Title: Chemsex and diagnoses of syphilis, gonorrhoea, and chlamydia among men who have sex with men in the UK: a multivariable prediction model utilising causal inference methodology.

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Abbreviations: PrEP, pre-exposure prophylaxis; HIV, human immunodeficiency virus; MSM, men-who-have-sex-with-men; PLHIV, people living with HIV; STI, sexually transmitted infection; WHO, World Health Organization; NHS, National Health Service; EMIS, The European Men-who-have-sex-with-men Internet Survey.

Footnote Page

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Key messages:

1. Reporting of recent (≤12 months) multi-partner chemsex among MSM was similar in HIV-diagnosed (25%) and PrEP users (28%), while much lower among other MSM (5%).
2. Recent multi-partner chemsex had adjusted odds ratios of between 1.9-4.0 (dependent on MSM subgroup) with recent syphilis, gonorrhoea and chlamydia diagnoses.
3. Recent exclusively dyadic chemsex had much weaker associations than multi-partner chemsex. Therefore, men engaged in multi-partner sex should be priorities for future tailored chemsex interventions.
4. Drug use services and HIV/PrEP/Sexual health services have closely overlapping client groups among MSM and may greatly benefit from service integration.

ABSTRACT

Introduction: In the last decade diagnoses of most sexually transmitted infections (STIs) have risen among men-who-have-sex-with-men (MSM). Although a significant proportion of this is likely due to increased STI screening, understanding the role of behavioural drivers remains critical. We measure associations between stimulant use to enhance and prolong sexual experiences (chemsex) and bacterial STI diagnoses in UK MSM, individually considering HIV-diagnosed MSM, PrEP users and other MSM.

Methods: We used UK 2017-18 European MSM Internet Survey data (n=9,375). We constructed causal inference models using multivariable logistic regression, calculating adjusted odds ratios (aORs) and 95% confidence intervals (95%CI) of associations between participation in recent (≤12 months): exclusively dyadic or multi-partner chemsex versus no chemsex; with recent self-reported diagnoses of syphilis, gonorrhoea, and chlamydia.

Results: Among MSM with an HIV-diagnosis 25% of users indicated recent multi-partner chemsex, versus 28% of PrEP users and 5% of other MSM. Adjusting for age; ethnicity; UK-birth; cis-trans status; sexual identity; education; settlement size; and relationship status; participation in recent multi-partner chemsex versus no chemsex was associated with greater odds of recent syphilis, gonorrhoea and chlamydia diagnosis. aORs for recent syphilis, gonorrhoea and chlamydia diagnoses were; 2.6 (95%CI;1.7-4.1), 3.9 (95%CI;2.6-5.8), and 2.9 (95%CI;1.9-4.3) respectively in HIV-diagnosed MSM; 1.9 (95%CI;1.1-3.3), 2.9 (95%CI;2.0-4.2), and 1.9 (95%CI;1.3-2.8) respectively in PrEP users; and 4.0 (95%CI;2.3-6.9), 2.7 (95%CI;1.9-3.8) and 2.3 (95%CI;1.6-3.4) respectively in other MSM. Conversely, exclusively dyadic chemsex had no significant associations with bacterial STI diagnoses among HIV-diagnosed MSM, only gonorrhoea [aOR 2.4 (95%CI;1.2-4.7)] among PrEP users and syphilis [aOR 2.8 (95%CI;1.4-5.6)] among other MSM.

Discussion: Multi-partner chemsex may drive the association between chemsex and bacterial STI diagnoses and thus should be the focus of future tailored chemsex interventions. Additionally, PrEP acceptability among MSM, and particularly chemsex participants has generated an emergent group suitable for such interventions.

Key words: Sexual and Gender Minorities, Syphilis, Gonorrhoea/Gonorrhea, Chlamydia trachomatis, HIV Infections, Men-who-have-sex-with-men, Chemsex, Pre-Exposure Prophylaxis, Illicit drugs, Substance-Related Disorders, Sexual Health.

Introduction

Across England, between 2015 and 2019 the total number of bacterial STIs (inclusive of syphilis, gonorrhoea and chlamydia) diagnosed among men-who-have-sex-with-men (MSM) increased from 39,283 to 62,915, representing a 60% increase. Contributing to this, syphilis diagnoses increased by 40%, gonorrhoea by 51% and chlamydia by 83%. Rates of gonorrhoea diagnoses in MSM also having increased 6.4-fold between 2009 and 2018.[1]

Among MSM, substances are sometimes used to enhance and prolong sexual intercourse, commonly referred to as 'chemsex'.[2] In the UK, the most common chemsex substances are crystal methamphetamine (crystal meth), gamma-hydroxybutyric acid/gamma-butyrolactone (GHB/GBL), and mephedrone (MCAT), however other substances (often stimulants) are used.[3-5] In the UK chemsex occurs more frequently among HIV-positive than HIV-negative MSM.[6,7]

Due to the decrease in inhibitions, the prolonged nature of mucosal contact during chemsex sessions, and the substantial opportunity for multi-partner encounters involving condomless sex, there is increased STI transmission risk.[8-12] Injecting of substances, known as 'slamming', carries significantly greater risk of bloodborne viruses such as HIV, hepatitis B and hepatitis C, especially when injecting equipment is shared.[13] However, injecting practices are unlikely to drive the transmission of bacterial STIs. Internationally, studies have shown chemsex to be associated with syphilis, gonorrhoea, and chlamydia aquisiton.[14,15] Further UK based data highlights increased odds of gonorrhoea diagnosis associated with use of crystal meth and GHB/GBL.[16,17] However, limitations of these have included: aggregation of bacterial STIs as a single outcome due to small samples; focus on a single STI;[16] or the inability to assess the subgroups of MSM, including PrEP users,[17] who may have different levels of interactions with sexual health services and differences in related needs.

Public health responses to bacterial STIs require a multidisciplinary approach, transmission prevention strategies, screening and diagnostics, and intelligent allocation of antibiotics.[18] As such we need to identify key risk factors among MSM to signal which individuals would benefit from extra sexual health services and support.[19]

The objective of this study is to examine the associations and potential effect of participation in chemsex on the acquisition of syphilis, gonorrhoea, and chlamydia to help address the relatively sparse amount of quantitative data available.[6,7]

Methods

Study Population

We used data from UK-based respondents to the European MSM Internet Survey (EMIS-2017). EMIS-2017 was an online self-completion survey, predominantly advertised through online dating applications, conducted in 33 languages with 127,000 participants from all countries of Europe recruited between 15 October 2017 and 31 January 2018 (www.emis2017.eu).[20,21] Eligibility for the survey included that respondents had to indicate they wished to take part in the survey by confirming that: they had read and understood the nature and purpose of the study; identified as a man; were at or over the age of homosexual consent in the country they lived in (16 in the UK); have had sex with men and/or were sexually attracted to men. In our analysis we only used data from respondents who indicated current residence in the UK. Further eligibility criteria for this analysis included responses with non-discrepant answers, had ever engaged in sexual activity with a man and had no missing data to questions regarding the exposure variable or adjusted covariates.

Outcome and Exposure

Our exposure is participation in chemsex in the previous 12 months (henceforth, 'recently'). We categorise our exposure variable into 'no recent chemsex', 'recent exclusively dyadic chemsex' (with one partner at a time), and 'recent multiple-partner chemsex'. We form these categorisations by combining responses for participation in chemsex, in line with EMIS-2017 question phrasing as 'using a stimulant drug to make sex more intense or last longer', stimulant drugs constituting of: ecstasy/MDMA, cocaine; amphetamine (speed); crystal methamphetamine (Tina, Pervitin); mephedrone; and ketamine, and responses to an additional question concerning the combination of stimulant drugs and sex with 'more than one man at the same time'.

Our outcome variables are recent (within the previous 12 months) self-reported diagnoses of bacterial STIs. EMIS-2017 recorded the recency of a respondent's latest diagnosis (if any) for syphilis, gonorrhoea, and chlamydia. For each of these bacterial STIs we then construct a binary variable, taking a positive value if diagnosis occurred recently.

Covariates

Covariates identified which were measured in EMIS-2017 were: age, categorised as <25, 25-39, and ≥40; ethnicity, categorised as White British, White other, Asian, Black, Mixed, and Other; UK-born, yes or no; cis-trans status, categorised from current gender identity of participants as either a cis man (assigned male at birth and identifies as a man) or a trans man (assigned female at birth and identifies as a man, or identifies as a trans man regardless of sex assigned at birth); sexual identity, categorised as homosexual, bisexual, or other; time spent in full-time post-16 education, categorised as <2 years, 2-5 years, and >5 years; population of current place of residence (settlement size), categorised as <100,000, 100,000-999,999 and ≥1,000,000; relationship status, categorised as having a steady partner ('a lover or spouse that means you are not 'single'"), single, or other ('I'm not sure/it's complicated'); HIV-diagnosis and current PrEP use (daily or when needed), categorised as HIV-diagnosed, or as not HIV-diagnosed, with those who are not HIV-diagnosed further stratified by current PrEP use into PrEP users and PrEP non-users; condom use during anal intercourse with non-steady partners in the previous 12 months, categorised as consistent, inconsistent or never; number of non-steady sexual partners in the previous 12 months (any sexual activity), categorised as ≤10 or >10. Other covariates identified which were not directly measured by EMIS-2017 include: frequency of sexual activity (including all types of sexual activity and with all partners); frequency of STI testing; and actual acquisition of each bacterial STI. A subset of these covariates is adjusted for in our main analysis based on the rules of causal inference applied to the causal graph (Figure 1).[22,23]

Data Analysis

First, we describe the number of the respondents meeting the eligibility criteria and thus included in the analysis, along with demographic characteristics of this study population. We then build a causal graph to define the set of covariates needed to adjust on, in order to control known confounding using the rules of causal inference (Figure 1).[22,23] Using causal inference methodology, we identified the set of covariates to adjust on to be: age; ethnicity; UK-born; cis-trans status; sexual identity; education; settlement size; relationship status; HIV status and PrEP use. However, we stratify rather than adjust our results by HIV-diagnosis status and PrEP use to examine these groups individually. The covariates adjusted upon were all directly obtained from the EMIS-2017 dataset.

We calculate the adjusted odds ratios (aORs) with 95% confidence intervals (95%CIs) of participation versus non-participation in recent chemsex with recent diagnoses of bacterial STIs using multivariable logistic regression models, with input variables following from the necessary adjustment set identified by the constructed causal graph. Variables were added in the same order in each multivariable model depending on the proximity to our primary outcome. Complete-case analysis was performed, excluding respondents from the model where there were missing data entries for any of the model variables.

We also performed sensitivity analyses on our main results using available data on the remaining covariates, where in addition to the set of parameters identified necessary for adjustment identified by the causal graph we also adjusted for: (1) consistency of condom use during anal intercourse with non-steady partners; (2) number of recent non-steady partners. This was to examine results which could arise from alternative 'causal graph' structures resulting from alternative assumptions about the relationship between identified covariates. Fully expanded tables for all models, including the sensitivity analyses and an aggregated model for all MSM can be found in the supplementary material (Tables S1-S8).

Analysis was carried out in STATA v15. Ethical approval for the original study was granted by the LSHTM Research Ethics Committee. Informed consent from participants was included in the survey via a tick box.

Results

Study population

The UK dataset consisted of 11,889 respondents. To increase the quality of the data we excluded 1,034 respondents with logically inconsistent responses across variables relating to age and number of sexual partners. We excluded a further 235 who did not indicate ever having had any sexual contact with another man. Lastly, we excluded 1,169 responses with missing data associated with adjusted covariates (included in the main or sensitivity analyses) and 76 responses with missing data regarding recent chemsex exposure. Resulting in a total of 9,375 eligible responses. As can be seen in Table 1, 99% of respondents were cis-male, 16% were <25, 40% were 25-39 and 44% were ≥40. 76% identified as White British and 73% were born in the UK. 84% identified as gay/homosexual and 53% were single. 10% had diagnosed HIV, while 8% of MSM were PrEP users. Among all MSM, 13% reported having engaged in chemsex recently (in the past 12 months). Of those who had participated in recent chemsex, 65% reported at least one instance of recent multi-partner chemsex.

Chemsex and bacterial STI acquisition

Multivariable logistic regression models (Table 2 and supplementary Tables S1-S4) show that participation in recent multi-partner chemsex versus no recent chemsex have associated aORs of 2.6 (95%CI; 1.7-4.1; p<0.001) for syphilis 3.9 (95%CI; 2.6-5.8; p<0.001) for gonorrhoea and 2.9 (95%CI; 1.9-4.3; p<0.001) for chlamydia diagnoses in HIV-diagnosed MSM and aORs of 1.9 (95%CI; 1.1-3.3; p=0.018) for syphilis 2.9 (95%CI; 2.0-4.2; p<0.001) for gonorrhoea and 1.9 (95%CI; 1.3-2.8; p=0.001) for chlamydia diagnoses in PrEP users. This contrasts to aORs of 4.0 (95%CI; 2.3-6.9; p<0.001) for syphilis, 2.7 (95%CI; 1.9-3.8; p<0.001) for gonorrhoea; and 2.3 (95%CI; 1.6-3.4; p<0.001) for chlamydia diagnoses among other MSM. Conversely, exclusively dyadic chemsex had no significant associations

with bacterial STI diagnoses among HIV-diagnosed MSM, only gonorrhoea [aOR 2.4 (95%CI; 1.2-4.7; p=0.014)] among PrEP users and syphilis [aOR 2.8 (95%CI; 1.4-5.6; p=0.002)] among other MSM.

Sensitivity analyses (Table 3 and supplementary Tables S5-S8), indicate that associations between recent syphilis and gonorrhoea diagnoses with recent multi-partner chemsex remain significant, although these associations are weakened, particularly in the group with the lowest STI rates. However, the association between a recent chlamydia diagnosis and recent multi-partner chemsex among PrEP non-users becomes non-significant when also adjusting for the number of recent non-steady partners or consistency of condom use. This may suggest that multi-partner chemsex is in parts a proxy for the number of sexual partners and associated STI testing activities.

Discussion

This study found that all MSM subgroups included men reporting recent use of stimulants to prolong or enhance sexual intercourse in a setting with multiple sexual partners had higher odds of recently being diagnosed with syphilis, gonorrhoea and chlamydia. The associations for recent exclusively dyadic chemsex compared with no chemsex were consistently much weaker and were only significant among PrEP users for gonorrhoea and among PrEP non-users for syphilis. Among all MSM who had participated in any recent chemsex, 65% had participated in multi-partner chemsex. While, 25% of all HIV-diagnosed MSM and 28% of PrEP users had participated in multi-partner chemsex, as compared to only 5% of other MSM.

The results of our study are consistent with previous UK data from EMIS-2010 looking at gonorrhoea diagnoses, which found an associated aORs of 1.9-2.2 if respondents had participated in chemsex (varying by specific substance used during chemsex).[16] Furthermore, our study projects similar observations to a London study which found 2.8-fold increased adjusted odds of 'bacterial STI' acquisition among chemsex participants.[11] Outside of the UK, a recent study from Amsterdam has also highlighted that engagement in chemsex in the past 6 months had a crude odds ratio of 1.7 for

diagnosis with a bacterial STI,[15] while a study from Norway that also used self-reported STI diagnoses calculates an aORs of 4.9 and 1.6 for syphilis and chlamydia diagnoses respectively among recent participants in chemsex.[24] This analysis however is the first to show an association between participation in chemsex and its association with all bacterial STIs by MSM subgroup.

Given participation in chemsex seems to increase the risk of acquiring bacterial STIs, interventions aimed at empowering MSM to understand the risks of bacterial STIs could be extremely beneficial.[25] However, MSM have been shown to be less concerned by the risks of bacterial STIs than those of HIV and hepatitis C, although levels of concern have been shown to be associated with knowledge regarding individual STIs.[25] HIV-negative MSM in particular have much lower levels of knowledge concerning the risks of bacterial STIs.[26] Furthermore, chemsex has also been associated with a range of morbidities, such as addiction, HIV, hepatitis C and other harms (for example, in users of methamphetamines, suicidal ideation)[24,27] which may pose further challenges in encouraging chemsex participants to prioritise consideration of the additional risks of bacterial STIs.

Our analysis expands the evidence for highlighting the inequalities of bacterial STI diagnoses among subgroups of MSM. HIV-diagnosed MSM and PrEP users proportionally were 5 to 6 times more likely to have a recent diagnosis of syphilis, gonorrhoea or chlamydia than other MSM. Given that over a quarter of HIV-diagnosed MSM and PrEP users participated in recent multi-partner chemsex and the highly elevated odds of bacterial STI diagnoses associated with this activity in every group, our results also highlight the critical importance of offering comprehensive harm reduction strategies targeted at bacterial STIs alongside PrEP and HIV care. Antibiotic-PrEP is one such potential solution and is a growing research area. However, reservations remain regarding implications on long-term side effects as well as antimicrobial resistance,[28] with robust evidence lacking in favour of antibiotic-PrEP. It is notable and of high concern that a small minority of MSM are self-sourcing antibiotics online for this purpose already.[28] We must ensure that conventional wisdom and professional advice do not fall by

the wayside as MSM begin to translate the success of HIV-related PrEP to bacterial STIs and self-source antibiotic-PrEP.

EMIS-2017 contains a wealth of demographic and behavioural data and was completed by over 11,000 MSM in the UK.[20,21] This has been an important factor in being able to control confounding while achieving the statistical power necessary to examine these research questions and perform detailed subgroup analysis. The data are recent, which is important due to sexual and drug use behaviours being subject to constant evolution.[29]

However, as with all large MSM datasets which include detailed sexual behaviour, the EMIS-2017 dataset is likely to be biased towards more highly educated and higher risk MSM.[29] MSM frequenting internet sites used for recruitment, and in particular dating sites, may also differ with regard to chemsex, bacterial STI rates or other covariates compared to MSM more generally. Whilst the findings are not generalisable to the wider MSM population, respondents do represent the target group of highly sexually active and therefore most at-risk men.

Furthermore, chemsex is a social category into which different stakeholders put different behaviours.[30] Our definition is based on qualitative research with men in South London who self-identified as engaging in chemsex.[8] We acknowledge that other stakeholders may define chemsex differently, both in terms of the types of drugs used (ie. to include drugs other than stimulants) and to exclude the motivations of intensification and temporal extension (or indeed to include other motivations or specific sexual behaviours).

Another strength of our analysis is the use of causal inference. Although EMIS-2017 data is cross-sectional in nature and thus that exact time ordering was not always possible to establish, much of the ordering can be assumed. For instance, sociodemographic factors, such as age, ethnicity, sexual identity, education, and whether the respondent was born in the UK were assumed to be present prior to the completion of the survey, and indeed true prior to the 12 month period of interest for our

exposure and outcome. Our exposure and outcome measure however, had a recall period of 12 months, which does mean that temporal ordering of these events cannot strictly be established. However, chemsex has specific mechanisms by which it leads to the acquisition of bacterial STIs leading to a confident assertion of causality between our exposure and outcome. An accurate measure of our causal effect size however will be limited by our ability to say for certain in what order people participated in chemsex or were diagnosed with an STI. However, 47% of respondents who indicated participating in chemsex in the last 12 months, did so in the past 4 weeks, which indicates chemsex is an ongoing behaviour. What we can say with confidence however is that we have accurately described the association of our exposure and outcome variable while controlling for known confounders. Our results are likely to provide a good estimate for the causal effect of recent chemsex on recent STI diagnosis, but with the assertion limited by the above reasoning. We also performed sensitivity analyses including additional covariates which were available from the EMIS-2017 data, to provide alternative models which could arise from varying covariate relationship assumptions within the 'causal graph'. Encouragingly, the majority of associations between recent multi-partner chemsex and recent syphilis remained significant, giving us further confidence in our findings.

Variables were all self-reported, which is generally the standard method of collection for sexual and drug related behaviours, even though self-reported data is affected by recall bias alongside respondent understanding and familiarity with the content of the questions posed. However, formal infection diagnosis data would have been advantageous, as although there is a direct connection between STI acquisition and STI diagnosis, we acknowledge that respondents who may have had undiagnosed bacterial STIs in this period may not be equally distributed across our model variables. This is particularly important as most PrEP using MSM and, to a lesser extent HIV-diagnosed men, undergo standardised clinical testing routines, thus increasing the chance that asymptomatic and/or self-limiting STIs are diagnosed. This explains the inverse order of aORs for chemsex when compared to the rates of diagnosed STIs across the three sub-groups. Ascertaining actual STI acquisition versus diagnosis of STIs in a sample of this size would be extremely challenging, however we believe those

being diagnosed will generally be representative of those who will have acquired bacterial STIs. Other unknown or unmeasured confounding may also have played a role in limiting the accuracy of our results however every effort was made to minimise this impact. This would include possible self-sourced antibiotics taken as chemoprophylaxis which may be an important factor in understanding STI acquisition going forward.

In conclusion, recent exclusively dyadic chemsex had much weaker associations than multi-partner chemsex with diagnosis of bacterial STIs, indicating that men engaged in multi-partner chemsex should be primarily targeted for future tailored interventions. Drug use services and health services tailored to HIV-diagnosed MSM and PrEP users have closely overlapping client groups and may benefit from service integration.

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Demographics and adjusted variables	Number of individuals (% of total individuals)	Number of individuals participating in any recent chemsex (% of subgroup)	Number of individuals participating in only recent dyadic chemsex (% of subgroup)	Number of individuals participating in recent multi-partner chemsex (% of subgroup)
Total	**9,375 (100)**	**1217 (13)**	**425 (5)**	**792 (8)**
Age				
<25	1,514 (16)	110 (7)	51 (3)	59 (4)
25-40	3,710 (40)	504 (14)	158 (4)	346 (9)
>40	4,101 (44)	603 (15)	216 (5)	387 (9)
Ethnicity				
White British	7,075 (76)	862 (12)	302 (4)	560 (8)
White Other	1,592 (17)	247 (16)	79 (5)	168 (11)
Asian	288 (3)	39 (14)	15 (5)	24 (8)
Black	133 (1)	19 (14)	9 (7)	12 (9)
Mixed	127 (1)	25 (20)	11 (9)	14 (11)
Other/missing	160 (2)	23 (16)	9 (6)	14 (9)
Born in the UK				
Yes	6,855 (73)	839 (12)	302 (5)	537 (8)
No	2,520 (27)	378 (15)	123 (4)	255 (10)
Cis-trans status*				
Cis man	9,259 (99)	1,206 (13)	417 (5)	789 (9)
Trans man	116 (1)	11 (9)	8 (7)	3 (3)
Sexual identity				
Gay/homosexual	7,887 (84)	1,074 (14)	362 (5)	712 (9)
Bisexual	1,071 (11)	100 (9)	44 (4)	56 (5)
Other	417 (5)	43 (10)	19 (5)	24 (6)
Time spent in full time post-16 education				
<2 years	1,169 (13)	152 (13)	48 (4)	104 (9)
2-5 years	4,395 (47)	536 (12)	205 (5)	331 (8)
>5 years	3,811 (41)	529 (14)	172 (5)	353 (9)
Settlement size				
Small (<100,000)	3,117 (33)	282 (9)	103 (3)	178 (6)
Medium (100,000 – 999,999)	3,424 (37)	384 (11)	148 (4)	236 (7)
Large (>1,000,000)	2,834 (30)	552 (19)	174 (6)	378 (13)
Relationship status				
Single	4,966 (53)	664 (13)	240 (4)	424 (9)
Steady partner	3,828(41)	464 (12)	159 (5)	305 (8)
Other	581 (6)	89 (15)	26 (5)	63 (11)
PrEP use and HIV Status				
PrEP non-users**	7,669 (82)	643 (8)	299 (4)	344 (5)
PrEP users**	740 (8)	250 (34)	44 (6)	206 (28)
HIV-diagnosed	966 (10)	324 (34)	82 (8)	242 (25)
Condom use during anal intercourse with non-steady partners				
Not applicable	3,355 (36)	195 (6)	134 (4)	61 (2)
Always	1,823 (20)	120 (7)	56 (3)	64 (4)
Inconsistent	3,423 (36)	716 (21)	186 (5)	530 (16)
Never	774 (8)	186 (24)	49 (6)	137 (18)
Non-steady partners in the past 12 months				
0	2,388 (26)	127 (5)	87 (4)	40 (2)
1-10	4,047 (43)	399 (10)	184 (5)	215 (5)
>10	2,940 (31)	691 (24)	154 (5)	537 (18)

Table 1: Descriptive data of covariates of the study sample. *cis-trans status is categorised from current-gender identity of participants as either a cis man (ie. assigned male at birth and identifies

as a man) or a trans man (ie. assigned female at birth and identifies as a man, or identifies as a trans man regardless of sex assigned at birth). **PrEP users and MSM not using PrEP only include MSM who have never been diagnosed with HIV.

MSM Subgroup and participation in chemsex in the past 12 months	n (% of total individuals)	Syphilis in past 12 months n (% of subgroup)	aOR* (95%CI)	p value†	Gonorrhoea in past 12 months n (% of subgroup)	aOR* (95%CI)	p value†	Chlamydia in past 12 months n (% of subgroup)	aOR* (95%CI)	p value†
HIV-diagnosed MSM										
No chemsex	642 (66)	48 (8)	1.0		66 (10)	1.0		69 (11)	1.0	
Yes, exclusively dyadic chemsex	82 (8)	4 (5)	0.5 (0.2-1.5)	0.225	11 (13)	1.2 (0.6-2.5)	0.596	5 (6)	0.5 (0.2-1.3)	0.171
Yes, including multiple partners	242 (25)	46 (19)	2.6 (1.7-4.1)	<0.001	78 (32)	3.9 (2.6-5.8)	<0.001	66 (28)	2.9 (1.9-4.3)	<0.001
PrEP users**										
No chemsex	490 (66)	37 (8)	1.0		97 (20)	1.0		106 (22)	1.0	
Yes, exclusively dyadic chemsex	44 (6)	3 (7)	0.9 (0.3-3.0)	0.817	15 (34)	2.4 (1.2-4.7)	0.014	8 (18)	0.7 (0.3-1.7)	0.468
Yes, including multiple partners	206 (28)	27 (13)	1.9 (1.1-3.3)	0.018	84 (42)	2.9 (2.0-4.2)	<0.001	69 (34)	1.9 (1.3-2.8)	0.001
PrEP non-users**										
No chemsex	7,026 (92)	80 (1)	1.0		337 (5)	1.0		285 (4)	1.0	
Yes, exclusively dyadic chemsex	299 (4)	10 (3)	2.8 (1.4-5.6)	0.002	22 (7)	1.6 (1.0-2.5)	0.058	12 (4)	0.9 (0.5-1.7)	0.836
Yes, including multiple partners	344 (4)	17 (5)	4.0 (2.3-6.9)	<0.001	43 (13)	2.7 (1.9-3.8)	<0.001	33 (10)	2.3 (1.6-3.4)	<0.001

Table 2: Multivariable analyses for association between recent (in the past 12 months) diagnosis of gonorrhoea, syphilis and chlamydia. With chemsex categorised as: no participation in recent chemsex; recent chemsex with no instances of recent multi-partner chemsex; and at least once instance of recent multi-partner chemsex. Variables adjusted for include: age; ethnicity; UK-born; cis-trans status; sexual identity; education level; settlement size; and relationship status, with results shown separately for key subgroups of the MSM population. *Calculated from logistic regression. †Likelihood ratio test. CI Confidence Interval; OR Odds Ratio. ** PrEP users and MSM not using PrEP only include MSM who have never been diagnosed with HIV.

Sensitivity scenario and MSM subgroup	Syphilis in the past 12 months aOR* (95%CI)	p value†	Gonorrhoea in past 12 months aOR* (95%CI)	p value†	Chlamydia in past 12 months aOR* (95%CI)	p value†
No additional adjustments						
HIV-diagnosed MSM	2.6 (1.7-4.1)	<0.001	3.9 (2.6-5.8)	<0.001	2.9 (1.9-4.3)	<0.001
PrEP users***	1.9 (1.1-3.3)	0.018	2.9 (2.0-4.2)	<0.001	1.9 (1.3-2.8)	0.001
PrEP non-users***	4.0 (2.3-6.9)	<0.001	2.7 (1.9-3.8)	<0.001	2.3 (1.6-3.4)	<0.001
Additionally adjusting for consistency of condom use with non-steady partners**						
HIV-diagnosed MSM	1.9 (1.2-3.1)	0.006	2.6 (1.7-3.9)	<0.001	2.0 (1.3-3.0)	0.001
PrEP users***	1.8 (1.0-3.1)	0.035	2.8 (1.9-4.1)	<0.001	1.7 (1.2-2.5)	0.005
PrEP non-users***	2.9 (1.6-5.0)	<0.001	1.7 (1.2-2.4)	0.003	1.4 (0.9-2.0)	0.110
Additionally adjusting for number of non-steady partners**						
HIV-diagnosed MSM	1.8 (1.1-2.8)	0.020	2.4 (1.6-3.7)	<0.001	1.7 (1.1-2.6)	0.011
PrEP users***	1.9 (1.1-3.3)	0.020	2.6 (1.8-3.9)	<0.001	1.7 (1.2-2.5)	0.004
PrEP non-users***	2.9 (1.7-5.1)	<0.001	1.7 (1.2-2.5)	0.002	1.5 (1.0-2.2)	0.059
Additionally adjusting for number and consistency of condom use with non-steady partners**						
HIV-diagnosed MSM	1.6 (1.0-2.7)	0.043	2.2 (1.5-3.4)	<0.001	1.6 (1.1-2.5)	0.027
PrEP users***	1.8 (1.0-3.1)	0.035	2.7 (1.8-3.9)	<0.001	1.6 (1.1-2.4)	0.013
PrEP non-users***	2.5 (1.4-4.4)	0.001	1.5 (1.0-2.1)	0.029	1.2 (0.8-1.8)	0.362

Table 3: Sensitivity analyses for association between recent (in the past 12 months) diagnosis of gonorrhoea, syphilis and chlamydia with recent multi-partner chemsex in MSM. Results shown versus the comparator of no recent chemsex. *Adjusted odds ratios calculated from logistic regression. **Base variables adjusted for: age; ethnicity; UK-born; cis-trans status; sexual identity; education level; settlement size; and relationship status. †Likelihood ratio test. CI Confidence Interval; OR Odds Ratio. ***PrEP non-users and PrEP users only includes MSM who have never been diagnosed with HIV.