

## SHORT REPORT

# High HIV incidence in men who have sex with men following an early syphilis diagnosis: is there room for pre-exposure prophylaxis as a prevention strategy?

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**ABSTRACT**

**Objectives** HIV pre-exposure prophylaxis (PrEP) is becoming a pivotal strategy for HIV prevention. Understanding the impact of risk factors for HIV transmission to identify those at highest risk would favour the implementation of PrEP, currently limited by costs. In this service evaluation, we estimated the incidence of bacterial STIs in men who have sex with men (MSM) diagnosed with early syphilis attending a London sexual health clinic according to their HIV status. In addition, we estimated the incidence of HIV infection in HIV-negative MSM, following a diagnosis of early syphilis.

**Methods** We undertook a retrospective case note review of all MSM patients diagnosed with early syphilis between January and June 2014. A number of sexual health screens and diagnoses of chlamydia, gonorrhoea and HIV were prospectively analysed following the syphilis diagnosis.

**Results** 206 MSM were diagnosed with early syphilis. 110 (53%) were HIV-negative at baseline, 96 (47%) were HIV-positive. Only age (37 vs 32 years,  $p=0.0005$ ) was significantly different according to HIV status of MSM at baseline. In HIV-negative versus HIV-positive MSM, incidence of rectal chlamydia infection at follow-up was 27 cases vs 50/100 person-years of follow-up (PYFU) ( $p=0.0039$ ), 33 vs 66/100 PYFU ( $p=0.0044$ ) for rectal gonorrhoea and 10 vs 26/100 PYFU ( $p=0.0044$ ) for syphilis reinfection, respectively. Total follow-up for 110 HIV-negative MSM was 144 person-years. HIV incidence was 8.3/100 PYFU (CI 4.2 to 14).

**Conclusions** A diagnosis of early syphilis carries a high risk of consequent HIV seroconversion and should warrant prioritised access to prevention measures such as PrEP and regular STI screening to prevent HIV transmission.

**INTRODUCTION**

HIV pre-exposure prophylaxis (PrEP) along with treatment as prevention is becoming the mainstay of combination strategies for HIV prevention.<sup>1</sup> PrEP has been shown to be 86% effective in reducing HIV acquisition in men who have sex with men (MSM) in two large trials,<sup>2 3</sup> and understanding how to better identify high-risk MSM who should receive PrEP could improve its cost-effectiveness, which appears to be the major obstacle to a widespread implementation.<sup>4 5</sup>

Recent acquisition of certain STIs is associated with increased HIV incidence in MSM.<sup>6</sup> In particular, rectal chlamydia or gonorrhoea infection can increase the risk of HIV seroconversion up to eight times.<sup>7</sup> Syphilis infection has also been found to be an independent risk factor for future HIV acquisition.<sup>8–10</sup> Data on real-life practice<sup>10</sup> confirm the increased risk of HIV acquisition with rectal STIs and syphilis, previously demonstrated in controlled studies, mostly where PrEP efficacy was the primary end point. Nonetheless, studies performed in a National Health Service context are lacking.

UK national guidance on the management of syphilis recommends that all people with syphilis be offered sexual health screening including HIV testing.<sup>11</sup> This service evaluation assesses the HIV and STI rates in people presenting with syphilis. We estimate the incidence of bacterial STIs in MSM diagnosed with early syphilis, according to their HIV status. In addition, we calculate the incidence of HIV infection in HIV-negative MSM following a diagnosis of early syphilis.

**METHODS**

The study was conducted at 56 Dean Street (56DS), a large HIV and sexual health clinic in London, UK.

All MSM, irrespective of their baseline HIV status, who received a diagnosis of primary, secondary or early latent syphilis between January and June 2014, were identified using our electronic database. We undertook a retrospective case note review of patient records and extracted data on subsequent management. Numbers of sexual health screens and Chlamydia trachomatis (CT), Neisseria gonorrhoeae (GC), HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) diagnoses were prospectively analysed. Samples for gonorrhoea and chlamydia testing were processed by nucleic acid amplification tests. Syphilis diagnosis was serological or clinical (confirmed by PCR on swab or serology), and the serological response was subsequently monitored. All patients who were HIV-negative were offered HIV test at baseline, according to the risk: third generation point-of-care test or fourth generation serology. Those resulting positive for either baseline HIV test were considered in the group of patients who



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were HIV-positive. At follow-up, incident syphilis was defined as at least a fourfold increase in Rapid plasma reagin test (RPR) titre from prior test and documentation of prior treatment appropriate for the stage of syphilis. All individuals received treatment in accordance with the BASHH guidelines.<sup>11</sup> We used the following tests to measure the differences between baseline characteristics according to HIV status: Mann-Whitney U test (age and number of sexual partners),  $\chi^2$  tests (syphilis stage), Z-test (penicillin treatment, drug use). We calculated 95% exact CIs and p values for incidence rates using Poisson distribution. This evaluation assesses current practice using existing data, and as such ethical approval was not sought.

## RESULTS

A total of 206 MSM were diagnosed with early syphilis between January and June 2014: primary (64, 31%), secondary (45, 22%), early latent (97, 47%). Their median age was 35 (IQR: 29–41 years), with a median number of sexual partners in the previous 3 months of 4 (IQR: 2–8). The majority (191, 93%) received treatment with 2.4 Millions of units (MU) benzathine penicillin intramuscularly. A total of 87 (42%) had reported recreational drug use during sexual activity in the previous 3 months; 110 (53%) were HIV-negative at baseline, 96 (47%) were HIV-positive (n=93) or were diagnosed with HIV at the time of syphilis diagnosis (n=3) (see [table 1](#)).

Three patients were HIV–HCV coinfectd, one monoinfected HCV and two monoinfected HBV at baseline. HIV-positive MSM with early syphilis were older than HIV-negative MSM (37 vs 32 years, p=0.0005). Otherwise, there were no differences in baseline characteristics according to the HIV status of MSM.

According to HIV status at baseline, subsequent incidence of rectal chlamydia infection was respectively 27 cases in HIV-negative vs 50 in HIV-positive/100 person-years follow-up

(PYFU) (p=0.004), 33 vs 66/100 PYFU for rectal gonorrhoea (p=0.0044) and 10 vs 26/100 PYFU for syphilis reinfection (p=0.004). Until February 2016, total follow-up for 110 HIV-negative MSM was 144 person-years. Among these, 12 (11%) developed a subsequent HIV infection, equating to an HIV incidence of 8.3/100 PYFU (95% CI 4.2 to 14). Of these, seven had a subsequent negative HIV test prior to their HIV diagnosis. Of the remaining five, the last negative HIV test was at baseline syphilis diagnosis. Of these, four were diagnosed more than 100 days later. One patient had a negative fourth generation HIV test at syphilis diagnosis and a subsequent positive p24 antigen 19 days later with symptoms of acute HIV infection.

## DISCUSSION

Our study highlights early syphilis as a risk factor for HIV acquisition in MSM, predicting a HIV incidence of 8.3/100 PYFU in a real-life setting. Nearly half of the population presented here are regular users of recreational drugs during sex (chemsex). MSM with early syphilis who attend our service have high rates of subsequent bacterial rectal STIs and syphilis reinfection, respectively of HIV status.

Our data confirm those seen in controlled studies. Syphilis was an independent predictor of HIV acquisition (HR 4.67) in a cohort in San Diego, USA, although a subanalysis of risk factors for HIV in those infected with syphilis was not performed.<sup>9</sup> Syphilis also emerged as an independent risk factor for HIV acquisition, although to a lesser extent, in similar studies of larger populations: Pathela *et al*<sup>10</sup> found a 5.6/100 PYFU incidence of HIV in MSM in New York City, USA, while in iPrEX, Solomon *et al*<sup>8</sup> found a 7.3/100 PYFU incidence. Here, the impact of PrEP in patients with a syphilis diagnosis was also measured.

As in other studies assessing the incidence of HIV following a diagnosis of STIs, our estimates of incidence may be underestimated, given the possibility that MSM in our cohort may have tested elsewhere. Also, our study findings may need to be contextualised for our clinical setting. Our sexual health clinic is located in Soho, London, and attracts a large proportion of London's MSM community: 56DS diagnoses 1 in 6 of the UK's HIV in MSM and serves a large number of sexually active HIV-positive individuals, as seen in nearly 50% of our early syphilis diagnoses.

Identifying key risk factors for HIV acquisition allows us to better target prevention strategies, particularly in a context of limited economic resources. Our HIV incidence following a diagnosis of early syphilis is comparable with the deferred arm of the PROUD study (9.0/100 person-years),<sup>2</sup> and with the incidence following postexposure prophylaxis use (7.6/100 person-years).<sup>12</sup> This suggests that intensive risk reduction and PrEP would be beneficial in HIV-negative MSM with early syphilis by reducing their risk of HIV acquisition.

In our population, high levels of subsequent bacterial rectal STIs, along with a rising problem of 'chemsex' use, suggest that the approach must be on multiple levels, supporting the inclusion of regular STI screening in PrEP management guidelines and chemsex support.

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**Contributors** NG and GW contributed to ideation, data collection, writing and analysis of this study. AG contributed with data collection. NN and AMCO contributed with the analysis and editing.

**Competing interests** None declared.

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**Table 1** Characteristics of patients with early syphilis according to their baseline HIV status.

n (%)	Syphilis in HIV-positive n=96 (47%)	Syphilis in HIV-negative n=110 (53%)	p Value
Age, median years (IQR)	37 (33–42)	32 (28–40)	0.0005
Syphilis stage			0.57
Primary (%)	30 (31)	34 (31)	
Secondary (%)	18 (19)	27 (25)	
Early latent (%)	48 (50)	49 (45)	
Treatment with benzathine penicillin (%)	86 (90)	105 (95)	0.11
Median number of sexual partners in last 3 month (IQR)	4 (2–9)	4 (2–7)	0.91
Reported drug use (%)	45 (47)	42 (38)	0.21
Mephedrone (%)	32 (33)	33 (30)	
GHB/GBL (%)	27 (28)	24 (22)	
Crystal metamphetamine (%)	28 (29)	20 (18)	
Intravenous drug use (%)	18 (19)	17 (15)	
Rectal chlamydia infection (incidence/100 PYFU, CI)	50 (36–68)	27 (19–36)	0.004
Rectal gonorrhoea infection (incidence/100 PYFU, CI)	66 (50–87)	33 (25–44)	0.004
Syphilis reinfection (incidence/100 PYFU, CI)	26 (16–40)	10 (5.7–17)	0.004
HIV infection (incidence/100 PYFU, CI)	n/a	8.3 (4.2–14)	

GHB/GBL, Gamma hydroxybutyrate/Gamma butyrolactone; PYFU, person-years of follow-up.

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**STI**

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