics that offer comprehensive services to MSM are available in many European metropolitan areas and have demonstrated high uptake of their services [86]. MSM-competent health clinics that offer comprehensive services have plausibility through removing barriers that prevent MSM from seeking care or from disclosing relevant personal information once in care [87].

Voluntary anonymous partner notification

No studies evaluating voluntary anonymous partner notification were found. Acceptability, defined as willingness of index patients to notify their sex partners about living with HIV, has been shown to be high among MSM in Europe [88,89]. Voluntary anonymous partner notification has a plausible effect by enabling early diagnosis, treatment and care, which benefits the individual person as well likely interrupting the transmission chain, thereby reducing HIV incidence.

Campaigns for lesbian, gay, bisexual, transgender and intersex equality

No studies have fully evaluated structural interventions for MSM defined as activities promoting equality through education, media awareness campaigns and policy regarding an HIV-preventative effect. Education programmes focusing on changing straight-identified men and women's perceptions of the heterosexual majority and challenging gender norms have been shown to be successful in decreasing stigma against LGBTI [90,91]. Implementation data are not available. Anti-stigma and LGBTI rights promotion have public health plausibility by removing structural barriers and providing a climate where MSM can access preventive and care service without fear of stigma.

Female condom use for anal intercourse

In comparisons with male condoms, one study reports the female condom to have no significantly different breakage at anal intercourse, but to have a higher rate of slippage OR: 2.7; 95% CI 1.2–5.8 (n=76) [92] No implementation data from Europe were found. The intervention has plausibility as a barrier method for HIV transmission. Female condoms potentially offer a protection method controlled by the receptive partner at anal intercourse. Higher rates of slippage, pain and discomfort when using the female condom at anal intercourse have been reported compared with using male latex condoms, which is a potential risk/harm with female condom use at anal intercourse [92]. There is a need for safety and efficacy studies of a female condom developed particularly for anal intercourse.

Interventions assigned an insufficient recommendation (HASTE grade 3)

An insufficient level of evidence available, HASTE grade 3, was assigned to four interventions: serosorting, avoiding taking semen in the mouth/unprotected oral sex, avoiding use of poppers at UAI and avoiding alcohol binge drinking.

Serosorting

A systematic review including three observational studies [27] found that serosorting (i.e. only engaging in unprotected intercourse with individuals thought to have the same HIV status), increased HIV transmission by 79% compared with condom use. However, compared with no condom use, serosorting reduced HIV transmission by 53% [27, 93]. The Explore trial performed among MSM in six cities in the United States (US) found that serosorting was associated with a modest reduction in HIV acquisition for HIV-negative MSM (OR: 0.88; 95% CI 0.81–0.95) [94]. Some European men have reported in studies that they use serosorting as a risk management approach [95, 96]. Serosorting may not have an effect due to low testing rates and the low possibility of detecting primary HIV infection. There is a risk that individuals may rely on a negative HIV test result that is not accurate. Serosorting among people living with HIV can be associated with an increased risk of STIs, which have been shown to cause a peak in HIV viral load in semen among individuals on ART, which could affect HIV onward transmission [97]. Public health plausibility is undefined.

Avoiding semen in the mouth/unprotected oral sex

A prospective cohort study including 2,189 high-risk MSM in the US between 1992 and 1994 (2,633 person years) reported a 0.06% risk of HIV at receptive oral sex with a sexual partner living with HIV and a 0.04% (95% CI 0.01–0.17) risk with a sexual partner of unknown serostatus [102]. A cross-sectional study including 239 MSM reporting only oral sex over the past six months (1999–2001) detected no HIV. No implementation data are available [136].

There is biological plausibility that not taking semen in the mouth and thereby limiting the contact between semen with possible HIV virus content and the oral mucosa could potentially remove this opportunity for transmission. However, transmission rates reported are between 0% and 0.04%, which is lower than estimated per contact risk of HIV at receptive anal intercourse with a condom (0.18%; 95% CI 0.10–0.28) The low risk of transmission implies that the avoidance of taking semen in the mouth would not have a significant effect on transmission [11].

Avoiding use of nitrite inhalants/poppers at unprotected anal intercourse

No efficacy data were available. Consistent high usage of poppers across European settings was self-reported in the EMIS 2010 study [36]. The pathway by which nitrite inhalants could lead to transmission of HIV transmission is unclear. Nitrite inhalants cause peripheral vasodilatation and are believed to decrease anal sphincter tone, potentially leading to more traumatic sexual intercourse or more direct exposure to HIV target cells [98]. There are limited animal and human data suggesting that nitrite inhalants may cause transient immunosuppression or alter cytokine profiles, which could enhance transmission of HIV across mucosal barriers [99,100]. Nitrite inhalants have been reported to be associated with high-risk sexual behaviour for STI/HIV including higher number of partners [101-103]. Frequent use of sex drugs may imply a high-risk marker of behavioural disinhibition that includes unprotected receptive anal intercourse with multiple partners [98,104]. Thereby, there is limited evidence supporting biological plausibility.

Interventions to reduce alcohol binge drinking

An RCT evaluated a combined intervention among MSM living with HIV promoting two target behaviours, abstinence from/reduction in alcohol use and safe sex practices, compared with an unexposed control group (n=253). The intervention had no effect on UAI [105]. Implementation data were not available. There is plausibility that alcohol binge drinking may cause disinhibition that can lead to increased sexual risk behaviour. Thus, behavioural interventions that decrease alcohol consumption might lead to a decrease in UAI.

Discussion

This systematic review of HIV prevention interventions among MSM found that four of the 24 interventions reviewed could be assigned a HASTE grade 1, equal to a strong recommendation. Another four interventions could be assigned grade 2a, equal to a probable recommendation. In addition, another seven interventions were assigned grade 2b, a possible recommendation. Unambiguous recommendations can be made to MSM to use condoms and condom-compatible lubricant when engaging in anal intercourse, to test frequently for HIV and STIs, to use ART if living with HIV, and, if uninfected, to use PEP if exposed to HIV. Recommendations can be made to service commissioners and providers to provide MSM with access to HIV testing, to provide medical care including ART to PLWH, to provide PEP to those not infected, and to provide or make otherwise accessible condoms and lubricant. Interventions which promote HIV testing, condom use, ART and PEP can also be recommended. Evidence-based delivery modes include peer-led interventions, educational outreach and group work programmes, with specific peer-led programmes for men living with HIV.

An important consideration in HIV prevention programme planning is that there are synergies and dependency between the recommended interventions, indicating that combining interventions into programmes is desirable [106]. For example, biomedical interventions dependent on HIV serostatus (e.g. ART, PrEP, PEP) need to be implemented in combination with easy access to the provision of VCT. An HIV-testing service itself can achieve high coverage through peer outreach and social marketing. Therefore, interventions should be packaged together to enhance their potential full effect to prevent HIV.

There was a striking lack of European effectiveness studies, where interventions are examined outside an RCT setting. Additional research into the areas of effectiveness in the European context is needed inform HIV prevention decision-making and programme planning. These are required both regarding new interventions, such as the implementation of PrEP programmes, and to report results of follow-up on already-implemented interventions such as early initiation of ART, PEP, and voluntary anonymous partner notification.

The challenge of scaling up ART for MSM with HIV in Europe includes both more widespread and more frequent HIV-testing, as well as increasing ART accessibility to men testing positive. In 2013, 37% of the MSM diagnosed with HIV in the EU/EEA were diagnosed late (defined as CD4 cell count<350/µL), indicating that many men who acquire HIV are unaware of their infection for some time [107]. Models using data from the 2010 United Kingdom national cohort of MSM living with HIV suggest that extending ART to MSM diagnosed with HIV with CD4 counts<500 cells/µL would have reduced the overall proportion of infectious men from 35% to 29%. However reducing the undiagnosed population by 50% would have reduced this to 21%, which serves to emphasise the importance of frequent HIV testing [108].

Comprehensive community education programmes linking peer community outreach work with easy access to HIV-testing and treatment are key components of universal coverage of antiretroviral treatment and treatment as prevention. As HIV self-tests become authorised for use in European countries, they may contribute to increased testing and linkage to care. A French study reported that accessing an unauthorised HIV self-test was associated with living one's sex life with men in total secrecy and having had unprotected anal intercourse with men during the last 12 months, indicating that for particular groups of MSM, autonomous self-testing may reduce barriers to testing [109]. The majority of literature on VCT included in this review was published before 2000, indicating a need for more contemporary published studies evaluating delivery of HIV testing among MSM in Europe.

Drug approval by the European Medicines Agency for emtricitabine and tenofovir disoproxil fumarate (TDF/FTC), brand-named Truvada, to be used for pre-exposure prophylaxis is currently pending. It has been approved by the US Food and Drug Administration since July 2012. Studies among MSM in France and the UK have showed a high interest in and acceptability for PreP among MSM [110,111]. Half of 842 HIV-negative MSM in London reported that they would consider using PrEP if it became available as a daily pill [111]. The long-term health effects of TDF/FTC in HIV-uninfected men and men who become HIV-infected while taking PrEP needs evaluation [112-114]. The PROUD clinical trial in the UK and the IPERGAY clinical trial in France and Canada report that PrEP is highly protective against HIV acquisition among HIV-negative MSM and that PrEP use was not associated with increased number of sexual partners, decreased condom use, or increased incidence of STIs [115,116]. PROUD and IPERGAY data were not available when this review was performed but should be taken into account when providing guidance on PrEP.

In Europe, structural barriers including human rights violations, homophobia, direct and indirect discrimination and obstructive policies and laws all limit the

effectiveness of HIV intervention programmes, by reducing service uptake and by compromising the quality of services. In the European Survey of Lesbian, Gay, Bisexual and Transgender persons conducted in 2012, 38% of European MSM respondents said that they were not open with any healthcare provider about their sexual orientation; the percentage of men saying this was 70% or higher in several EU countries, including Lithuania, Slovakia, Romania, Poland, and Latvia [117]. Structural interventions aiming to decrease stigma and discrimination against MSM could result in an open climate where MSM feel safe to disclose their sexual practice and enrol in prevention and treatment programmes. Evaluation research is needed to guide how structural interventions for MSM in Europe would best be designed and implemented. As LGBTI rights improve in diverse European settings there will be opportunities for evaluating the health impacts that might be achieved due to structural and policy changes, and these should not be missed.

More descriptive data are needed on morbidity, wellbeing and health service use among MSM and MSM sub-populations. To minimise selection bias inherent in sampling strategies such as purposive or voluntary recruitment, combinations of sampling strategies that complement each other may increase validity. These may include the inclusion of sexual identity and practice variables in service monitoring, respondent driven sampling in real-life or on the web and time-location sampling.

This systematic review of HIV prevention interventions among MSM aimed for a comprehensive evidence-based multidisciplinary approach. The HASTE grading framework that is designed to evaluate HIV interventions among MSM allowed for an inclusive approach employing three tiers of data, and was particularly helpful for highlighting the importance of implementation data. In the grading process, we spent time thoroughly discussing the differences between HASTE grade 2a probable, 2b possible and 2c pending for recommendation. These grades overlap somewhat, and careful consideration is required when assigning them.

Behavioural and biological outcomes were assigned the same value according to the inclusion criteria for this review. As HIV incidence studies are rare, this review argues that all available efficacy data are relevant to include if the specific outcome variables are transparently reported. Reliance on self-reports of sexual risk behaviour is however subject to recall bias and social desirability bias, which may have diluted the measured effects of some interventions [118]. Most studies applied a short recall duration, which has been shown to maximise self-report accuracy and thereby diminish recall bias [119].

In this review it was notable that studies usually evaluated a mix of different (often related or entangled) interventions rather than a single component intervention. Similarly, outcome data in intervention studies are usually combined without disaggregating results by, for example, knowledge of partners' HIV status. Hence the effects of different individual components as well as effects in MSM sub-groups might be diluted in some results.

Serosorting was assigned an insufficient grade of recommendation and is not to be considered as a HIV intervention that should be recommended for MSM. However, many MSM in Europe use this tactic and so communication around serosorting, including the risk of HIV transmission and acquisition as well as STI acquisition, is important to address in counselling and information to MSM.

Encouragingly, fifteen interventions were graded to be strongly, probably or possibly recommended. These interventions can complement each other to maximise their impact and to address prevention needs and preferences of a diverse population of MSM. Offering and implementing prevention packages in collaboration with community members is crucial to the success of national and sub-national prevention programmes in the EU/EEA. In the relatively resource-rich European setting, there is an opportunity to provide global leadership with regard to the regional scale-up of comprehensive effective HIV prevention interventions for MSM.

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Conflict of interest

Authors report no conflict of interest.

Authors' contributions

SS prepared the manuscript and managed revisions. MS and SS carried out the data collection. AT led the study team. All authors participated in the study design, the interpretation of data and revised the manuscript for intellectual content. All authors approved the final manuscript.

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Mitteilungen der Sanitätsverwaltung
Bundesministerium für Gesundheit Familie und Jugend, Vienna
Monthly, print only. In German.
http://www.bmgfj.gv.at/cms/site/thema.html?channel=CH0951

Belgium

Vlaams Infectieziektebulletin
Department of Infectious Diseases Control, Flanders
Quarterly, print and online. In Dutch, summaries in English.
http://www.infectieziektebulletin.be

Bulletin d'information de la section d'Epidémiologie
Institut Scientifique de la Santé Publique, Brussels
Monthly, online. In French.
http://www.iph.fgov.be/epidemio/epifr/episcoop/episcoop.htm

Bulgaria

Bulletin of the National Centre of Infectious and Parasitic Diseases, Sofia
Print version. In Bulgarian.
http://www.ncipd.org/

Cyprus

Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus
Medical and Public Health Services, Ministry of Health, Nicosia
Biannual, print and online. In Greek.
http://www.moh.gov.cy

Czech Republic

Zpravy CEM (Bulletin of the Centre of
Epidemiology and Microbiology)
Centrum Epidemiologie a Mikrobiologie Státního
Zdravotního Ústavu, Prague
Monthly, print and online. In Czech, titles in English.
http://www.szu.cz/cema/adefaultt.htm

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Denmark

EPI-NEWS
Department of Epidemiology, Statens Serum Institut, Copenhagen
Weekly, print and online. In Danish and English.
http://www.ssi.dk

Finland

Kansanterveyslaitos
Department of Infectious Disease Epidemiology, National Public Health Institute, Helsinki
Monthly, print and online. In Finnish.
http://www.ktl.fi/portal/suomi/osastot/infe/tutkimus/tartuntatautien_seuranta/tartuntatautilaakarin_kommentit/

France

Bulletin épidémiologique hebdomadaire
Institut de veille sanitaire, Saint-Maurice Cedex
Weekly, print and online. In French.
http://www.invs.sante.fr/beh/default.htm

Germany

Epidemiologisches Bulletin
Robert Koch-Institut, Berlin
Weekly, print and online. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

Greece

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Hellenic Centre for Disease Control and Prevention (HCDCP/KEELPNO), Athens
Monthly, online. In English and Greek.
http://www2.keelpno.gr/blog/?lang=en

Hungary

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National Center For Epidemiology, Budapest
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http://www.oek.hu/oek.web?to=839&nid=41&pid=7&lang=hun

Iceland

EPI-ICE
Landlæknisembættið
Directorate Of Health, Seltjarnarnes
Monthly, online. In Icelandic and English.
http://www.landlaeknir.is

Ireland

EPI-INSIGHT
Health Protection Surveillance Centre, Dublin
Monthly, print and online. In English.
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Italy

Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.iss.it/publ/noti/index.php?lang=1&tipo=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
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Latvia

Epidemiologijas Bileteni
Sabiedribas veselibas agentura
Public Health Agency, Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni

Lithuania

Epidemiologijos žinios
Užkreciamuju ligu profilaktikos ir kontroles centras
Center for Communicable Disease Prevention and Control, Vilnius
Online. In Lithuanian.
http://www.ulac.lt/index.php?pl=26

Netherlands

Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
National Institute of Public Health and the Environment, Bilthoven
Monthly, print and online. In Dutch.
http://www.rivm.nl/infectieziektenbulletin

Norway

MSIS-rapport
Folkehelseinstituttet, Oslo
Weekly, print and online. In Norwegian.
http://www.folkehelsa.no/nyhetsbrev/msis

Poland

Meldunki o zachorowaniach na choroby zakazne i zatruciach w Polsce
Panstwowy Zaklad Higieny,
National Institute of Hygiene, Warsaw
Fortnightly, online. In Polish and English.
http://www.pzh.gov.pl

Portugal

Saúde em Números
Ministério da Saúde,
Direcção-Geral da Saúde, Lisbon
Sporadic, print only. In Portuguese.
http://www.dgs.pt

Romania

Info Epidemiologia
Centrul pentru Prevenirea si Controlul Bolilor Transmisibile, National Centre of Communicable Diseases Prevention and Control, Institute of Public Health, Bucharest
Sporadic, print only. In Romanian.
Sporadic, print only. In Romanian.
http://www.insp.gov.ro/cnscbt/index.php?option=com_docman&Itemid=12

Slovenia

CNB Novice
Inštitut za varovanje zdravja, Center za nalezljive bolezni, Institute of Public Health, Center for Infectious Diseases, Ljubljana
Monthly, online. In Slovene.
http://www.ivz.si

Spain

Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid
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Sweden

Folkhälsomyndighetens nyhetsbrev
Folkhälsomyndigheten, Stockholm
Weekly, online. In Swedish.
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England and Wales

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Weekly, online only. In English.
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Monthly, print and online. In English.
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Scotland

Health Protection Scotland Weekly Report
Health Protection Scotland, Glasgow
Weekly, print and online. In English.
http://www.hps.scot.nhs.uk/ewr/

European Union

"Europa" is the official portal of the European Union. It provides up-to-date coverage of main events and information on activities and institutions of the European Union.
http://europa.eu

European Commission - Public Health

The website of European Commission Directorate General for Health and Consumer Protection (DG SANCO).
http://ec.europa.eu/health/

Health-EU Portal

The Health-EU Portal (the official public health portal of the European Union) includes a wide range of information and data on health-related issues and activities at both European and international level.
http://ec.europa.eu/health-eu/

European Centre for Disease Prevention and Control

European Centre for Disease Prevention and Control (ECDC)
The European Centre for Disease Prevention and Control (ECDC) was established in 2005. It is an EU agency with aim to strengthen Europe's defences against infectious diseases. It is seated in Stockholm, Sweden.
http://www.ecdc.europa.eu

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