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**Sex, drugs, and sexually transmitted infections: a cluster analysis among men who have sex with men in Amsterdam and surrounding urban regions, the Netherlands**

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## **Abstract (max 249/250)**

### **Background**

Men who have sex with men (MSM) are at high risk for sexually transmitted infections (STI) and often have sex while under the influence of drugs (sexualized drug use). We aimed to identify subgroups of MSM in Amsterdam and in surrounding urban regions with distinctive patterns of sexualized drug use and their association with STI.

### **Methods**

In this cross-sectional study, data on MSM were collected at STI clinics in the Netherlands between September-December 2017. Information on drug use, sociodemographics and sexual risk behavior, including lab-confirmed STI, -i.e. chlamydia, gonorrhea, syphilis and HIV- was collected and compared between Amsterdam and surrounding urban regions. *K*-median cluster analysis was used to identify subgroups with similar drug use patterns, which were then linked to sexual behavior and STI.

### **Results**

We included 4461 MSM who were median 35 years old (IQR=27-47) and were mostly Dutch (56.9%). Use of all drugs were reported more often in Amsterdam compared to surrounding regions ( $p < 0.001$ ). We identified five different subgroups based on sexualized drug use among Amsterdam participants and four subgroups in surrounding regions. In both regions, poly-drug use clusters were defined by higher numbers of sexual partners (median range 8-15 vs 4-6) and higher STI prevalence (range 23.1%-36.2% vs 18.7% - 20.6%) compared to clusters of no drug use or only alcohol use.

### **Conclusion**

Given the high prevalence of risk behavior and STIs, MSM in urban settings partaking in sexualized

drug use combining various drugs might benefit from tailored outreach, screening, and sex and drug use interventions.

## INTRODUCTION

Compared to the heterosexual population, men who have sex with men (MSM) are more likely to use recreational drugs and to engage in sexual activity associated with high risk of contracting sexually transmitted infections (STI)(1, 2). MSM who have sex while under the influence of drugs (hence forward sexualized drug use) are known to increase sexual risk behavior, such as condomless sex with a human immunodeficiency virus (HIV)-serodiscordant partner and to be at heightened risk of contracting STI and HIV (3-9). In particular, chemsex – usually defined as the use of  $\gamma$ -hydroxybutyrate (GHB)/ $\gamma$ -butyrolactone (GBL), methamphetamine (Crystal Meth) and mephedrone during sex – has been described as a major driver of STI/HIV infection(10) and a recent study has reported an increase in its use over the last few years(11). Of concern, chemsex is associated with drug overdosage, hospitalization for both physical and mental disorders, as well as other societal consequences (e.g. unemployment)(12, 13). Reasons for sexualized drug use often described by users are: increased sexual arousal, increased sexual confidence and enhanced performance(14, 15).

In a previous cross-sectional study of MSM in Amsterdam with high-risk sexual behavior, we were able to identify five clusters of reported sexualized drug use(16). Based on these clusters, STI prevalence was 22.9% among MSM with “polydrug” use, 17.5%-7.6% in clusters with more distinct patterns of drug use (i.e. erectile dysfunction drugs; alcohol and poppers; and alcohol alone), and 1.9% in a cluster with no drug or alcohol use during sex. Notwithstanding the potential use of these clusters as a means to identify individuals at risk of STI/HIV, these findings were obtained from cohort data of MSM who engaged in an ostensibly higher level of at-risk behavior than MSM in a non-research setting. Given that Amsterdam is an international metropole with a large MSM community, it remains to be determined if similar clustering patterns are also observed in MSM living in urban regions outside Amsterdam(17-19). Most studies on chemsex have been published on MSM residing in cities with large MSM populations, such as London, Barcelona and Manchester(1, 4, 5, 7-

9, 13-16) Therefore, the types and characteristics of drug use could be different in urban settings with smaller MSM populations. These differences could have implications on the effectiveness of interventions aimed to minimize harm related to sexualized drug use and allow for tailored approaches and test policies in different urban settings.

The aims of this study were (1) to assess differences in sexualized drug use among MSM in Amsterdam and surrounding urban regions (2) to assess patterns in sexualized drug use, as determined by identifying clusters of drug use, and (3) to assess associated risk behavior and STI prevalence.

## **METHODS**

### **Study design**

In the Netherlands, STI clinics managed by public health services (PHS) provide STI testing services anonymously and free of charge. Demographics and sexual behavior data are routinely collected. Data from 24 clinics covering all regions of the Netherlands are merged into a centralized, nation-wide database by the National Institute of Public Health and the Environment (RIVM).

In this cross-sectional study, data were restricted to MSM attending Dutch STI clinics for three consecutive months between September-December 2017. During this period, additional data on drug use were collected. Ethical approval for the study was not necessary following Dutch law, as the study used routinely collected, de-identified surveillance data.

### **Data collection and definitions**

Socio-demographic characteristics and information on sexual behavior and other STI risk factors in the preceding 6 months were routinely collected, including number of partners, being

notified by a sex partner or having STI-related symptoms. MSM were defined based on self-declared sexual behavior (having had sex with a man in the last 6 months). STI screening included nucleic acid amplification testing (NAAT) for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at three anatomical locations (pharyngeal, urethral and anorectal) and serum testing for syphilis and HIV.

Data on drug use were collected either via computer-assisted self-interviewing or during consultation by a health care professional. All MSM were asked if they used drugs or were inebriated before or during sex in the past 6 months and if so, which drugs they used from a predefined list. This list included the following substances: alcohol, amphetamine (speed), cannabis, cocaine, GHB/GBL, ketamine, methamphetamine (crystal meth), mephedrone, nitrites, 3,4-methylenedioxy-N-methylamphetamine (XTC/MDMA) or other drugs. Any drug use was defined as self-declared use of at least one of the drugs mentioned above, including alcohol, within the past six months.

Educational level was divided into low (primary school and lower secondary vocational education), medium (intermediate secondary general education, higher secondary general education, senior secondary vocational education and pre-university secondary education) or high (higher professional or university education). Ethnicity was defined according to Statistics Netherlands on the basis of country of birth and maternal and paternal country of birth(20).

### **Statistical analysis**

To prevent reporting bias from centers with excessive missing data, only STI clinics where more than 90% of visitors had data on drug use were included. We then defined two geographical regions based on testing centers with available data: Amsterdam and surrounding urban regions (all STI



clinics outside the Amsterdam region). Participant characteristics were described and compared between those from Amsterdam versus surrounding urban regions. For individuals with more than one visit during the study period, any visit after the initial visit was excluded.

To define drug use clusters, we employed a *k*-medians clustering algorithm with the Jaccard similarity measure (specified for binomially distributed data)(21) using the 'flexclust' package in R(22). The optimal number of clusters,  $k=(2, 3, \dots, 10)$ , was based on maximizing the Caliński and Harabasz pseudo-F index (with larger indices representing more distinct clustering). The reproducibility of the clustering method was tested by repeating the *k*-median segmentation algorithm on 50 bootstrapped dataset replicas and calculating the adjusted Rand indices (measuring the similarity of the clusters from bootstrapped data to those obtained from the original data)(23). The final choice of *k* was determined by a high Caliński and Harabasz pseudo-F index and high density peak of bootstrapped adjusted Rand indices. After defining *k*, cluster groups were assigned to each observation based on the similarity measure above, meaning that every individual in the analysis was classified into one of the identified clusters.

Correlations between drugs used were determined using tetrachoric correlations and visualized in networks using Cytoscape v3.6.1 (24).

Demographic characteristics, sexual behavior and STI prevalence were compared between the identified cluster groups. All comparisons were tested using Pearson's  $\chi^2$  test for categorical variables and rank-sum tests for continuous variables, unless specified otherwise. In sensitivity analysis we repeated cluster analysis without MSM who were notified by a sex partner or had STI related symptoms. Moreover, multinomial logistic regression was used to correct STI prevalence for age, ethnicity and HIV-status.

Statistical analyses were performed with STATA Intercooled 13.1 (STATA Corporation, College Station, TX, USA) and R (v3.4.1, R Foundation for Statistical Computing, Vienna, Austria). Significance was defined as a *p*-value <0.05.

## RESULTS

### Description of the study population

Between September 2017 and December 2017, 11300 consultations involving MSM were recorded. Five centers recorded >90% data on drug use (mean 99.6%, range=98.9%-100%). The other 19 centers had a mean 45.9% (range=28.8%-76.5%) of consultations with available drug use data and were excluded. This resulted in 5060 of 11300 (44.8%) consultations performed at included centers. We excluded 582 repeat visits during the study period and 17 visits without data on drug use. Thus, 4461 MSM were analyzed: 3201 from the Amsterdam PHS and 1260 from PHS in surrounding urban regions (Flevoland, Hollands Noorden, Den Haag and Utrecht).

Participant characteristics are summarized in Table 1. The overall median age was 35 years (IQR=27-47), 43.1% were of non-Dutch ethnicity and 64.6% had a high educational level. In Amsterdam, participants were more often known to be HIV-positive (19.0% vs 8.3%, *p*<0.001) than in the surrounding urban regions and reported less often having sex with both women and men (8.3% vs 20.0%, *p*<0.001). STI prevalence did not differ per region (22.3% in Amsterdam vs 21.4% in the surrounding urban regions, *p*=0.540). Of the 3714 individuals without a previous HIV-positive diagnosis, 32 (0.9%) were newly diagnosed with HIV.

### Description of drug use

In total, 2445/4461 (54.8%) participants reported sexualized drug use in the preceding 6 months and 234 (5.3%) of whom reported using 5 types of drugs or more. For each drug, a higher proportion was

used in Amsterdam than in the surrounding urban regions ( $p < 0.001$  for all). Alcohol was most often reported respectively in Amsterdam vs surrounding urban regions (42.9% vs 28.6%), followed by XTC (20.2% vs 14.1%), GHB/GBL (17.7% vs 10.2%) and nitrites (19.3% vs 8.3%). Methamphetamine (3.1% vs 0.8%) and mephedrone (1.9% vs 0.5%) were the least frequently reported drugs.

### **Patterns of drug use in Amsterdam and surrounding urban regions**

In Amsterdam, we distinguished five distinct clusters of drug use (Figure 1a). The first cluster ( $n=1287$ , 40.2%) included MSM reporting no or sparse drug use, which was defined herein as “no drug” users. The second cluster ( $n=732$ , 22.9%) consisted of MSM reporting use of mainly alcohol (“alcohol” users). In the third cluster ( $n=469$ , 14.7%), MSM reported use of mostly alcohol, cannabis and nitrites (“alcohol and soft drugs” users), while MSM in the fourth cluster ( $n=380$ , 11.9%) reported mainly XTC, GHB/GBL and alcohol (“XTC, GHB/GBL and alcohol” users). MSM in the fifth cluster ( $n=333$ , 10.4%) reported use of several drugs, including GHB/GBL, nitrites, ketamine, cocaine and methylamphetamine, but relatively low levels of alcohol use (“polydrug” users). Correlation network demonstrated low correlations between alcohol, cannabis and other drugs, but relatively high correlations between ketamine, GHB/GBL and XTC. (Figure 1b).

In the surrounding urban regions, four distinct patterns of drug use emerged (Figure 2a). The first cluster ( $n=732$ , 58.1%) consisted of MSM showing no sexualized drug use (“no drugs” cluster), while the second cluster ( $n=306$ , 24.3%) consisted of MSM using mainly alcohol (“alcohol” cluster). MSM in the third cluster ( $n=94$ , 7.4%) reported use of a broad range of drugs, including cocaine, XTC and GHB/GBL, but was mostly defined by high use of nitrites and alcohol (“polydrug and poppers”). In the fourth cluster ( $n=128$ , 10.2%), MSM reported high use of GHB/GBL and XTC (“GHB/GBL and XTC” cluster). Correlation network analysis again demonstrated relatively high correlations between ketamine, GHB/GBL and methylamphetamine but also between cocaine and amphetamine (Figure 2b).

In a sensitivity analysis, excluding MSM visiting STI clinics with symptoms or after a partner notification rendered comparable results (data not shown).

### **Association of drug-use clusters with sexual behavior and STIs in Amsterdam and surrounding urban regions.**

In Amsterdam, demographic characteristics, sexual behavior and STI prevalence are reported per cluster in Table 2. Compared to “no drug” users, “polydrug” users were more often of Dutch ethnicity (62.2% vs 49.7%,  $p < 0.001$ ) and reported more sexual partners in the preceding 6 months (median 15, IQR=6-30 vs. 5, IQR=3-10,  $p < 0.001$ ) and lower condom use during the last sex act (76.7% vs 59.9%,  $p < 0.001$ ). “Alcohol” users were younger ( $p < 0.001$ ) and more often HIV negative ( $p < 0.001$ ) compared to MSM in other clusters.

“Polydrug” users had the highest proportion diagnosed with an STI (27.3%), which was significantly higher compared to “no drug” users (20.6%,  $p = 0.008$ ) or “alcohol” users (20.3%,  $p = 0.010$ ), but not significantly different from “alcohol and soft drugs” (23.1%,  $p = 0.175$ ) or “XTC, GHB/GBL and alcohol” users (26.6%,  $p = 0.822$ ). No differences in proportion with newly diagnosed HIV were found between clusters ( $p = 0.870$ ). Differences in STI prevalence remained when adjusting for age, HIV-status and ethnicity (see appendix figure 1a).

In the surrounding urban regions, as shown in Table 3, MSM in the “GHB/GBL + XTC” cluster reported the highest number of sexual partners (median 10, IQR=5-15). This was significantly higher than those in the “no drugs” (median 4, IQR=3-8,  $p < 0.001$ ) and “alcohol” clusters (median 5, IQR=3-8,  $p < 0.001$ ) but not significantly higher than those in the “polydrug and nitrites” cluster (median 8, IQR=4-16,  $p = 0.667$ ). MSM in the “alcohol” cluster were younger (median age 28, IQR=23-35) than those in other clusters (median age 37, IQR=26-49,  $p < 0.001$ ).

STI prevalence differed significantly across clusters and was highest in the "GHB/GBL + XTC" cluster (36.2%) and lowest in the "no drugs" cluster (18.7%). Of note, more newly diagnosed HIV infections were found in the "GHB and XTC" cluster compared to the "no drugs" cluster (3.8% vs 0.4%,  $p=0.001$ ). Differences in STI prevalence were similar when adjusting for age, HIV-status and ethnicity (see appendix figure 1b).

## DISCUSSION

Using a large database of STI clinic visitors across the Netherlands, we identified five distinct patterns of drug use in Amsterdam and four patterns in surrounding urban regions. In both regions, MSM belonging to clusters involved in low levels of drug use ("no drugs" clusters) or only alcohol use ("alcohol" clusters) reported lower sexual risk behavior and were less likely to be diagnosed with an STI compared to MSM belonging to other clusters. MSM in clusters established on the use of a combination of different drugs ("Alcohol + poppers", "Polydrug and Poppers", "Polydrug", "XTC + GHB + Alcohol" and "GHB + XTC" clusters) reported higher number of sexual partners and had a higher proportion with detected STIs.

Importantly, we demonstrate that drug use during sexual activity is common among MSM, with 54.8% reporting having used drugs during sex in the preceding 6 months. Examining previous data of MSM at the STI clinic in Amsterdam from 2008-2009, use of GHB/GBL, XTC, and cocaine were similar to our study, but use of nitrites and cannabis were substantially lower compared to the current analysis (38.3% to 19.3% for nitrites and 21.1% to 12.7% for cannabis)(5). This is in contrast to Sewell et al who found an increased use of GHB/GBL from 13.1% to 19.8% between 2013 until 2016 in the UK(11). The discrepancy between studies could be explained by geographical location, the

already relatively high levels of drug use in Amsterdam(g) or a possible recruitment bias as study locations gained awareness as chemsex support centers over time(11).

We noticed marked differences in sexualized drug use between Amsterdam and the surrounding urban regions. Drug use is much more common in Amsterdam than in the surrounding urban regions, hence the importance of stratifying cluster analysis on these regions. Indeed, there were similarities in identified clusters, namely no drug use and only alcohol use. Nevertheless, we did observe nuances in polydrug use when comparing regions. In Amsterdam, more diverse subgroups were identified with different combinations, while in the surrounding urban regions, polydrug use seemed to be limited to a combination of specific drugs, like nitrites, GHB/GBL and XTC. Moreover, in the surrounding urban regions, some of the clusters from Amsterdam were not observed, particularly 'alcohol and poppers' and 'GHB+XTC' clusters. The reasons for such regional differences are difficult to explain. Possibly, the role of peers and partners, along with positive norms for drinking and drug-taking, could shape individual patterns of use, which could be further enhanced by structural or environmental proximity for excessive alcohol and illicit drugs(14, 25) – these external factors could play out differently within regions.

Previous research has consistently identified groups of MSM engaging in polydrug use(6, 7, 16, 26). Some of these studies have also linked polydrug use to sexual behavior(7) or STI prevalence, either self-reported(6) or laboratory-confirmed(16). We add to these previous studies by demonstrating the link between a broad range of clusters and sexual behavior. Although different clusters of "polydrug" use were uncovered between Amsterdam and surroundings, its association with STI prevalence was maintained in both regions. It is generally considered that 'chemsex', one of the more common forms of polydrug use, is the hallmark of increased STI risk(27). Our data would contend that STI risk could lie outside the definition of 'chemsex' and could be quite high even among individuals using other combinations of drugs, particular in non-metropolitan settings.

Public health interventions, such as pre-exposure prophylaxis against HIV in MSM, are soon to roll out in the Netherlands and based on Dutch recommendations, would coincide with STI screening 4 times a year(28). As increasing demand for STI associated care in the Netherlands could be likely, increasing healthcare costs warrant more efficient methods for screening(29). Targeting interventions, particularly among individuals with specific profiles of drug use, could be helpful; however, given that STI prevalence was at 18.7%-20.6%% in the no drug use clusters, other factors would likely be needed to identify MSM at high-risk of having an STI. In addition, the polydrug clusters express the need for STI clinics to collaborate with specialized drug dependency services in order to offer a more appropriate response for the complex needs of some clients.

Several limitations of our study need to be mentioned. First, we recognize this study is not representative for all MSM in the Netherlands, both due to missing data of the remaining STI centers and of MSM not attending STI clinics. MSM in the overall population might show lower sexual risk and drug-use behavior. Second, our previous analysis in high-risk MSM from Amsterdam demonstrated a cluster with high levels of EDD use combined with medium levels of nitrites(16). Since information on EDD use was not collected in the presented database, we were unable to further elaborate the role of these drugs in our study population. Third, data on frequency of use, drug dependency and drug-related harm were lacking. Nevertheless, previous research has suggested low levels of dependency for GHB/GBL, mephedrone, and methyl amphetamine in Amsterdam(1). Lastly, the intent of drug use was not asked, as some studies define chemsex as intentionally using drugs to facilitate or enhance sexual encounters(8, 15). Its association with behavioral or prevalent STI could be rather different. Despite these limitations, our study is one of the first with detailed epidemiologic and behavioral data within the context of a national network of STI clinics, enabling us to compare different geographical regions. This framework also allowed us to include laboratory confirmed STIs, whereas many other studies rely on self-reported STI or only on sexual behavior(4, 6, 7, 9).

Since drug policies are liberal in the Netherlands compared to other countries, drug use might be more openly discussed, making underreporting less likely in our study population(30).

In conclusion, several patterns of sexualized drug use among MSM were identified, with noticeable differences between Amsterdam versus surrounding urban areas. These drug use patterns were closely linked to sexual behavior and STI prevalence. Clusters involving polydrug use, be it in specific combinations or widely varying drugs, were consistently associated with prevalent STIs in both regions. STI risk could be quite high even among individuals using other combinations of drugs than the definition of 'chemsex', particularly in non-metropolitan settings. Nevertheless, further research is required to determine how these clusters could be used to identify individuals for tailored drug-based STI screening and prevention programs.

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### **Competing interest:**

The Public Health Service of Amsterdam received study drug from Gilead for the Amsterdam Pre-exposure prophylaxis (AMPrEP) demonstration project.

### **Contributors:**

RA and SD designed the study. FvA coordinated national data collection. RA and AB performed the data analysis and drafted the manuscript, supported by MvR. All authors commented on drafts of the manuscript and approved the final version.



## Tables and figures

**Table 1. Demographics, sexual behavior, sexual transmitted infections (STI) and drug use of 4461 MSM visiting STI clinics in Amsterdam and surrounding area's (Sept-Dec 2017)**

	Amsterdam (N=3201)		Surrounding STI clinics of Amster- dam <sup>#</sup> (N=1260)		P value
	n	%*	n	%*	
<b>Age (years)</b>					
Median [IQR]	36	[28-47]	33	[25-47]	<0.001
<b>Ethnicity</b>					
Non-Dutch	1480	46.2 %	443	35.2 %	<0.001
Dutch	1721	53.8 %	817	64.8 %	
<b>Educational level <sup>a</sup></b>					
Low & Middle	897	30.9 %	550	46.3 %	<0.001
High	2003	69.1 %	638	53.7 %	
<b>HIV-status <sup>b</sup></b>					
Positive	608	19.0%	105	8.3%	<0.001
Negative	2593	81.0%	1155	91.7%	
<b>Reason for consultation</b>					
Notified of an STI	734	22.9%	235	18.7%	0.002
STI-related symptoms	685	21.4%	204	16.2%	<0.001
<b>Sexual partners</b>					
Men only	2934	91.7%	1008	80.0%	<0.001
Both men and women	267	8.3%	252	20.0%	
<b>Median number of sex partners <sup>c</sup></b>					
Median [IQR]	7	[4-15]	5	[3-10]	<0.001
<b>Condom use during last sex act</b>					
No condom use	2022	64.0%	716	61.1%	0.077
<b>STI diagnosed</b>					
Chlamydia any site	315/3200	9.8%	120/1260	9.5%	0.746
Pharyngeal	48/3193	1.5%	13/1234	1.1%	0.250

Urethral	112/3195	3.5%	32/1252	2.6%	0.101
Anorectal	227/3190	7.1%	93/1209	7.7%	0.511
Of which LGV	25/188	13.3%	4/74	5.4%	0.173
Gonorrhoea any site	389/3205	12.2%	141/1260	11.1%	0.331
Pharyngeal	201/3194	6.3%	55/1235	4.5%	0.019
Urethral	103/3196	3.2%	39/1255	3.1%	0.844
Anorectal	261/3184	8.2%	103/1210	8.5%	0.735
Syphilis <sup>d</sup>	102/3197	3.2%	57/1258	4.5%	0.030
Any bacterial STI <sup>e</sup>	713/3196	22.3%	270/1258	21.4%	0.540
New HIV diagnosis	21/2571	0.8%	11/1143	1.0%	0.658
<b>Drug use during sex <sup>c</sup></b>					
Alcohol	1372	42.9%	360	28.6%	<0.001
Amphetamine	159	5.0%	32	2.5%	<0.001
Cannabis	405	12.7%	107	8.5%	<0.001
Cocaine	386	12.1%	57	4.5%	<0.001
GHB/GBL	565	17.7%	128	10.2%	<0.001
Ketamine	208	6.5%	30	2.4%	<0.001
Nitrites	618	19.3%	105	8.3%	<0.001
Mephedrone	60	1.9%	6	0.5%	<0.001
Methylamfetamine	100	3.1%	10	0.8%	<0.001
XTC	647	20.2%	178	14.1%	<0.001
Other	59	1.8%	18	1.4%	0.338
<b>Number of different drugs used <sup>f</sup></b>					<0.001
0	1285	40.1%	731	58.0%	
1	724	22.6%	258	20.5%	
2	488	15.3%	152	12.1%	
3	334	10.4%	65	5.2%	
4	163	5.1%	27	2.1%	
≥5	207	6.5%	27	2.1%	

# GGD Den Haag, Flevoland, Hollands Noorden and region Utrecht <sup>a</sup> 373 missing, <sup>b</sup> does not include new diagnoses, <sup>c</sup> in the past 6 months, <sup>d</sup> includes all stadia, <sup>e</sup> includes chlamydia, gonorrhoea and syphilis diagnoses, <sup>f</sup> includes alcohol

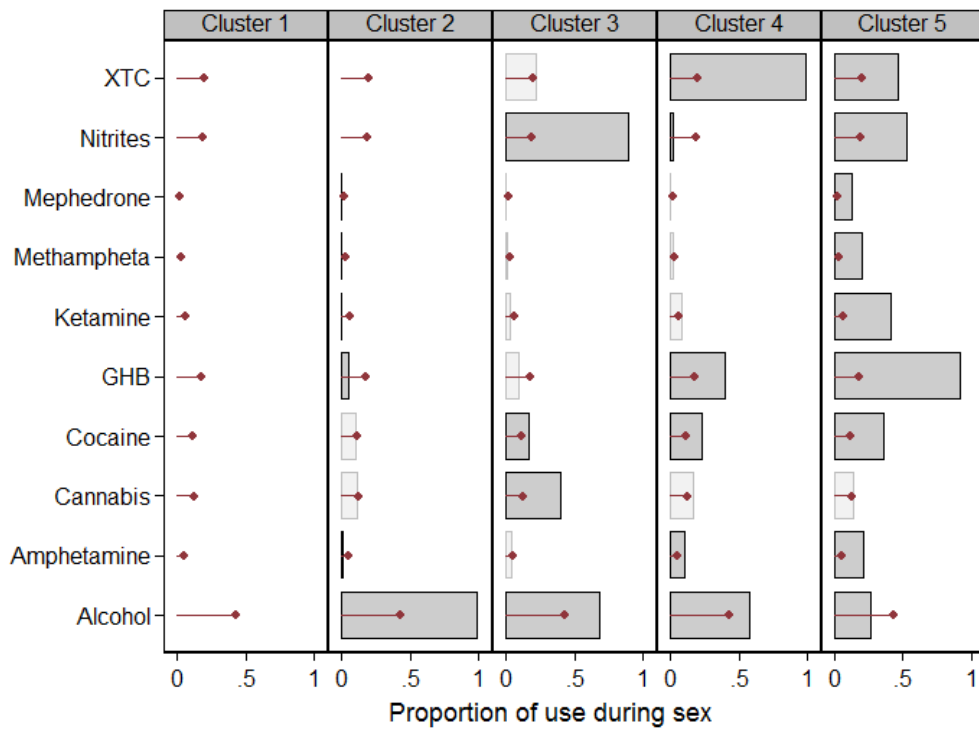


Figure 1A: Patterns of drugs use among 3201 men who have sex with men having an STI consultation at the STI clinic of Amsterdam.

• The overall percentage of specific drug use among MSM in all clusters.

Bars indicate proportion of MSM within a cluster who use a specific drug. Darker bars represent distinguishing characteristics of the cluster.

Clusters 1 “No drugs”; Cluster 2 “Alcohol”; Cluster 3 “Alcohol + soft drugs”; Cluster 4 “XTC+GHB+Alcohol”; Cluster 5 “Polydrug”

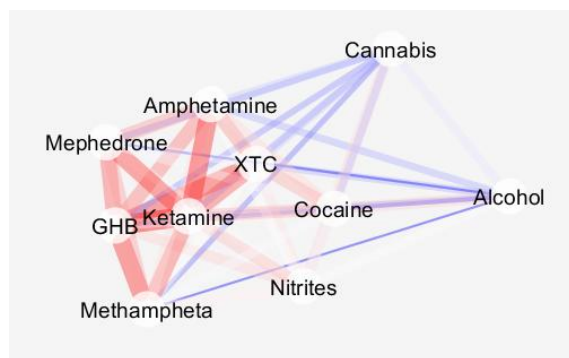


Figure 1B: Correlation networks between drugs when used during sex in Amsterdam.

Positive and negative correlations of all MSM (independent of clusters) are depicted in red and blue, respectively. Stronger correlations have thicker lines and colored shading.

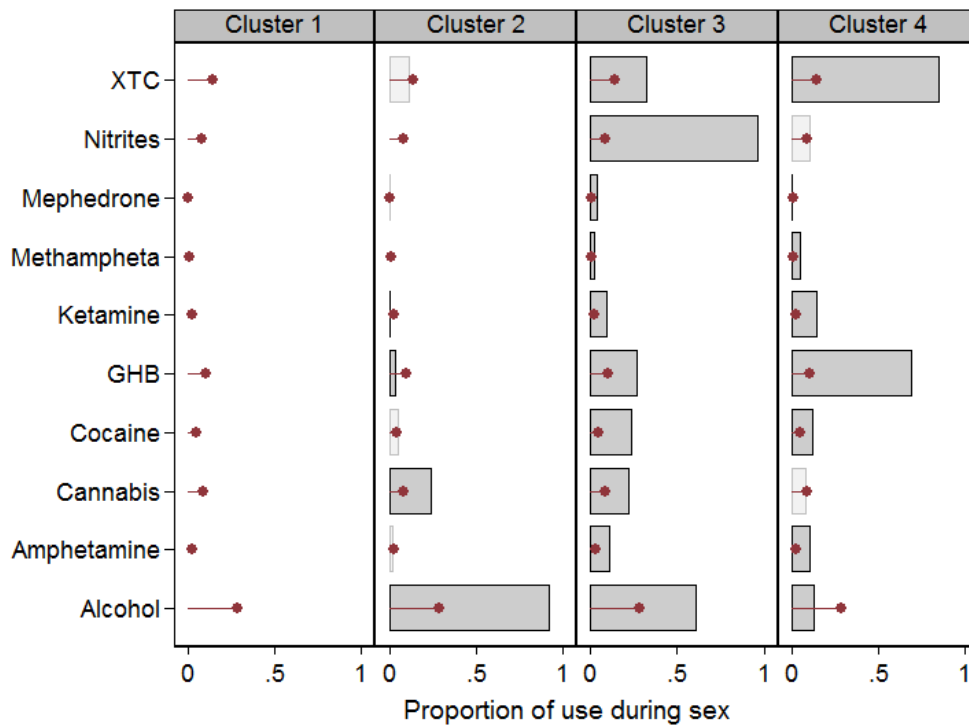


Figure 2A: Patterns of drugs use among 1260 men who have sex with men having an STI consultation at the STI clinic in the surrounding urban regions of Amsterdam.

• The overall percentage of specific drug use among MSM in all clusters.

Bars indicate proportion of MSM within a cluster who use a specific drug. Darker bars represent distinguishing characteristics of the cluster.

Clusters 1 “No drugs”; Cluster 2 “Alcohol”; Cluster 3 “Polydrug and poppers”; Cluster 4 “GHB+XTC”

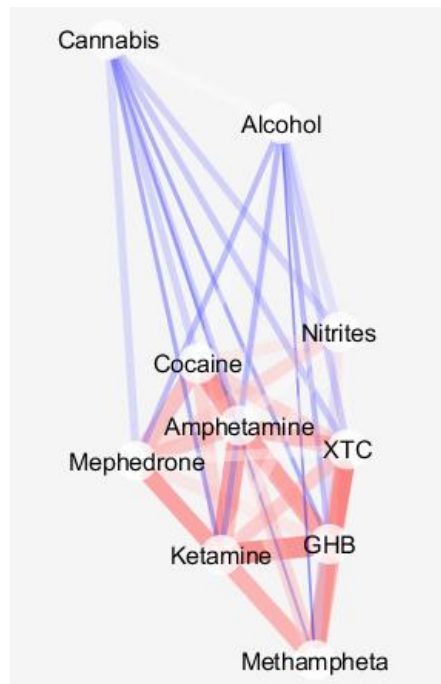


Figure 2B: Correlation networks between drugs when used during sex in surrounding urban regions of Amsterdam.

Positive and negative correlations of all MSM (independent of clusters) are depicted in red and blue, respectively. Stronger correlations have thicker lines and colored shading.

**Table 2. Characteristics of 5 clusters among 3207 MSM attending STI clinics in Amsterdam.**

	Cluster 1 N=1287 No drugs		Cluster 2 N=732 Alcohol		Cluster 3 N=469 Alcohol + soft drugs		Cluster 4 N=380 XTC + GHB + Alcohol		Cluster 5 N=333 Polydrug		P-value
	N	%	N	%	N	%	N	%	N	%	
<b>SOCIO-DEMOGRAPHIC CHARACTERISTICS</b>											
<b>Age in years</b>											<0.001
Median [IQR]	38	[29-49]	31	[26-41]	37	[28-47]	36	[28-46]	40	[30-49]	
<b>Ethnicity</b>											0.005
Dutch	640	49.7%	418	57.1%	243	51.8%	213	56.1%	207	62.2%	
Turkey/Morocco	56	4.4%	27	3.7%	14	3.0%	14	3.7%	6	1.8%	
Dutch Antilles	106	8.3%	38	5.2%	24	5.1%	31	8.2%	15	4.5%	
Eastern Europe	41	3.2%	28	3.8%	20	4.3%	12	3.2%	7	2.1%	
Sub Saharan Africa	27	2.1%	13	1.8%	12	2.6%	5	1.3%	3	0.9%	
Middle & South America	73	5.7%	35	4.8%	37	7.9%	21	5.5%	16	4.8%	
Asia	127	9.9%	57	7.8%	33	7.0%	36	9.5%	31	9.3%	
Western other	214	16.7%	113	15.5%	86	18.3%	48	12.6%	48	14.4%	
<b>Educational level <sup>a</sup></b>											0.059
Low & Middle	388	33.6%	190	29.0%	119	27.7%	113	32.8%	87	27.7%	
High	768	66.4%	465	71.0%	311	72.3%	232	67.3%	227	72.3%	
<b>HIV status <sup>b</sup></b>											<0.001
Positive	217	16.9%	87	11.9%	106	22.6%	86	22.6%	112	33.6%	
<b>Reason of consultation</b>											
Partner notification	276	21.5%	162	22.1%	94	20.0%	104	27.4%	98	29.4%	0.003
STI related symptoms	261	20.3%	167	22.8%	93	19.8%	83	21.8%	81	24.3%	0.373
<b>SEXUAL BEHAVIOR CHARACTERISTICS in the past 6 months</b>											
<b>Sexual partners</b>											<0.001
Both male and female partners	91	7.1%	92	12.6%	31	6.6%	43	11.3%	10	3.0%	
<b>Condom use during last sex act</b>											<0.001
No condom use/condom failure	757	59.9%	446	62.0%	285	61.2%	278	73.9%	253	76.7%	

<b>Number of sex partners</b>											<0.001
Median [IQR]	5	[3-10]	6	[3-10]	10	[6-20]	10	[5-18]	15	[6-30]	
<b>SEXUALLY TRANSMITTED INFECTIONS (STI)</b>											
<b>Chlamydia any site</b>	127	9.9%	63	8.6%	44	9.4%	40	10.5%	41	12.3%	0.425
Pharyngeal	17	1.3%	7	1.0%	11	2.4%	5	1.3%	8	2.4%	0.208
Urethral	45	3.5%	29	4.0%	9	1.9%	18	4.8%	11	3.3%	0.220
Anorectal	87	6.8%	45	6.2%	36	7.7%	29	7.7%	30	9.0%	0.486
Of which LGV	11/75	14.7%	4/35	11.4%	6/31	19.4%	2/19	10.5%	2/28	7.1%	0.688
<b>Gonorrhea any site</b>	125	9.7%	84	11.5%	63	13.4%	59	15.5%	58	17.4%	<0.001
Pharyngeal	61	4.8%	49	6.7%	25	5.3%	30	7.9%	36	10.8%	0.001
Urethral	38	3.0%	20	2.7%	20	4.3%	13	3.4%	12	3.6%	0.605
Anorectal	79	6.2%	48	6.6%	46	9.8%	42	11.1%	46	13.9%	<0.001
<b>Syphilis</b>	46	3.6%	17	2.3%	17	3.6%	15	4.0%	7	2.1%	0.322
Primary/secondary/recent	34	2.6%	14	1.9%	16	3.4%	13	3.4%	7	2.1%	0.421
Latens tarda/unknown stadium	12	0.9%	3	0.4%	1	0.2%	2	0.5%	0	0%	0.174
<b>Any bacterial STI</b>	265	20.6%	148	20.3%	108	23.1%	101	26.6%	91	27.3%	0.012
<b>Any bacterial STI adjusted<sup>d</sup></b>		21.5%		19.7%		22.6%		25.8%		26.4%	
<b>New HIV diagnosis</b>	9/1056	0.9%	5/641	0.8%	4/360	1.1%	1/293	0.3%	2/221	0.9%	0.870

<sup>a</sup> 304 missing, <sup>b</sup> does not include new diagnoses, <sup>c</sup> was not used when making clusters, <sup>d</sup> adjusted for age, ethnicity (dutch vs non-dutch) and HIV status, using multinomial logistic regression analysis. Abbreviations: MSM, Man who have sex with men; IQR, Inter quartile ranges; STI, sexually transmitted infection; GHB,  $\gamma$ -hydroxybutyrate; GBL,  $\gamma$ -butyrolactone; XTC, ecstasy; MDMA, 3,4-Methylenedioxymethamphetamine.

**Table 3. Characteristics of 4 clusters among 1271 MSM attending STI clinics in the surrounding urban regions of Amsterdam.**

	Cluster 1 N=732 No drugs		Cluster 2 N=306 Alcohol		Cluster 3 N=94 Polydrug and Poppers		Cluster 4 N=128 GHB + XTC		P-value
	N	%	N	%	N	%	N	%	
<b>SOCIO-DEMOGRAPHIC CHARACTERISTICS</b>									
<b>Age in years</b>	<0.001								
Median [IQR]	36	[26-49]	28	[23-35]	35	[25-46]	41	[29-52]	
<b>Ethnicity</b>	0.205								
Dutch	459	62.9%	195	63.7%	65	69.2%	98	76.6%	
Turkey/Morocco	23	3.2%	16	5.2%	4	4.3%	3	2.3%	
Dutch Antilles	67	9.2%	23	7.5%	1	1.1%	8	6.3%	
Eastern Europe	18	2.5%	8	2.6%	3	3.2%	2	1.6%	
Sub Saharan Africa	17	2.3%	4	1.3%	0	0%	1	0.8%	
Middle & South America	20	2.7%	10	3.3%	2	2.1%	2	1.6%	
Asia	60	8.2%	20	6.5%	11	11.7%	8	6.3%	
Western other	66	9.0%	30	9.8%	8	8.5%	6	4.7%	
<b>Educational level <sup>a</sup></b>	0.008								
Low & Middle	302	44.1%	129	44.2%	46	51.7%	73	59.8%	
High	383	55.9%	163	55.8%	43	48.3%	49	40.2%	
<b>HIV status <sup>b</sup></b>	<0.001								
Positive	46	6.3%	22	7.2%	15	16.0%	22	17.2%	
<b>Reason of consultation</b>									
Partner notification	138	18.9%	47	15.4%	13	13.8%	37	28.9%	0.006
STI related symptoms	108	14.8%	63	20.6%	14	14.9%	19	14.8%	0.124
<b>SEXUAL BEHAVIOR CHARACTERISTICS in the past 6 months</b>									
<b>Sexual partners</b>	<0.001								
Both male and female partners	120	16.4%	86	28.1%	16	17.0%	30	23.4%	
<b>Condom use during last sex act</b>	0.001								
No condom use/condom failure	411	60.4%	164	57.3%	47	55.3%	94	77.7%	
<b>Number of sex partners</b>	<0.001								

Median [IQR]	4	[3-8]	5	[3-8]	8	[4-15]	10	[5-15]	
<b>DRUG USE DURING SEX (6m)</b>									
Other <sup>c</sup>	3.9%	1	5	1.6%	7	7.5%	5	3.9%	<0.001
Median number of drugs used [IQR]	[1-3]	0	1	[1-2]	2	[2-4]	2	[1-3]	<0.001
<b>SEXUALLY TRANSMITTED INFECTIONS (STI)</b>									
<b>Chlamydia any site</b>	59	8.1%	30	9.8%	9	9.6%	22	17.2%	0.014
Pharyngeal	6	0.8%	2	0.7%	1	1.1%	4	3.2%	0.103
Urethral	20	2.7%	6	2.0%	0	0%	6	4.7%	0.154
Anorectal	42	6.0%	25	8.6%	8	8.6%	18	14.3%	0.012
Of which LGV	0/32	0%	2/19	10.5%	1/7	14.3%	1/16	6.3%	0.272
<b>Gonorrhoea any site</b>	66	9.0%	33	10.8%	14	14.9%	27	21.1%	0.001
Pharyngeal	26	3.6%	9	3.0%	9	9.6%	11	8.7%	0.003
Urethral	19	2.6%	8	2.6%	2	2.1%	10	7.9%	0.013
Anorectal	48	6.9%	24	8.3%	10	10.8%	21	16.7%	0.003
<b>Syphilis</b>	35	4.8%	12	3.9%	7	7.5%	3	2.4%	0.308
Primary/secondary/recent	22	3.0%	10	3.3%	6	6.4%	3	2.3%	0.333
Latens tarda/unknown stadium	13	1.8%	2	0.7%	1	1.1%	0	0%	0.252
<b>Any bacterial STI</b>	137	18.7%	62	20.3%	25	26.6%	46	36.2%	<0.001
<b>Any bacterial STI adjusted <sup>d</sup></b>		19.2%		19.4%		25.7%		35.8%	
<b>New HIV diagnosis</b>	3	0.4%	3	1.1%	1	1.3%	4	3.8%	0.013

<sup>a</sup> 74 missing, <sup>b</sup> does not include new diagnoses, <sup>c</sup> was not used when making clusters, <sup>d</sup> adjusted for age, ethnicity (dutch vs non-dutch) and HIV status, using multinomial logistic regression analysis. Abbreviations: MSM, Man who have sex with men; IQR, Inter quartile ranges; STI, sexually transmitted infection; GHB,  $\gamma$ -hydroxybutyrate; GBL,  $\gamma$ -butyrolactone; XTC, ecstasy; MDMA, 3,4-Methylenedioxymethamphetamine.



## Supplemental figures

Figure 1a (appendix): Prevalence of STI per cluster adjusted for age, ethnicity and HIV-status among 3207 MSM attending the STI clinic in Amsterdam.

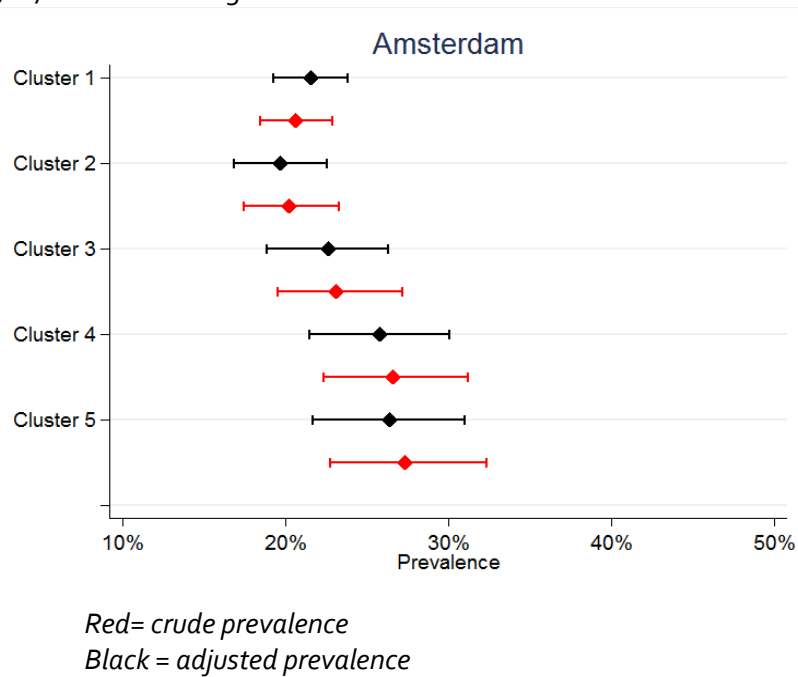
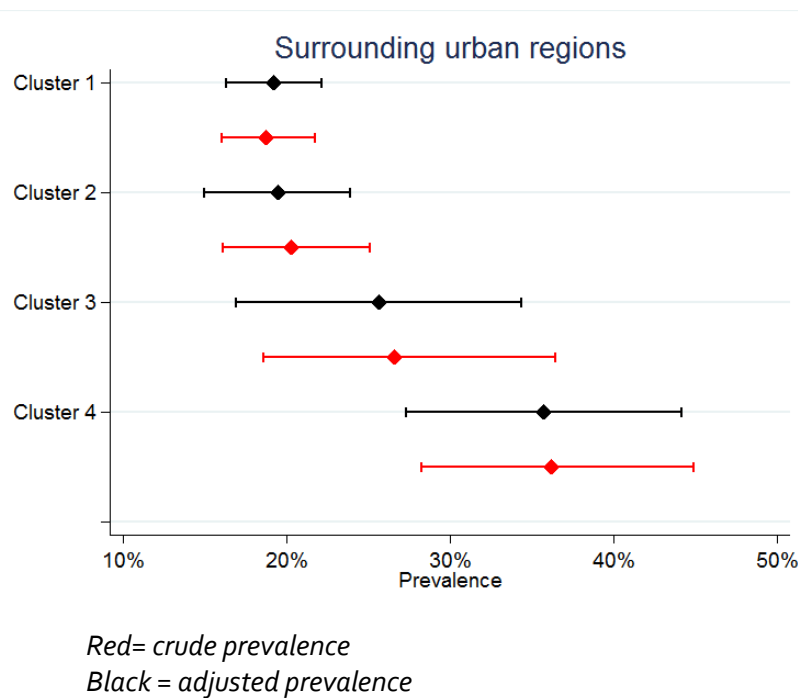


Figure 1b (appendix): Prevalence of STI per cluster adjusted for age, ethnicity and HIV-status among 3207 MSM attending STI clinics in surrounding urban regions.



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