HIV incidence in an open national cohort of men who have sex with men attending STI clinics in England

Running Head: HIV incidence among MSM attending STI clinics in England

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Abstract

Objective: To determine HIV incidence among men who have sex with men (MSM) who repeat test for HIV at sexually transmitted infection (STI) clinics in England, and identify associated factors.
Design/methods: Annual HIV incidence and 95% confidence interval (CI) was calculated for a national cohort of MSM who tested HIV negative at any STI clinic in England in 2012 and had a follow up test within one year using routinely collected data. Cox regression analyses were performed to identify predictors of HIV acquisition and population attributable risk for HIV was calculated for predictors.
Results: In 2012, 85,500 MSM not known to be HIV positive attended any STI clinic in England, and 31% tested for HIV at least twice within a year at the same clinic. HIV incidence was 2.0/100 person-years (py) (95%CI 1.8-2.2) among repeat testers. Incidence was higher among MSM of black ethnicity (3.2/100 py); and those with a bacterial STI diagnosis at the initial attendance (3.2/100 py). MSM with a previous syphilis or gonorrhoea infection were at significantly greater risk of acquiring HIV in the subsequent year (adjusted hazard ratio: 4.1 95%CI 2.0-8.3 and 2.1 95%CI 1.4-3.2, respectively). The predictors accounted for 37% of HIV infections.
Conclusions: Annual HIV incidence among MSM attending STI clinics in England is high. Previous STIs were predictors of HIV acquisition but only accounted for one in five infections. More discriminatory behavioural predictors of HIV acquisition could provide better triaging of HIV prevention services for MSM attending STI clinics.

INTRODUCTION

Into the fourth decade of the HIV epidemic in the United Kingdom (UK), men who have sex with men (MSM) remain most at risk of HIV and the group among whom controlling the HIV epidemic remains a public health priority.(1) In 2012, 3,230 new HIV diagnoses were reported among MSM in the UK. (2) In the same year, over 34,000 MSM were living with diagnosed HIV infection and coverage of antiretroviral therapy, which is freely available, was 86%.

Most MSM are tested for and diagnosed with HIV in free and confidential sexually transmitted infection (STI) clinics, of which there are 215 in England. Available behavioural data show STI clinics serve a MSM population who report higher frequency of sexual risk behaviours, such as reporting 10 or more sexual partners in the last year,(3) reporting casual condomless sex partners or not exclusively serosorting in the last year, (4) than men who do not attend clinics.

New HIV diagnoses, however, do not necessarily reflect HIV incidence as they include long-standing and recently acquired infections and are also influenced by the volume of HIV testing performed. HIV incidence is considered the most important measure to describe the current HIV epidemic and identify sub-groups at greatest risk of infection. Incidence estimates among MSM clinic attendees in England from the last decade ranged between 2%-3% (5;6) while more recent estimates from the general MSM population show incidence to be less than 1%.(7-9) The behavioural data and incidence estimates highlight that MSM attending STI clinics are at higher risk and devising a method that allows HIV incidence to be routinely measured is key to monitoring the epidemic in this population and ensuring clinics can direct prevention services appropriately.

We employ a simple approach to estimate HIV incidence, which uses data from recently established national surveillance from STI clinics in England. These data can readily provide recent incidence measures and additionally allow characteristics associated with acquisition of HIV infection to be further investigated. Here, we determine HIV incidence in an open national cohort of MSM attending STI clinics in England in 2012 and identify predictors for HIV acquisition to help identify sub-groups among who HIV prevention services can be directed for the greatest impact on HIV transmission.

METHODS

Data source

The national reporting system of patient-level data known as the Genitourinary Medicine Clinic Activity Dataset (GUMCAD) was set up in all STI clinics in England from 2008 and a full description is available elsewhere.(10) Briefly, all clinics provide data quarterly to Public Health England. The database contains socio-demographic (age group, ethnicity, region of residence), HIV testing and STI screening and diagnosis information on patients attending STI clinics in England. Patient identifiers are anonymised so that patients can only be longitudinally linked and followed within clinics using a unique clinic identification number generated by the local clinic computer system. Thus, identification of individuals across clinics is not possible.

In this paper, two analyses have been conducted using GUMCAD. The first provides an overview of the characteristics of the HIV negative MSM population attending any of the 215 STI clinics in England in 2012 and the second estimates HIV incidence in the subset of the negative population who had at least two HIV tests within 12 months at the same clinic.

HIV negative MSM

MSM attending any STI clinic in England in 2012 and who were not known to be HIV positive were identified in GUMCAD. These were men with no previous clinical record indicating a HIV diagnosis from the same clinic and/or with a HIV negative test at the first visit in 2012. We also used any records available after the first attendance in 2012 to establish the HIV status of the individual if it was not clear from their clinical history or if no clinical history was available.

Socio-demographic characteristics were summarised and proportions of available clinical risk markers examined. Clinical risk markers related to the year prior to the initial attendance in 2012 (for those who previously attended in 2011) and to the initial attendance in 2012. Markers included an acute STI diagnosis and having a prior HIV test and/or sexual health screen. An acute STI diagnosis included: chlamydia, gonorrhoea, syphilis (primary, secondary and early latent), lymphogranuloma venereum (LGV), non-specific genital infection (NSGI), chancroid, first episode of genital warts and genital herpes and donovanosis.

Repeat testers and HIV incidence

MSM who tested HIV negative at any STI clinic in 2012 and had another test more than 42 days later at the same clinic were followed from the date of their earliest HIV test for up to one year until they either seroconverted or until their last attendance in the 12 month period after their first test. Any HIV test within 42 days of the first test was considered to belong to the same testing episode. An episode of care lasts 42 days to allow for disparities in dates reported for HIV/STI tests, diagnoses and treatments. A seroconversion was a new HIV diagnosis occurring after the last HIV negative test.

The Kaplan–Meier method was used to calculate HIV incidence in 2012. Incidence rates were calculated for sub-groups including by previous clinic attendance history and expressed per 100 person-years (py) with 95% confidence intervals (CI). In univariate analyses, associations between HIV incidence and clinical and demographic characteristics were evaluated using the log rank test.. Variables with marginal associations ($p<0.1$) were included in multivariable Cox regression analyses. Repeat testers who had not attended in the prior year were combined with those who did attend but were not diagnosed with a STI or did not have a HIV test. We combined them as HIV incidence did not differ in the two groups suggesting their risk for HIV was comparable. A stepwise backward approach was used to sequentially remove variables not significant ($p>0.05$) in order of the p value magnitude. Adjusted hazard ratios (aHR) and 95%CI were reported for risk markers significantly associated with HIV acquisition ($p<0.05$ using the likelihood ratio test).

Absolute numbers in the text have been rounded to the nearest hundred; actual numbers are presented in the tables. All statistical analyses were conducted using STATA 13.1 (StataCorp, College Station, TX).

The relative contribution of each predictive factor was determined by calculating population attributable risk (PAR), which combines the adjusted HR and the prevalence of the variable among repeat testers using the formula: prevalence(HR-1)/ prevalence (HR-1)+1.(11)

RESULTS

HIV negative MSM

In 2012, 85,500 MSM not known to be HIV positive attended any STI clinic in England (Figure 1). The mean age of attendees was 34 years (standard deviation (SD) 21.2). Eighty per cent were of white ethnicity, over two-thirds were born in the UK and almost half were resident in London (47%). Of the other ethnic groups, 5% were of black ethnicity; with 45% of them black Caribbean, 35% black African and the remainder of other black ethnicity.

For 57% of men, this was the first recorded attendance at a STI clinic since 2008, while 25% had attended the same clinic in the year prior to their initial attendance in 2012. After the initial attendance in 2012, only 41% re-attended the same clinic within 12 months (but more than 42 days after the first attendance) (median attendances per annum: 3, interquartile range (IQR) 2-4). Of all MSM not known to be HIV positive, 14% did not test for HIV at the first attendance in 2012 or in the following 12 months, 56% tested for HIV once and the remainder tested at least twice ("repeat testers") (Figure 1).

The demographic profile of the repeat (26,200) and non-repeat testers (59,300) differed by age (≥35 years: 37% vs 40%, respectively, $p<0.001$), birth in the UK (69% vs 66%, respectively, $p<0.001$) or residency in London (46% vs 50%, respectively, $p<0.001$). Eighty per cent of both groups were of white ethnicity. A third of repeat testers had also tested in the previous year compared to 17% of non-repeat testers ($p<0.001$). Forty-eight per cent had never attended (since 2008) compared to 61% of non-repeat testers ($p<0.001$). A tenth of repeat testers were diagnosed with an acute STI in the previous year compared to 6% of non-repeat testers ($p<0.001$).

Figure 1 Flow chart of MSM attending the same STI clinic* in England in 2012 and HIV seroconversion rates among repeat testers

*Attendance history and HIV testing information for men attending other clinics is not available in GUMCAD

Repeat testers

The 26,200 (31%) MSM who repeat tested for HIV within a year and at the same clinic were included in the HIV incidence analyses. Just over a quarter were young (15-24 years), a further 38% were aged 25-34 years and the remaining 34% were 35 years or older.

At the first attendance in 2012, 19% were diagnosed with an acute STI. Of all repeat testers, 9,300 (rounded to nearest hundred) (35%) had attended the same clinic in the year prior to their first attendance in 2012 (Figure 1). Of these, 95% had tested for HIV or had a STI screen, 26% were diagnosed with a bacterial STI, of which 20% were rectal infections. 417 (4.5%) MSM had taken PEP in the previous year.

HIV incidence

The 26,200 repeat testers MSM contributed 16,400 person years (py) of follow-up time. Median follow-up time was 0.65 person years (Interquartile range: 0.43-0.84). There were 324 seroconversions during follow-up, giving an HIV incidence of 2.0/100 py (95%CI 1.8-2.2) in 2012. Incidence differed by sub-groups (Table 1). Incidence was higher among MSM of black ethnicity (3.2/100 py), those born abroad (2.5/100 py) and those diagnosed with a bacterial STI at the initial attendance (3.2/100 py). Incidence was non-significantly higher among MSM attending in the prior year (2.3/100 py, 95%CI 1.9-2.7) compared to those who did not attend in the prior year (1.8/100 py, 95%CI 1.6-2.1).

Table 1 Socio-demographic, clinical characteristics and HIV incidence among MSM repeat testing at the same STI clinic, England, 2012 (n=26,192)

[a] Exact numbers presented. Missing information not included in the proportions.
[b] Univariate analyses exclude individuals with missing information
[c] Bacterial STI includes chlamydia, gonorrhoea, syphilis (primary, secondary and early latent), lymphogranuloma venereum (LGV), non-specific genital infection (NSGI), chancroid, and donovanosis

[d] Acute STI includes all the above and first episode of genital warts and herpes

HIV incidence was significantly higher among MSM who were diagnosed with an acute STI in the previous year (3.4/100 py) and in particular among those with a previous chlamydia (4.5/100 py), gonorrhoea (4.3/100 py) and syphilis infection (7.1/100 py) (Table 2). Incidence did not differ by genital infection of warts or herpes.

Table 2 HIV incidence among a subset of MSM repeat testing at the same STI clinic with clinical history from the prior year, England, 2012 (n=9,309)

[a] Bacterial STI includes: chlamydia, gonorrhoea, syphilis (primary, secondary and early latent), lymphogranuloma venereum (LGV), non-specific genital infection (NSGI), chancroid, and donovanosis
[b] Acute STI includes all the above and first episode of genital warts and herpes
[c] Rectal infections include gonorrhoea, chlamydia, NSGI and LGV

Predictors of HIV acquisition and Population Attributable Risk

In multivariable analyses, a bacterial STI and a rectal STI at the initial attendance in 2012 were associated with increased risk of acquiring HIV in the subsequent year (aHR:1.4 and 2.1, respectively) (Table 3). Two clinical markers from the previous year were also predictive of HIV infection: a previous syphilis or gonorrhoea infection. MSM previously diagnosed with syphilis were more than four times at greater risk of going on to acquire HIV (aHR: 4.1, 95%CI 2.1-8.3). Finally, of the demographic variables, men living in London were 1.4 times more likely to acquire HIV (95%CI 1.1-1.8).

The population attributable risk for HIV was 2.1% (95%CI 0.7-4.8) for syphilis, whereas a previous gonorrhoea infection accounted for almost 4% of infections among all repeat testers. The clinical markers from the previous year together accounted for 6% of all HIV infections, while those at the initial attendance accounted for another 12%. Living in London accounted for the greatest proportion (19%). Therefore, in total, the risk predictors accounted for over a third of all infections occurring in the population.

Table 3 Predictors of HIV seroconversion among MSM repeat testing at the same STI clinic, England, 2012 (n=24,234*)

*In the final model, residence was the only variable with incomplete information and those without residence information were excluded n.s.: not significant (p>0.05)
[a]PAR only calculated for risk factors significant in multivariable analyses

DISCUSSION

Our study uniquely uses data from a large national open cohort of MSM to provide insight into the characteristics of HIV negative MSM attending STI clinics in England. It also provides an indication of HIV risk and incidence in a subset that regularly test for HIV in the setting where HIV prevention can most suitably be delivered. Annual HIV incidence was high, at 2% among repeat testing MSM with significantly higher incidence in groups such as MSM diagnosed with a rectal STI in the prior year (5.4%). MSM diagnosed with a rectal STI at the initial attendance in 2012 were twice as likely to acquire HIV in the following year and men with a previous syphilis infection were more than four times at increased risk. Together, the risk factors accounted for 37% of all HIV infections observed in the population.

There are several limitations to this study. First, GUMCAD can only be used to follow up individuals within clinics and not between clinics. Movement between clinics is likely to be particularly common in urban areas such as London where the availability of more clinics will impact clinic choice.(12) Recent data collected from a small number of STI clinics suggests that 9% of MSM attended another STI clinic in the previous year. (13) Thus the number of MSM who repeat test within a year at the same clinic is probably an underestimate of repeat HIV testing among MSM generally and could partly explain why 14% did not have a HIV test at their first attendance. HIV incidence estimates may also be underestimated if MSM at higher risk of HIV acquisition are also more likely to attend more than one STI clinic for HIV testing. However, we cannot ascertain whether this is the case from the available data. Further, without the ability to identify individuals attending more than one clinic, the study population in 2012 may have been overestimated. Second, assuming 85% of all new HIV diagnoses among MSM were made in STI clinics, there were approximately 2,390 new HIV diagnoses in England reported to national HIV surveillance in 2012 compared to 2,000 to GUMCAD.(14)

Therefore a small number of seroconversions may be missing from this analysis. The discrepancies between the two surveillance systems are likely due to the differences in the reporting pathways. Third, by grouping MSM without clinical history with MSM attending in the prior year but without HIV tests or STI diagnoses, we may have misclassified some MSM who could have been diagnosed at other clinics in the prior year. However, this approach increases the similarity between this group and MSM attending in the prior year with a diagnosis and any bias in the results would be towards an underestimation of the effect of prior history on HIV risk. We conducted sensitivity analyses to determine risk factors for MSM with clinical history (n=9,300) and found four of the same five risk factors. The exception was a rectal bacterial infection at the initial attendance, which was only a risk factor for all repeat testers. Additionally, the magnitude of the effect was very similar. Fourth, incidence estimates reported here cannot be generalised beyond our population of MSM who repeat test at the same clinic. Finally, we didn't have any behavioural information for MSM attending STI clinics as this information is not routinely collected in national surveillance. Sexual behaviours, such as condomless receptive anal intercourse (RAI),(15)condomless RAI with HIV serodiscordant partners (16) and increasing partner numbers,(16-18) are known risk factors for HIV acquisition and would have accounted for a greater proportion of the HIV infections observed in the population.

Our incidence estimate is consistent with other studies among MSM clinic attendees in England from 2001 (2.5/100 py, 95%CI 1.7-3.5) (6) and 2004 (3%, 95%CI 1.9-4.6).(5) While these two studies employed a different methodology to estimate incidence, their results suggest incidence has remained relatively stable and high over the past 10 years among men attending STI clinics.(19) Our estimates are also comparable with those from cohorts of MSM in Portugal (2.8/100 py),(20) Spain (2.4/100 py),(21) Germany (3.3%) (22) and the US (2.4/100 py) (23) but higher than among clinic attending MSM in Australia (1.3/100 py).(24) Different mathematical models have been developed

to estimate HIV incidence among the general MSM population. These have reported incidence rates of 0.9%, (95%CI 0.5-1.3%) in the general MSM population aged 15-44 in England and Wales, in 2007,(9) mean annual incidence of 0.5% between 1998-2010 among MSM in the UK (8) and approximately 0.3% (2,500 new infections) among MSM in England and Wales in 2010.(7) These estimates highlight that incidence in clinic attending MSM is approximately two- to seven-fold higher than in the general MSM population.

This analysis was conducted amongst repeat testers; a diverse population of men seeking HIV testing services for different reasons. GUMCAD does not collect information on the reason for testing; however men may test frequently as they continue to engage in high-risk behaviours or as a reassurance mechanism. Community surveys indicate that over half of MSM regularly tested as part of their sexual health check while 36% tested following a risk event.(25) Furthermore, men reporting at least four tests in the last two years were also more likely to report at least 10 sexual and 10 anal intercourse partners than those testing 0-1 times indicating a higher risk population of frequent testers. Other studies have also found some association between being a repeat tester and reporting risky sexual behaviours when compared to first time testers.(26;27) Our data suggest repeat testers, while demographically similar to non-repeat testers, may be a higher risk population. A greater proportion had tested for HIV and was diagnosed with an acute STI in the previous year. However, we did not have behavioural data to conclusively determine if sexual behaviours differed between the two populations.

We were able to identify strata of MSM who were at high risk of HIV acquisition. Previous gonorrhoea and syphilis infections have been reported as predictors of infection (17;28;29) and were also shown here to increase the risk of acquiring HIV two- to four-fold. Rectal infections were also associated with HIV acquisition, similar to the results of a study in New York.(30) Rectal

infections reflect the practice of risky sexual behaviours including condomless RAI. The estimated per-act probability of acquiring HIV when engaging in condomless RAI is 138/10,000 exposures to an infected source; the most associated with a sexual exposure.(31)

Geographic location was the only socio-demographic factor associated with increased risk with London residents at higher risk than residents elsewhere in the UK. This finding may be explained by geographic differences in HIV prevalence and behaviours. HIV prevalence was significantly higher in London (2013: 132/1,000 aged 15-59 years) than the rest of the UK (39/1,000),(32) thus although the proportion of MSM living in London unaware of their infection is lower than outside London, , onward transmission of HIV is likely to be higher in London. Further, the proportion of undiagnosed MSM who had tested for HIV in the past year in London has significantly increased since 2000 suggesting that in recent years a greater number of infections in this population were acquired in the year following the last HIV test.(4) The proportion of MSM from community samples in London reporting condomless anal intercourse in the last year increased from 43% to 53% between 2000 and 2013.(4) This compares to 40% among MSM in Scotland in 2008.(33) There is also some evidence that other behaviours such as recreational drug use has also increased among core groups of MSM in London.(34)

While gonorrhoea, syphilis and rectal infections predicted for HIV infection, their low occurrence in the population resulted in small population attributable risks and most HIV infections were not predicted by STI history. High risk behaviours, including condomless RAI, which occur more frequently in the population and are strongly associated with HIV acquisition, have a higher PAR (11). Therefore, capturing behavioural information would be more useful than the currently available clinical outcomes especially for identifying high risk MSM in clinical settings and guiding better decision making for HIV prevention.(35) A clinical audit indicated that routine collation,

nationally, of this information should be possible as the majority of STI clinics do collect recent sexual behaviours for MSM.(36) The collection of some sexual behavioural information is currently being piloted in a small number of STI clinics with the view to expand data collection from all STI clinics in the country.

Our findings may particularly be useful to clinicians who should consider targeting HIV prevention services to repeat testers and core sub-groups within this population. Our results may also support policy makers developing guidelines for individuals eligible for pre-exposure prophylaxis (PrEP) following a recent UK trial which found PrEP to be highly effective at reducing HIV infection among MSM.(37) Men with a history of bacterial STIs, particularly syphilis, were at increased risk of subsequently acquiring HIV infection. Approximately 2,500 repeat testing MSM were diagnosed with a bacterial STI in the prior year; a number which could reasonably be enrolled into a PrEP programme that offers comprehensive HIV and STI prevention.

A large number of HIV negative MSM annually attend STI clinics in England, with at least a third testing for HIV twice within a year at the same clinic. Among these repeat testers we demonstrated high HIV incidence and highlighted some heterogeneity in HIV risk. Using clinical history with additional behavioural data could allow more nuanced risk stratification of MSM, which in turn could better enable clinicians to direct intensified HIV prevention to higher risk MSM who are in greatest need of these services to facilitate a reduction in HIV incidence.

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