

Factors associated with reporting antibiotic use as STI prophylaxis among HIV PrEP users: findings from a cross-sectional online community survey, May–July 2019, UK

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ABSTRACT

Objectives The use of antibiotics as pre-exposure or postexposure prophylaxis for sexually transmitted infection (STI) prevention (STI prophylaxis) is not currently recommended in the UK, but there is evidence that self-prescribing occurs among those at greatest risk. We present the prevalence and factors associated with STI prophylaxis among a community sample of HIV pre-exposure prophylaxis (PrEP) users.

Methods The 2019 online PrEP User Survey ran between 17 May and 1 July. Eligible participants included UK residents reporting HIV PrEP use or having tried to obtain HIV PrEP since January 2017. STI prophylaxis use was defined as reporting buying antibiotics to prevent STIs, either privately or through the internet; this question was only asked to HIV PrEP users. Factors associated with STI prophylaxis use were assessed using univariable and multivariable logistic regression.

Results Overall, 9% (167/1856) of HIV PrEP users reported STI prophylaxis use; 97% were gay or bisexual men, 84% reported white ethnicity, 55% resided in London and 69% were aged ≥ 35 years. Factors associated with STI prophylaxis included: reporting ≥ 5 compared with 1–4 condomless sex partners in the past 6 months (12% vs 5.6%, adjusted odds ratio (aOR)=1.80; 95% CI 1.22 to 2.64), reporting chemsex drug use compared with no sexualised drug use in the past 12 months (13% vs 6.0%, aOR=1.88; 95% CI 1.20 to 2.93) and reporting an STI diagnosis in the past 12 months (12% vs 6.6%, aOR=1.54; 95% CI 1.08 to 2.18). Variables not significant in multivariable analyses included: ethnicity, age, residence and HIV PrEP sourcing.

Conclusions Approximately 1 in 10 HIV PrEP users from this community sample reported self-prescribed STI prophylaxis. STI prophylaxis was associated with sexual behaviour known to facilitate STI transmission and with a history of recent STIs acquisition. Given the potential risk of antimicrobial resistance, sexual health clinicians should consider asking attendees, especially HIV PrEP users, about the use of antibiotics as STI prophylaxis, to inform appropriate counselling, testing and management.

INTRODUCTION

There is growing concern over the burden of bacterial sexually transmitted infections (STIs) reported among individuals using HIV pre-exposure prophylaxis (HIV PrEP) to prevent HIV.^{1–3} A meta-analysis of STI prevalence and incidence among individuals using HIV PrEP estimated a pooled STI prevalence of 24% among individuals initiating HIV PrEP and a pooled STI incidence of 72.2 per 100 person-years during persistent HIV PrEP use.³

In the same way that antiretroviral therapy is used to prevent HIV infection in the forms of PrEP and postexposure prophylaxis (PEP), there is evidence that antibiotics for STI treatment could be used to prevent STIs. Doxycycline is a tetracycline antibiotic, which is commonly used as primary prevention (pre-exposure and PEP) for several infectious diseases⁴ and bacterial STIs treatment, but more recently has been assessed by studies as a preventative intervention for STIs.⁵ A substudy of the ANRS-IPERGAY trial in France among 232 high risk men who have sex with men (MSM) using HIV PrEP, showed that Doxycycline postexposure prophylaxis (Doxy-PEP) following condomless sex, was effective in reducing incidence of a first episode of chlamydia and syphilis but not gonorrhoea.⁶ Use of Doxycycline as pre-exposure prophylaxis (Doxy-PrEP) significantly reduced the number of gonorrhoea, chlamydia and syphilis diagnoses within the intervention arm among MSM with HIV in a small randomised controlled trial in the USA.⁷ However, this study is limited by the small sample size ($n=30$) and because participants received financial incentives for remaining STI negative.

A key concern about STI prophylaxis use is that any potential reduction in an individual's acquisition of specific STIs may be outweighed by harms associated with widespread, unprescribed and unmonitored use of tetracycline antibiotics. In 2017, Public Health England (PHE) and The British Association for Sexual Health and HIV advised against Doxy-PEP use due to the risk of increasing antimicrobial resistance (AMR) in STI pathogens and other bacterial species.⁸ Isolates collected through PHE's Gonococcal Resistance to Antimicrobials



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Surveillance Programme in 2018 showed 53% were resistant to tetracycline;⁹ therefore, Doxy-PEP/PrEP is unlikely to be effective at preventing *Neisseria gonorrhoeae* infection. Treatment success rates with tetracyclines for *Chlamydia trachomatis* and *Treponema pallidum* remain high with limited evidence for tetracycline resistance.¹⁰ Although tetracyclines have limited efficacy in clearing *Mycoplasma genitalium*, they are used in treatment regimens and AMR is a major concern in this organism.¹¹ Additionally, unanswered questions remain surrounding the efficacy, safety, appropriate dose, target population, acceptability, cost-effectiveness and risk-benefit of Doxy-PEP/PrEP in the general population.⁵

In the UK, patients can access antibiotics through prescription from healthcare professionals (HCPs), although more recently online pharmacies are selling generic Doxycycline directly to the public, without prescription or oversight from HCPs. Despite uncertainties over effectiveness and safety and lack of endorsement by professional organisations, emerging evidence suggests key populations are already self-prescribing STI prophylaxis.¹²⁻¹⁴ Little is known about who are using it, how these individuals become aware of the availability of antibiotics privately without prescription and motivations for use. Potential reasons for STI prophylaxis use could be increased awareness and community discussions about STI burden in specific risk groups and the ease of informal access online. Private HIV PrEP users could be alerted to online pharmacies selling antibiotics if purchasing HIV PrEP through the same internet retailer.

The PrEP User Survey aims to capture experiences of using and accessing HIV PrEP among people living in the UK. We used 2019 survey data to estimate the prevalence and predictors of STI prophylaxis use among UK HIV PrEP users, to add to our knowledge on STI prophylaxis and inform the public health response to STI and AMR control.

METHODS

The PrEP User Survey is an online, cross-sectional survey that was first conducted in 2017, led by PrEPster and iwantPrEPnow (community-based organisations educating about PrEP and PrEP access in the UK) to inform their PrEP activism activities. In 2018 and 2019, PHE joined the collaboration. Participation was voluntary and the information provided and experience of completing the anonymous, online survey ensured that consent was implied. The survey aims to characterise and capture experiences of HIV PrEP users, explore barriers to use and to estimate the current number of UK users, irrespective of the source of PrEP (publicly funded programmes or privately purchased).¹⁵

This analysis used data exclusively from the 2019 survey round, following previous surveys in 2017 and 2018. The survey recruits participants from the iwantPrEPnow mailing list, generated from individuals requesting updates on PrEP availability via the iwantPrEPnow website, and the PrEPster mailing list generated from individuals attending PrEPster events and given permission to be contacted about future events and activity, including research participation requests. The 2019 survey additionally recruited participants through social media (Facebook, Instagram, Twitter) and Grindr (a geosocial networking application); participants were eligible if they were UK residents and reported HIV PrEP use or unsuccessfully trying to obtain HIV PrEP since January 2017. Recruitment for 2019 took place from 17 May to 1 July; data were collected on participant demographics, HIV PrEP use and access, sexual behaviour, HIV and STI testing practices and STI diagnoses.

This analysis only includes individuals from the 2019 survey round who reported HIV PrEP use since January 2017. STI prophylaxis use was defined by an affirmative response to the question introduced in 2019: 'Do you buy antibiotics to prevent STI infections, either privately or through the internet?'. The term 'antibiotics' was used instead of Doxycycline, as previous studies suggest individuals also purchase other antibiotics for STI prophylaxis.^{12,14} Only individuals reporting HIV PrEP use in the 2019 survey were asked about STI Prophylaxis use; hence, our analyses do not include those who tried but were unable to obtain HIV PrEP.

Factors associated with STI prophylaxis use were identified using logistic regression. Variables were considered for inclusion in multivariable analyses if they were of interest (ie, deemed important predictors for STI prophylaxis use) and/or significant at $p < 0.100$ in univariable analyses. A backwards stepwise approach was used for the final multivariable model, with variables retained if significant at $p < 0.050$ using the likelihood-ratio test. Data were analysed using STATA 15.1 (College Station, Texas, USA).

RESULTS

Sample characteristics of HIV PrEP users

Overall, 2389 participants submitted responses between 17 May and 1 July 2019; 1856 (78%) individuals reported HIV PrEP use since January 2017. A description of these participants is detailed in online supplemental table 1. The majority identified as white gay or bisexual men, aged ≥ 35 years, living in England.

STI prophylaxis users versus non-STI prophylaxis users

Of the 1856 HIV PrEP users, 167 (9%) reported STI prophylaxis (1681 reported no STI prophylaxis use and 8 did not answer) (online supplemental table 2). Of the 167 STI prophylaxis users, the majority (97%, 162/167) reported male gender and identified as gay or bisexual, 84% (141/167) reported white ethnicity, 69% (115/167) were aged ≥ 35 years. Similar gender, sexual orientation ethnicity and age breakdowns were reported among non-STI prophylaxis users. Of participants who identified with a gender different to that assigned at birth ($n=23$), none reported STI prophylaxis.

Most STI prophylaxis users (60%, 101/167) were recruited through iwantPrEPnow and PrEPster mailing lists, with the remaining recruited through Grindr (17%, 29/167), social media (15%, 25/167) and other means (7%, 11/167). Smaller proportions of non-STI prophylaxis users were recruited through mailing lists (52%, 878/1681) with a larger proportion recruited through Grindr (23%, 387/1681) ($p=0.155$). Just over half of STI prophylaxis users reported living in London (54%, 91/167), 41% (69/167) in England outside London and 4.2% (7/167) in Scotland, Wales and Northern Ireland. Smaller proportions of non-STI prophylaxis users lived in London (47%, 798/1681, $p=0.375$).

Just over half of STI prophylaxis users last sourced HIV PrEP through the Impact Trial in England¹⁶ or another publicly funded programme in devolved administrations (58%, 97/167) and 42% (70/167) through online purchase or other private sources. Similar HIV PrEP sources were reported among non-STI prophylaxis users. Just over a quarter (26%, 44/167) of STI prophylaxis users reported sharing or selling HIV PrEP compared with 15% (253/1,681) among non-STI prophylaxis users ($p < 0.001$). Similar proportions reported taking HIV PrEP daily in both STI prophylaxis and non-STI prophylaxis groups (75% and 75%, respectively).

The majority of STI prophylaxis users and non-STI prophylaxis users reported condomless sex in the past 6 months (96% and 95%, respectively); however, a larger proportion of STI prophylaxis users reported ≥ 5 condomless sex partners (72% vs 41%, respectively, $p < 0.001$). Three-quarters (75%, 125/167) reported using drugs just before or during sex in the past 12 months compared with 61% (1027/1681) among non-STI prophylaxis users ($p < 0.001$). A third (33%, 55/167) reported using ≥ 1 chemsex-associated drugs compared with a fifth (22%, 364/1681) among non-STI prophylaxis users ($p < 0.001$). Injecting drug use in the last 12 months was reported among 9.0% and 3.9% of STI prophylaxis users and non-STI prophylaxis users, respectively ($p < 0.001$).

A slightly larger proportion of STI prophylaxis users (81%, 135/167) reported ≥ 3 HIV tests in the last year compared with non-STI prophylaxis users (77%, 1286/1681, $p = 0.031$) and similar proportions reported having their last HIV test at a sexual health clinic (SHC) (86% and 87%, respectively). Just under two-thirds reported having ≥ 3 STI tests in the last year in both STI prophylaxis users and non-users (65% and 64% respectively), with the majority having their last test STI test at a SHC (89% and 90% respectively). A larger proportion of STI prophylaxis users (63%, 105/167) reported an STI diagnosis in the last 12 months compared with non-STI prophylaxis users (48%, 805/1,681, $p < 0.001$). Among those reporting STI diagnoses, a higher proportion reported a chlamydia diagnosis among STI prophylaxis users compared with non-STI prophylaxis users (66% vs 60.4%, $p < 0.001$) and a lower proportion reported a gonorrhoea diagnosis among STI prophylaxis users (57% vs 67%, $p = 0.279$).

Factors associated with STI prophylaxis use

In univariable analyses, higher odds of STI prophylaxis use were observed among HIV PrEP users reporting the following: being aged 35–44 compared with < 35 years, reporting ≥ 5 compared with between 1 and 4 condomless sex partners in the last 6 months, chemsex and injecting drug use compared with no drug use just before or after sex in the last 12 months and an STI diagnosis in the last 12 months (online supplemental table 2). Lower odds of STI prophylaxis use were observed among HIV PrEP users reporting < 3 compared with no HIV tests in the last 12 months. These variables were included in the multivariable analyses. Gender, sexual orientation, method of survey recruitment, HIV PrEP source, PrEP dosing regimen, transactional sex, SHC attendance, setting of last HIV or STI test, number of STI tests in the last year, STI diagnoses other than Chlamydia and sex life satisfaction were not significantly associated with STI Prophylaxis use. Sharing or selling HIV PrEP and being diagnosed with Chlamydia were significantly associated with STI Prophylaxis use in univariable analyses but were not included in multivariable analyses as they were not a priori variables of interest. Residence and ethnicity, although not significantly associated with the outcome in the univariable analyses, were included as a priori variables of interest. Injecting drug use was not retained in the final multivariable model due to collinearity with chemsex. Residence, ethnicity, number of HIV tests in the last 12 months and age were also not retained as they significantly reduced the goodness of fit of the model at $p \geq 0.050$ using the likelihood-ratio test.

In the final multivariable model, statistically significant associations were observed between reporting STI prophylaxis use and reporting ≥ 5 compared with 1–4 condomless sex partners in the past 6 months (aOR=1.80 (95% CI 1.22 to 2.64), $p = 0.003$),

using ≥ 1 chemsex-associated drugs just before or during sex compared with no sexualised drug use in the past 12 months (aOR=1.88 (95% CI 1.20 to 2.93), $p = 0.006$) and reporting an STI diagnosis in the last 12 months (aOR=1.54 (95% CI 1.08 to 2.18), $p = 0.016$).

DISCUSSION

To our knowledge, this is the largest community-based study exploring STI prophylaxis use among HIV PrEP users. Our findings show 9.0% (167/1856) of individuals among our cohort of high-risk HIV PrEP users in 2019 reported privately purchasing antibiotics to prevent STIs. Most notably, we also found STI prophylaxis use to be geographically widespread in the UK and associated with higher risk for HIV/STIs: multiple condomless sex partners, chemsex and STI diagnoses.

This analysis has various strengths. In addition to the relatively large sample size compared with other STI prophylaxis research, our PrEP User Survey had wide geographical coverage and is an annual, established survey. Community sampling methods allowed access to diverse HIV PrEP user groups across the UK, not limited to SHC attendees. The survey was piloted using small focus groups and data were anonymously self-reported, reducing social desirability bias. We collected extensive information on sexual behaviour and sexual health, allowing us to explore a variety of risk factors and build a comprehensive profile of survey participants, taking our knowledge further than previous surveys examining predictors of STI prophylaxis.^{12–14}

Our survey also has limitations. As we recruited individuals online, and predominantly MSM, there is potential for participation and self-selection bias, meaning our sample and findings may not be representative of all UK HIV PrEP users. Our recruitment included promotion through PrEPster and iwantPrEPnow mailing lists, potentially skewing our sample towards higher-risk MSM seeking information on HIV PrEP. Our survey was only conducted in English and therefore not representative of non-English speaking HIV PrEP users. Cognitive testing of the STI prophylaxis use question was not performed and may have led to misinterpretation. The question also refers to *buying* antibiotics and may not have captured STI prophylaxis users accessing antibiotics through other informal channels. We also did not capture other key variables related to STI prophylaxis such as specific antibiotics used, access routes, how they were used (eg, as pre-exposure or postexposure prophylaxis, daily or on-demand dosing), how often and for how long. These data could help us understand the likely effectiveness of individual STI prophylaxis practices and methods of use. As we restricted our survey question on STI prophylaxis to HIV PrEP users, our findings are not generalisable to other populations, including non-HIV PrEP users and MSM living with diagnosed HIV.

Our 9% prevalence of STI prophylaxis use is similar to smaller studies quantifying STI prophylaxis use in SHC attendees attending HIV PrEP follow-up. In 2018, 9.9% ($n = 105$) of 1065 MSM HIV PrEP users attending a SHC in Melbourne, Australia, reported Doxycycline prophylaxis in the last month.¹³ Also in 2018, 8% ($n = 46$) of 106 MSM HIV PrEP users attending a SHC in London, UK, reported taking antibiotics to prevent STIs.¹² A study among 321 MSM recruited through eight STI clinics in the Netherlands in 2018 observed a smaller prevalence estimate (2.2%, $n = 7$) reporting STI prophylaxis; however, this study included MSM not taking HIV PrEP.¹⁴ These three studies provide useful references for STI prophylaxis prevalence and risk factors, but cannot be directly compared for various reasons. First, they were conducted among SHC attendees and may have different demographics, risk

behaviours, risk perception and how these are reported, compared with our community sample. The Dutch study did not restrict to HIV PrEP users; therefore, risk profiles in their sample will differ. Questions on STI prophylaxis were phrased differently between studies, likely leading to differing interpretations, for example the Dutch and London studies asked about antibiotic use as STI prophylaxis, whereas the Melbourne study limited to Doxycycline use. Sample sizes were also smaller compared with our survey, potentially decreasing the power to detect effects. Our survey is more recent and may reflect changes in behaviours, HIV PrEP use, infection epidemiology and STI prophylaxis awareness since the other surveys were conducted.

Our research indicates reported STI prophylaxis use is more common among HIV PrEP users at higher risk of HIV/STIs, as we observed significant associations with reporting ≥ 5 condomless sex partners in the past 6 months, and chemsex and reported STI diagnoses in the last 12 months. Although not retained in the final multivariable model, injecting drug use was associated with STI prophylaxis in our univariable analyses, as was observed in the Melbourne study multivariable model.¹³ These associations with higher STI risk behaviours may reflect HIV PrEP users having an increased awareness of risk behaviours, assessing their individual heightened risk for STIs, and mitigating against that risk through self-prescription of antibiotics. A recent meta-analysis of studies reporting sexual risk outcomes in HIV PrEP users found that commencing HIV PrEP led to an increase in anorectal STIs, suggesting HIV PrEP use is associated with a decline in condom use for anal sex.¹ This altered risk perception and behaviour change may also be mirrored in STI prophylaxis initiation, whereby users engage in increased STI risk behaviours due to the perception that antibiotic use has a protective effect on the risk of STI acquisition. Additionally, those engaging in higher STI risk behaviours may be less risk averse, and more likely to use STI prophylaxis, despite a paucity of evidence supporting its effectiveness and no endorsement from professional and public health bodies.

Interestingly, ethnicity, age and residence were not significantly associated with STI prophylaxis in the multivariable analysis. This suggests that STI prophylaxis use may be geographically widespread and dispersed across age, residence and ethnic groups. We expected private HIV PrEP use to be associated with STI prophylaxis, as these individuals are already sourcing HIV PrEP through the internet or other informal routes; however, no significant association was observed.

Although it appears STI prophylaxis is an emerging phenomenon among higher-risk MSM, there are growing concerns over the potential of widespread STI prophylaxis use to select AMR in STIs and other bacterial pathogens. Future research quantifying this risk are welcomed. Frequent antimicrobial exposure for STI treatment in MSM is thought to facilitate development of resistance in target and non-target organisms, such as *Shigella* spp.^{17 18} More evidence is also needed to determine the effectiveness of antibiotics as Pre-Exposure STI prophylaxis for individual STI pathogens. As STI prophylaxis users in our cohort obtained antibiotics privately, it is likely they were not clinically advised on individual need and the appropriate use of these medicines. There are also concerns over drug integrity, dosage, storage, transportation and supporting information on safe and correct use by suppliers. The UK currently does not recommend the use of antibiotics as STI prophylaxis; hence, individuals may be reluctant to disclose this to clinicians, hindering provision of appropriate support. Routine data collection of STI prophylaxis use among SHC attendees as part of sexual history could inform clinical risk assessment and provision of appropriate clinical advice on testing frequency and test of cure, as well as good

antimicrobial stewardship. Additionally, awareness and public health education on the informal use and abuse of antibiotics, for both patients and providers, would be beneficial.

Our study provides scope for further research. We did not ask which antibiotics participants were using, where they were sourced, how they were used, frequency and length of use, adherence and motivations for use, which should be explored in future surveys. Subsequent survey rounds could also provide insight into trends in STI prophylaxis use and extent of use in other groups, including non-HIV PrEP users. Furthermore, larger, more robust studies on the effectiveness of STI prophylaxis on the incidence of different STIs, and the long-term impact of frequent antibiotic use on target and non-target organisms, are urgently needed.

Key messages

- ▶ Sexually transmitted infection (STI) prophylaxis describes the use of antibiotics to prevent STI acquisition; however, national estimates of its use among HIV pre-exposure prophylaxis (PrEP) users has not been quantified.
- ▶ Small studies have reported effectiveness of STI prophylaxis in reducing incidence of certain STIs, but there are concerns over its potential to contribute to antimicrobial resistance.
- ▶ Nine per cent of HIV PrEP users in the UK reported STI prophylaxis, purchasing antibiotics to prevent STIs, either privately or through the internet.
- ▶ STI prophylaxis was associated with reporting ≥ 5 condomless sex partners (past 6 months), chemsex and STI diagnoses (past 12 months).

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Contributors All authors were involved in shaping the research and interpretation of findings. All authors reviewed the manuscript, provided critical feedback on revisions and contributed to writing. JMS was the principal investigator for the subanalysis on STI prophylaxis. COH was responsible for carrying out data analyses, writing manuscript drafts, incorporating author comments and was responsible for final draft publication. SC and HM provided support with statistical analyses. JMS, HM, HF, HA and GH provided key epidemiological and clinical advice on STI treatment and surveillance. WN and GO provided valuable insight into STI prophylaxis and HIV PrEP use in the community. VD, ONG, COH, GO, WN and SC are part of the PrEP User Survey team and are responsible for the overall aims of the survey, design, recruitment, management and analysis of results.

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