

Polydrug use is associated with new HIV infections among men who have sex with men in China: a multicenter cross-sectional survey

Xiang Mao

NHC KEY Laboratory of AIDS Immunology(China Medical University)

Sequoia I. Leuba

University of North Carolina at Chapel Hill

Qinghai Hu

NHC KEY Laboratory of AIDS Immunology(China Medical University)

Hongjing Yan

Jiangsu Province Center for Disease Control and Prevention

Zhe Wang

Henan Province Center for Disease Control and Prevention

Lin Lu

Yunnan Centers for Disease Control and Prevention

Minghua Zhuang

Shanghai Municipal Center for Disease Control and Prevention

Xi Chen

Hunan Centers for Disease Control and Prevention

Jihua Fu

Shandong Center for Disease Control and Prevention

Wenqing Geng

NHC KEY Laboratory of AIDS Immunology(China Medical University)

Yongjun Jiang

NHC KEY Laboratory of AIDS Immunology(China Medical University)

Hong Shang (✉ hongshang100@hotmail.com)

NHC Key Laboratory of AIDS Immunology (China Medical University) <https://orcid.org/0000-0001-5333-8943>

Junjie Xu

NHC KEY Laboratory of AIDS Immunology(China Medical University)

Research article

Keywords: recreational drug use, polydrug use, Chinese MSM, recent HIV infection, HIV risk behaviors

Posted Date: July 5th, 2019

DOI: <https://doi.org/10.21203/rs.2.10999/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background Recreational drug use is popular among men who have sex with men (MSM), while there is limited information about polydrug use and its consequent impact on sexual health and human immunodeficiency virus (HIV) acquisition. Methods MSM were recruited from a multicenter cross-sectional survey conducted in seven Chinese cities. Participants were divided into four subgroups based on the number of recreational drugs (RDs) used in the past 6 months. "Polydrug use" was defined as simultaneous use of ≥ 2 types of RDs. Information on demographics and HIV high-risk behaviors (HIV-HRBs) was collected, and blood samples were tested for recent HIV infection by the BED capture enzyme immunoassay. Results A total of 4,496 Chinese MSM participated, of which 28.4% used RDs, and 5% were polydrug users. Polydrug users commonly took poppers with one or more types of other RDs (e.g. methamphetamine). Polydrug users were likely to be aged 26–30 years, have low educational attainment, be internal migrants, have a high monthly income, use versatile positions during anal intercourse, and have inadequate knowledge about prevention of HIV infection ($P < 0.05$ for all). As the number of RDs used in the past 6 months increased, the prevalence of HIV-HRBs increased ($P < 0.05$ for all). The odds of recent HIV infection were higher among those who used one type (aOR = 2.2, 95%CI: 1.5–3.0) or two types of RDs (2.3, 1.0–5.2) in the past 6 months compared with those who did not use RDs. The population-attributable fractions of most HIV-HRBs for recent HIV infection were higher among polydrug users compared with those who used only one type of RD or used no RD in the past 6 months. Conclusion The level and pattern of polydrug use among Chinese MSM were different from developed countries. Polydrug use had a dose-effect relationship with HIV-HRBs. Polydrug users who have greater levels of RDs use are more likely to engage in various sexual risks, thus may associated with new HIV infections.

Background

Compared with the general population, men who have sex with men (MSM) experience a disproportionately high burden of human immunodeficiency virus (HIV) infection [1-3]. Use of recreational drugs (RDs) among this population is regarded as a serious public health concern in China and overseas [4-6]. At the end of the twentieth century, RD use was popular among MSM in developed countries [7]. Currently, this phenomenon is expanding to MSM communities in China and other developing countries [5, 8-10]. RDs can enhance sexual function [11], increase sexual pleasure [12], and decrease pain during anal intercourse [13]. However, RD use has been reported to correlate with high-risk sexual behaviors and an increased chance of HIV infection [12-14].

In this context, "polydrug use" refers to use of multiple RDs simultaneously or during the same period of time to achieve a particular effect. Polydrug use has attracted worldwide attention with regard to prevention of HIV infection. Polydrug use can lead to a greater risk of transmission of HIV or other sexually transmitted infections than use of a single RD [15]. Polydrug use alters the mental state and decreases cognitive inhibition [16]. This action can lead to an increased prevalence of condom-less sex (CLS), CLS with HIV-positive partners, group sex, and the number of sexual partners among MSM [17, 18]. Compared with using a single RD, any combination of psychoactive drugs (e.g., methamphetamine, ecstasy) and physiologically actives substances (e.g., poppers, erectile-dysfunction agents) can increase the risk of HIV acquisition dramatically [19].

Despite the severity of this problem, most of the research on polydrug use has been in developed countries [4, 18] which, because of political, legal, and cultural differences, may not be applicable to developing countries [9, 20]. In addition, the HIV incidence among MSM is higher in developing countries than in developed countries [21], which suggests a need for studying the effects of polydrug use upon recent HIV infection in developing countries.

China is the largest developing country in the world. The HIV prevalence among China MSM shows an increasing trend and reached ~8% in 2015 [22]. Thus, it is imperative to understand the relationship between polydrug use and recent HIV infection among Chinese MSM to develop "tailored" interventions that control RD abuse specifically in the hope of mitigating the HIV epidemic. The present study aims to provide researchers and practitioners with information about patterns of polydrug use among Chinese MSM, as well as the impact of polydrug use on HIV high-risk behaviors and HIV acquisition.

Methods

Study participants and questionnaire

A multicenter cross-sectional survey was conducted among Chinese MSM in seven large cities in China (Shenyang, Ji'nan, Zhengzhou, Shanghai, Nanjing, Changsha, and Kunming) from June 2012 to June 2013. Details regarding recruitment, inclusion criteria, and the anonymous structured questionnaire of the survey have been published [23].

Knowledge about prevention of HIV infection was assessed by nine relevant questions. If the participant answered all questions correctly, he was defined as having "adequate" knowledge of prevention of HIV infection. Participants were asked about their use (nonmedical or recreational) of seven commonly used RDs in parties or during sexual contact in the past 6 months: poppers, ecstasy, methamphetamine, amphetamine, codeine, tramadol, and ketamine. Thus, participants were grouped based on the number of drugs used in the past 6 months (i.e., no drug, single drug, two types of drugs, and ≥ 3 types of drugs). "Polydrug use" was defined as using ≥ 2 types of drugs simultaneously in the past 6 months.

Laboratory testing

Samples of venous blood were collected from each participant to diagnose HIV-1 infection. HIV-seropositive specimens were demonstrated by western blotting. These HIV-seropositive samples were tested by the BED capture enzyme immunoassay (BED-CEIA) to ascertain if the HIV-1 infection was recent or established. Details of the testing procedure and calculation formula have been reported [23].

Statistical analyses

The chi-square test was used to determine the significance of differences in social demographics of the different subgroups. The Cochran–Armitage trend test was used to analyze the association between different subgroups and social demographics. We calculated the prevalence of nine defined HIV high-risk behaviors in each subgroup. We estimated the ratio of the prevalence of unadjusted HIV high-risk behaviors through the chi-square test, and adjusted this prevalence ratio for social demographics through multivariate logistic regression analysis. An alpha of 0.05 was considered significant. The HIV incidence was estimated using a formula to adjust sensitivity/specificity, and the time window to define recent HIV infection was 168 days. This formula and parameters were recommended by the Chinese Centers for Disease Control and Prevention [24]. Then, we used multivariable logistic regression to determine the adjusted odds ratios (AORs) and respective 95% confidence intervals (CIs) of the different subgroups. We adjusted for social demographics using recent or established HIV infection, as defined by the BED-CEIA, as the outcome. The population-attributable fractions (PAFs) of HIV high-risk behaviors for recent or established HIV infection in the different subgroups were calculated based on their odds ratios (ORs) using the punaf package in STATA [25]. Use of two types of RD in the past 6 months and use of ≥ 3 types of RD in the past 6 months were combined into the term “multiple drug use” (i.e., polydrug) category to reach sufficient numbers and statistical power to calculate PAFs. Statistical analyses were carried out using SAS 9.2 (SAS Institute, Cary, NC, USA) and STATA 13.0 (Stata Corporation, College Station, TX, USA).

Results

Prevalence and patterns of polydrug use

In total, 4,496 MSM participated in our study, and 1275 (28.4%) reported using RDs in the past 6 months. Of these, 82.4% ($n = 1050$, 23.4% of all participants) used one type of RD (one-type-RD-users, 1DUs), 12.2% (155, 3.4%) used two types of RDs (2DUs), and 5.5% (70, 1.6%) used ≥ 3 types of RDs (3DUs).

Among 1DUs, most used poppers (90.9%), followed by codeine (3.2%), and methamphetamine (2.8%). Among 2DUs, 91.6% used poppers, 57.4% used methamphetamines, and 23.9% used ecstasy. Among 3DUs, 95.7% used poppers, 74.3% used methamphetamines, and 71.4% used ecstasy. Among all participants, 5.0% ($n = 225$, 17.6% of RD users) used two or more types of RDs (i.e., polydrug use). These polydrug users commonly took poppers accompanied with one or more types of other RDs (e.g., methamphetamine) simultaneously or within the same time period (Figure 1).

Characteristics of polydrug users

MSM aged 26–30 years had the highest prevalence of RD use in the past 6 months for all types of RD use (i.e., 1DUs, 2DUs, and 3DUs). Except for between age and ≥ 3 types of RDs used ($P = 0.594$), there was a significant association between age and the different RD subgroups ($P < 0.001$ for all). Also, the proportion of MSM aged 26–30 years increased as the number of RDs used in the past 6 months increased ($P < 0.001$ for trend) (Table 1).

For all the other social demographics examined, participants who were internal migrants, had a monthly income ≥ 600 USD, used versatile positions during anal intercourse, and who had inadequate knowledge about prevention of HIV infection had the highest prevalence of for all types of RD use in the past 6 months. Also, the proportions of these demographics increased significantly as the number of RDs used in the past 6 months increased ($P < 0.05$ for trend). Although participants with educational attainment of junior school or below had the lowest prevalence for use of one type of RD in the past 6 months, the prevalence of use of two or more types of RDs in the past 6 months was significantly higher ($P < 0.05$ for all) (Table 1).

Characteristics of HIV high-risk behaviors

For almost all the HIV high-risk behaviors examined (e.g., seeking male sexual partners through the Internet in the past 6 months, having group sex in the past 6 months), the prevalence of HIV high-risk behavior was higher among those who used RDs in the past 6 months compared with those who did not, and there was a significant association between the HIV high-risk behavior and RD subgroup ($P < 0.05$ for all). In general, the prevalence of HIV high-risk behaviors increased as the number of RDs used in the past 6 months increased (Table 2).

Prevalence and incidence of HIV based on RD use

The HIV prevalence (13.7%, 95%CI: 11.7–15.9 vs. 8.8%, 95%CI: 7.8–9.8) and HIV incidence [13.1 infections per 100 person-years (PY), 95%CI: 9.8–16.3 vs. 7.7 infections per 100 PY, 95% CI: 6.3–9.1] were higher among 1DUs compared with participants who did not use RDs in the past 6 months. In contrast, the HIV prevalence (8.4%, 95%CI: 4.5–13.9; 7.1%, 95%CI: 2.4–15.9) and HIV incidence (9.7 infections per 100 PY, 95%CI: 2.5–16.9; 2.4 infections per 100 PY, 95%CI: 2.3–7.0) of 2DUs and of 3DUs were not significantly higher than those who did not use RDs or of 1DUs in the past 6 months (Table 3a).

Association between RD use and HIV infection

After adjustment for social demographics, 1DUs had higher odds of established HIV infection (AOR = 2.1, 95%CI: 1.5–2.8) and higher odds of recent HIV infection (AOR = 2.2, 95%CI: 1.5–3.0) compared with those who did not use RDs. 2DUs also had higher odds of recent HIV infection (AOR = 2.3, 95%CI: 1.0–

5.2) compared with those who did not use RDs. In contrast, 2DUs and 3DUs did not have significantly higher odds of established HIV infection compared with those who did not use RDs (Table 3b).

PAFs of high-risk behaviors for HIV infection

The PAFs of most HIV high-risk behaviors for recent HIV infection (except for men who had >2 male sexual partners in the past 6 months and those who had commercial sex in the past 6 months) were higher among polydrug users in the past 6 months compared with those who did not use RDs or among 1DUs. However, this relationship of higher PAFs of HIV high-risk behaviors as the number of RDs used in the past 6 months increased was not shown consistently in relation to established HIV infection. Finally, most of the PAFs of HIV high-risk behaviors for recent HIV infection were higher compared with the PAFs of the corresponding HIV high-risk behaviors for established HIV infection (Figure 2).

Discussion

We examined the patterns of use of different RD types among Chinese MSM and the impact of such RD use on HIV high-risk behaviors and HIV acquisition. We found that the prevalence of polydrug use among Chinese MSM (5.0%) was lower than the reported prevalence of polydrug use among MSM in western developed countries (~11.8%) [4]. Chinese MSM who used multiple RDs frequently used poppers along with one or more types of other RDs. As the number of RDs used in the past 6 months increased, the prevalence of various HIV high-risk behaviors also increased. In addition, the odds of recent HIV infection were higher among those who used RDs in the past 6 months compared with those who did not. Furthermore, the PAFs of most HIV high-risk behaviors for recent HIV infection were higher among those who were polydrug users compared with 1DUs or people who did not use RDs in the past 6 months. These data suggested that polydrug users who had greater levels of RD use were more likely to engage in substantially more risky sexual behaviors, and may be associated with a higher risk of HIV acquisition.

Our study has increased understanding of the characteristics of polydrug use in an MSM population in a developing country and its relationship with HIV infection. Previous studies have shown a correlation between RD use and HIV high-risk behaviors among MSM [7, 26]. Our study confirmed those results and showed that the increase in the number of RDs used for recreation was associated with an increase in the prevalence of HIV high-risk behaviors. The similar finding has been documented among HIV-positive MSM in the UK [17], but this relationship has not been examined in a developing country. In contrast with patterns of polydrug use among MSM in developed countries [17, 18, 27], Chinese MSM frequently use poppers. We found that 90% of MSM used poppers, and those who used multiple RDs frequently used poppers along with one or more types of other RDs (i.e., methamphetamine, ecstasy, codeine, and/or ketamine). Poppers are physiologically active substances that facilitate and enhance anal intercourse [4, 13]. They do not affect mental function or decision-making directly [28]. However, when poppers were used with other psychoactive drugs [4] such as methamphetamine, ecstasy, or ketamine, the prevalence of HIV high-risk behaviors increased significantly (Table 2). Most psychoactive drugs are stimulants and, thus, can alter the mental state [16], cause loss of muscle control [16], enhance sexual desires/sexual functions, and affect risk perception and decision-making [11, 12]. If psychoactive drugs are used with poppers (which relax the anal-sphincter muscles and reduce pain) simultaneously, MSM can experience more serious sexual disinhibition and, thus, anal intercourse may be more robust or last for longer, leading to an increased risk of HIV infection [28]. This pattern of polydrug use is popular among Chinese MSM, but was associated with more HIV high-risk behaviors in our study. Scholars have also found that using poppers with methamphetamine or amphetamine is associated with more unprotected sex acts [29] and, hence, is linked to higher risks of HIV seroconversion [30, 31].

The number of RDs used had a dose–effect relationship with HIV high-risk behaviors among participants. However, the possible relationship between HIV high-risk behaviors, the number of RDs used, and HIV infections was not clear. However, when we subdivided diagnosed HIV infections into recent and established HIV infections based on the BED-CEIA, we found a significant relationship between recent HIV infection and one type of RD used or two types of RD used compared with no RD used in the past 6 months. While, we did not find a significant relationship between recent HIV infection and 3DUs compared with those who did not use RDs, this finding could have been due to our small sample size, which would have led to low statistical power to detect the differences in our AOR estimates. In contrast, we found a significant relationship only between established HIV infection and one type of RD used in the past 6 months compared with no RD used. This result suggests that RDs used in the past 6 months were associated with recent HIV infection. This may have been because those polydrug users who are less risk-averse would have greater levels of RD use and to be more likely to engage in more sexually risky behaviors and, thus, may be associated with new HIV infections. To test our hypothesis, we further explored the differences between the effect of RD use on HIV infection by calculating the PAF of each HIV high-risk behavior for recent and established HIV infection. The PAF is used to estimate the contribution of a risk factor to a disease [32, 33]. Hence, the PAFs we calculated of HIV high-risk behaviors were the reduction in recent and established HIV infection in the overall Chinese MSM population if there was no exposure to the risk factor. The PAFs of most HIV high-risk behaviors for recent HIV infection were higher among participants who had used multiple types of RDs (i.e., polydrug users) than among participants who did not use RDs or among participants who used one type of RD in the past 6 months (Figure 2a). These results verified that certain HIV high-risk behaviors had higher contributions to recent HIV infection among MSM who used multiple types of RDs. Several longitudinal studies have found similar associations between polydrug use and recent HIV seroconversion [19, 34]. Newly infected individuals have a high level of viral load in plasma and few pronounced symptoms and, thus, are highly infectious, but detection of such people is difficult [35, 36]. In addition, MSM in this HIV seroconversion period have been found to participate frequently in HIV high-risk behaviors [36]. Thus, polydrug users will take more sexual risks and, thus, may be associated with new HIV infections and an increased risk of secondary HIV transmission.

Although the collected prevalence of polydrug use among Chinese MSM in our study was lower than the prevalence among MSM reported in developed countries (5.0% vs. ~11.8%) [4], the actual prevalence of polydrug use of Chinese MSM may have been underestimated due to two main reasons. First, most RDs are illegal in China, so participants may have been afraid of the repercussions of answering honestly about their use of multiple RDs (though participants were asked through an anonymous survey to minimize this bias in social acceptance). Second, we investigated only the seven most commonly used RDs

among Chinese MSM. There are many products used by MSM in which the presence of drugs is not clear, so MSM may have underestimated their RD use unknowingly. Thus, the estimated HIV incidence among polydrug users may also be underestimated because of this bias.

We elucidated the characteristics and possible mechanisms of HIV transmission among Chinese MSM who use RDs. We undertook this study in the hope of developing targeted interventions to address the HIV epidemic. We found that participants aged 26–30 years had a higher prevalence of overall RD use in the past 6 months (39.0%) and polydrug use in the past 6 months (7.2%) compared with any other age group examined. The number of identified HIV/AIDS cases among MSM aged 26–30 years in China increased rapidly from 2007 to 2015 [37]. Mao and colleagues found a high HIV incidence (~9 infections per 100 PY) among Chinese MSM aged 26–30 years [38]. RD use is associated with behaviors which increase the risk of HIV, so tailored methods reducing RD use must be implemented among Chinese MSM 26–30 years to reduce the risk of HIV acquisition. In addition, we found an association between a decrease in adequate knowledge about prevention of HIV infection and an increase in the number of RDs used in the past 6 months, suggesting that strategies focused on increasing knowledge about prevention of HIV infection should be targeted at polydrug users. Finally, many Chinese MSM in our study used poppers, which may have been due to the ease of buying this drug (they are not illegal in China) [20]. Thus, the Chinese government should restrict the sale of poppers to reduce RD use to diminish the effect of RD use on HIV transmission.

Our study had limitations. First, the proportion of participants who self-reported using multiple types of RDs was only 5%. The low number of polydrug users may have led to the inconsistencies found in the dose–effect relationship between HIV high-risk behaviors and drug subgroups; calculation of the incidence and prevalence of HIV infection by RD subgroups; association between HIV infection and RD subgroups. We speculate that a bias against social acceptance and misclassification because of unknown use of RDs may have limited our ability to develop statistically significant results and reduced the observed effect of polydrug use upon HIV infection. Second, the PAFs of HIV high-risk behaviors on recent or established HIV infection were estimated without addressing possible confounding by social demographics or addressing the possible non-independence of risk factors. Thus, our PAFs were thought to be due to a reduction in recent and established HIV infection in the overall Chinese MSM population if there was no exposure to the risk factor assuming all risk factors were independent of each other and not confounded by social demographics.

Conclusions

Chinese MSM who used multiple RDs frequently used poppers along with one or more types of other RDs. The number of RDs used in the past 6 months among Chinese MSM had a dose–effect relationship with HIV high-risk behaviors. Using one or two types of RDs was associated with increased odds of recent HIV infection compared with MSM who did not use RDs. We found polydrug use to be associated with higher PAFs for HIV high-risk behaviors for recent HIV infections, so polydrug use was more likely to be associated with new HIV infections. Strategies focusing on decreasing RD use among Chinese MSM and increased governmental control of RDs could reduce drug use and, thus, mitigate the HIV epidemic in China.

Abbreviations

MSM: men who have sex with men; **HIV:** human immunodeficiency virus; **RDs:** recreational drugs; **HIV-HRBs:** HIV high-risk behaviors; **CLS:** condom-less sex; **BED-CEIA:** BED capture enzyme immunoassay; **CIs:** confidence intervals; **AORs:** adjusted odds ratios; **PAFs:** population-attributable fractions; **ORs:** odds ratios; **1DUs:** one-type-RD-users; **2DUs:** two types of RDs users; **3DUs:** three or more types RDs users

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Review Board of the First Affiliated Hospital of China Medical University ([2011]-36; Shenyang, China). The study was undertaken in accordance with all relevant guidelines and regulations. Written informed consent was obtained from all participants before study commencement.

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

This study was funded by the Mega-Projects of National Science Research (13th Five-Year Plan [2017ZX10201101-002-007]), National Natural Science Foundation of China (81872674), National Science and Technology Major Project (2018ZX10101-001-001-003) and Central Public-Interest Scientific Institution Basal Research Fund of Chinese Academy of Medical Sciences (2018PT31042).

Authors' contributions

Conception and design of experiments: XM, HS, JJX, QHH; carried out the study and experiments: HJY, ZW, LL, MHZ, XC, JHF, WQG, YJJ; analyzed the data: XM, QHH, JJX; wrote and revised the manuscript: XM, SIL, JJX. All authors reviewed the manuscript.

References

1. Baral S, Sifakis F, Cleghorn F, Beyrer C. Elevated risk for HIV infection among men who have sex with men in low- and middle-income countries 2000-2006: A systematic review. *PLoS Med.* 2007;4(12):1901-11.

2. UNAIDS. 2015 China AIDS Response Progress Report. 2015.
http://www.unaids.org/sites/default/files/country/documents/CHN_narrative_report_2015.pdf. Accessed December 2, 2018.
3. UNAIDS. Prevention Gap Report. 2014. http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf. Accessed December 2, 2018.
4. Rosinska M, Gios L, Nostlinger C, Vanden Berghe W, Marcus U, Schink S, et al. Prevalence of drug use during sex amongst MSM in Europe: Results from a multi-site bio-behavioural survey. *Int J Drug Policy*. 2018;55:231-41.
5. Xu JJ, Qian HZ, Chu ZX, Zhang J, Hu QH, Jiang YJ, et al. Recreational Drug Use among Chinese Men Who Have Sex with Men: A Risky Combination with Unprotected Sex for Acquiring HIV Infection. *Biomed Res Int*. 2014;9.
6. Lampinen TM, Mattheis K, Chan K, Hogg RS. Nitrite inhalant use among young gay and bisexual men in Vancouver during a period of increasing HIV incidence. *BMC Public Health*. 2007;7:6.
7. Drumright LN, Patterson TL, Strathdee SA. Club drugs as causal risk factors for HIV acquisition among men who have sex with men: A review. *Subst Use Misuse*. 2006;41(10-12):1551-601.
8. Chen X, Li XL, Zheng J, Zhao JS, He JM, Zhang GQ, et al. Club Drugs and HIV/STD Infection: An Exploratory Analysis among Men Who Have Sex with Men in Changsha, China. *PLoS One*. 2015;10(5):9.
9. Nguyen TV, Van Khuu N, Nguyen PD, Tran HP, Phan HTT, Phan LT, et al. Sociodemographic Factors, Sexual Behaviors, and Alcohol and Recreational Drug Use Associated with HIV Among Men Who Have Sex with Men in Southern Vietnam. *AIDS Behav*. 2016;20(10):2357-71.
10. Bautista CT, Sanchez JL, Montano SM, Laguna-Torres VA, Lama JR, Sanchez JL, et al. Seroprevalence of and risk factors for HIV-1 infection among South American men who have sex with men. *Sex Transm Infect*. 2004;80(6):498-504.
11. Kurtz SP. Post-circuit blues: motivations and consequences of crystal meth use among gay men in Miami. *AIDS Behav*. 2005;9(1):63-72.
12. Green AI. "chem friendly": the institutional basis of "club-drug" use in a sample of urban gay men. *Deviant Behavior*. 2003;24(5):427-47.
13. Romanelli F, Smith KM, Thornton AC, Pomeroy C. Poppers: Epidemiology and clinical management of inhaled nitrite abuse. *Pharmacotherapy*. 2004;24(1):69-78.
14. Ross MW, Mattison AM, Franklin DR. Club drugs and sex on drugs are associated with different motivations for gay circuit party attendance in men. *Subst Use Misuse*. 2003;38(8):1173-83.
15. Gorman EM, Applegate T, Scrol A. Club Drug and Poly-Substance Abuse and HIV Among Gay/Bisexual Men. *Journal of Gay & Lesbian Social Services*. 2003;16(2):1-17.
16. Freese TE, Miotto K, Reback CJ. The effects and consequences of selected club drugs. *J Subst Abuse Treat*. 2002;23(2):151-56.
17. Daskalopoulou M, Rodger A, Phillips AN, Sherr L, Speakman A, Collins S, et al. Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: results from the cross-sectional ASTRA study. *Lancet HIV*. 2014;1(1):E22-E31.
18. Sewell J, Miltz A, Lampe FC, Cambiano V, Speakman A, Phillips AN, et al. Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. *Int J Drug Policy*. 2017;43:33-43.
19. Ostrow DG, Plankey MW, Cox C, Li XH, Shoptaw S, Jacobson LP, et al. Specific Sex Drug Combinations Contribute to the Majority of Recent HIV Seroconversions Among MSM in the MACS. *J AIDS*. 2009;51(3):349-55.
20. Zhang H, Tenga T, Lu HY, Zhao YJ, Liu HJ, Yin L, et al. Poppers use and risky sexual behaviors among men who have sex with men in Beijing, China. *Drug Alcohol Depend*. 2016;160:42-8.
21. Beyrer C, Baral SD, van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL, et al. Global epidemiology of HIV infection in men who have sex with men. *Lancet*. 2012;380(9839):367-77.
22. Tang SY, Tang WM, Meyers K, Chan P, Chen ZD, Tucker JD. HIV epidemiology and responses among men who have sex with men and transgender individuals in China: a scoping review. *BMC Infect Dis*. 2016;16:8.
23. Xu JJ, Tang WM, Zou HC, Mahapatra T, Hu QH, Fu GF, et al. High HIV incidence epidemic among men who have sex with men in china: results from a multi-site cross-sectional study. *Infect Dis Poverty*. 2016;5:11.
24. China CDC. National Guidelines for Serology-based Detection of HIV-1 Incidence in China. 2011.
http://ncaids.chinacdc.cn/fzyw_10256/jsgf/201608/W020171101497393625088.pdf Accessed December 2, 2018.
25. Newson RB. Attributable and unattributable risks and fractions and other scenario comparisons. *The Stata Journal*. 2013;13(4):672-98.
26. Bourne A, Weatherburn P. Substance use among men who have sex with men: patterns, motivations, impacts and intervention development need. *Sex Transm Infect*. 2017;93(5):342-46.
27. Halkitis PN, Palamar JJ, Mukherjee PP. Poly-club-drug use among gay and bisexual men: A longitudinal analysis. *Drug Alcohol Depend*. 2007;89(2-3):153-60.
28. French RS, Power R. Self-Reported Effects of Alkyl Nitrite Use: A Qualitative Study Amongst Targeted Groups. *Addiction Research*. 1997;5(6):519-48.
29. Semple SJ, Strathdee SA, Zians J, Patterson TL. Sexual risk behavior associated with co-administration of methamphetamine and other drugs in a sample of HIV-positive men who have sex with men. *Am J Addict*. 2009;18(1):65-72.
30. Plankey MW, Ostrow DG, Stall R, Cox C, Li XH, Peck JA, et al. The relationship between methamphetamine and popper use and risk of HIV seroconversion in the Multicenter AIDS Cohort Study. *J AIDS*. 2007;45(1):85-92.
31. Ackers ML, Greenberg AE, Lin CY, Bartholow BN, Goodman AH, Longhi M, et al. High and Persistent HIV Seroincidence in Men Who Have Sex with Men across 47 US Cities. *PLoS One*. 2012;7(4):7.

32. Goller JL, De Livera AM, Fairley CK, Guy RJ, Bradshaw CS, Chen MY, et al. Population attributable fraction of pelvic inflammatory disease associated with chlamydia and gonorrhoea: a cross-sectional analysis of Australian sexual health clinic data. *Sex Transm Infect.* 2016;92(7):525-31.
33. Azimi SS, Khalili D, Hadaegh F, Yavari P, Mehrabi Y, Azizi F. Calculating population attributable fraction for cardiovascular risk factors using different methods in a population based cohort study. *J Res Health Sci.* 2015;15(1):22-7.
34. Carey JW, Mejia R, Bingham T, Ciesielski C, Gelaude D, Herbst JH, et al. Drug use, high-risk sex behaviors, and increased risk for recent HIV infection among men who have sex with men in Chicago and Los Angeles. *AIDS Behav.* 2009;13(6):1084-96.
35. Buskin SE, Fida NG, Bennett AB, Golden MR, Stekler JD. Evaluating New Definitions of Acute and Early HIV Infection from HIV Surveillance Data. *Open AIDS J.* 2014;8:45-9.
36. Colfax GN, Buchbinder SP, Cornelisse PGA, Vittinghoff E, Mayer K, Celum C. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. *Aids.* 2002;16(11):1529-35.
37. Qin QQ, Guo W, Tang WM, Mahapatra T, Wang LY, Zhang NC, et al. Spatial Analysis of the Human Immunodeficiency Virus Epidemic among Men Who Have Sex with Men in China, 2006-2015. *Clin Infect Dis.* 2017;64(7):956-63.
38. Mao X, Wang Z, Hu Q, Huang C, Yan H, Wang Z, et al. HIV incidence is rapidly increasing with age among young men who have sex with men in China: a multicentre cross-sectional survey. *HIV Med.* 2018;19(8):513-22.

Tables

Table 1. Distribution of social demographics among different subgroups of RD use (N = 4496)

| Variable | ODUs (n = 3221) | | | | P | 1DUs (n = 1050) | | | | P | 2DUs (n = 155) | | | | P | Over | |
|---|-----------------|------|----------------------|-----------------------|--------|-----------------|------|------|---|--------|----------------|------|---|----|-----|------|--|
| | N | n | Overall proportion % | Subgroup proportion % | | n | % | % | n | | % | % | n | % | | | |
| Age (years) | | | | | <0.001 | | | | | <0.001 | | | | | | | |
| 18-25 | 1617 | 1123 | 69.4 | 34.9 | | 412 | 25.5 | 39.2 | | 59 | 3.6 | 38.1 | | 23 | 1.4 | | |
| 26-30 | 1181 | 721 | 61.0 | 22.4 | | 375 | 31.8 | 35.7 | | 63 | 5.3 | 40.6 | | 22 | 1.9 | | |
| >30 | 1698 | 1377 | 81.1 | 42.8 | | 263 | 15.5 | 25.0 | | 33 | 1.9 | 21.3 | | 25 | 1.5 | | |
| Residence | | | | | 0.001 | | | | | 0.022 | | | | | | | |
| Local cities | 1785 | 1327 | 74.3 | 41.2 | | 385 | 21.6 | 36.7 | | 45 | 2.5 | 29.0 | | 28 | 1.6 | | |
| Non-local cities | 2711 | 1894 | 69.9 | 58.8 | | 665 | 24.5 | 63.3 | | 110 | 4.1 | 71.0 | | 42 | 1.6 | | |
| Education | | | | | 0.072 | | | | | <0.001 | | | | | | | |
| Junior school or below | 916 | 674 | 73.6 | 20.9 | | 169 | 18.4 | 16.1 | | 45 | 4.9 | 29.0 | | 28 | 3.1 | | |
| High school | 1201 | 877 | 73.0 | 27.2 | | 269 | 22.4 | 25.6 | | 37 | 3.1 | 23.9 | | 18 | 1.5 | | |
| College or above | 2379 | 1670 | 70.2 | 51.8 | | 612 | 25.7 | 58.3 | | 73 | 3.1 | 47.1 | | 24 | 1.0 | | |
| Marital status | | | | | <0.001 | | | | | <0.001 | | | | | | | |
| Never married | 3303 | 2266 | 68.6 | 70.4 | | 860 | 26.0 | 81.9 | | 129 | 3.9 | 83.2 | | 48 | 1.5 | | |
| Married | 1193 | 955 | 80.1 | 29.6 | | 190 | 15.9 | 18.1 | | 26 | 2.2 | 16.8 | | 22 | 1.8 | | |
| Occupation | | | | | 0.187 | | | | | 0.599 | | | | | | | |
| Student | 565 | 418 | 74.0 | 13.0 | | 127 | 22.5 | 12.1 | | 16 | 2.8 | 10.3 | | 4 | 0.7 | | |
| Non-student | 3931 | 2803 | 71.3 | 87.0 | | 923 | 23.5 | 87.9 | | 139 | 3.5 | 89.7 | | 66 | 1.7 | | |
| Monthly income (USD) | | | | | <0.001 | | | | | <0.001 | | | | | | | |
| No income | 769 | 591 | 76.9 | 18.3 | | 146 | 19.0 | 13.9 | | 25 | 3.3 | 16.1 | | 7 | 0.9 | | |
| 1-599 | 2858 | 2069 | 72.4 | 64.2 | | 658 | 23.0 | 62.7 | | 94 | 3.3 | 60.7 | | 37 | 1.3 | | |
| ≥600 | 869 | 561 | 64.6 | 17.4 | | 246 | 28.3 | 23.4 | | 36 | 4.1 | 23.2 | | 26 | 3.0 | | |
| Primary sex position during AI^a | | | | | <0.001 | | | | | 0.001 | | | | | | | |
| Top | 1395 | 1053 | 75.5 | 33.4 | | 291 | 20.9 | 28.0 | | 34 | 2.4 | 23.1 | | 17 | 1.2 | | |
| Bottom | 988 | 725 | 73.4 | 23.1 | | 222 | 22.5 | 21.3 | | 31 | 3.1 | 21.1 | | 10 | 1.0 | | |
| Versatile | 2022 | 1371 | 67.8 | 43.5 | | 527 | 26.1 | 50.7 | | 82 | 4.1 | 55.8 | | 42 | 2.1 | | |
| HIV-prevention knowledge^b | | | | | <0.001 | | | | | 0.006 | | | | | | | |
| Inadequate | 2730 | 1861 | 68.2 | 57.8 | | 676 | 24.8 | 64.4 | | 128 | 4.7 | 82.6 | | 65 | 2.4 | | |
| Adequate | 1766 | 1360 | 77.0 | 42.2 | | 374 | 21.2 | 35.6 | | 27 | 1.5 | 17.4 | | 5 | 0.3 | | |

ODUs: No RDs used in the past 6 months; 1DUs: One type of RD (one-type-RD-users) used in the past 6 months; 2DUs: Two types of RDs used in the past 6 months; 3DUs: Three or more types of RDs used in the past 6 months. AI: anal intercourse. Unadjusted *P*-values were calculated by the chi-square test. The *P* for trend of social demographics changing in different subgroups was determined by the Cochran-Armitage trend test a. Ninety-one participants did not provide responses to this variable on the questionnaire, so it differs from total sample size; b. Knowledge of prevention of HIV infection was assessed by nine questions. If the participant answered all questions correctly, he/she was defined as having "adequate" knowledge. The questions were: (1) Is it possible for a person who looks healthy to carry HIV? (2) Is it

possible to be infected through transfusion of blood or blood products with HIV? (3) Is it possible to be infected through sharing needles with HIV-infected persons or AIDS patients? (4) Can proper use of condoms in each sexual activity reduce the risk of HIV transmission? (5) Can having sex with only a single HIV-uninfected sexual partner reduce the risk of HIV transmission? (6) Can a HIV-infected pregnant woman transmit HIV to her child? (7) Is it possible to be infected through eating with HIV-infected persons or AIDS patients? (8) Is it possible to be infected through mosquito bites? (9) If you know or suspect that your partner has AIDS, will you stop having sex with him?

Table 2. Prevalence and adjusted prevalence ratios of HIV high-risk behaviors among different subgroups (N = 4496)

0DUs: No RDs used in the past 6 months; 1DUs: One type of RD (one-type-RD-users) used in the past 6 months; 2DUs: Two types of RDs used in the past 6 months; 3DUs: Three or more types of RDs used in the past 6 months. AI: anal intercourse; Commercial sex: buying or selling sex services, including anal intercourse or oral intercourse; STI-related symptoms: abnormal pain or burning sensation upon micturition, urethra secretion, genital/anal skin damage or hyperplasia; Mucosally-traumatic sex: Mucosally-traumatic sex means sexual intercourse especially anal intercourse sometimes may be rougher or last for longer and caused vagina, anus, or rectum mucosal trauma, which could facilitate HIV/STIs transmission. The table includes information only for participants who answered a specific question, so sample sizes may differ because of missing data. Unadjusted *P*-values were calculated by the chi-squared test. a. Adjusted prevalence ratios were derived through multivariate logistic regression analysis with adjustment for the following social demographics: study site (Shanghai, Nanjing, Changsha, Zhengzhou, Ji'nan, Shenyang, and Kunming), age (18–25, 26–30, and >30 years), residence (local cities and non-local cities), education (junior school or below, high school, and college or above), marital status (never married and married), occupation (student and non-student), monthly income (no income, 1–599, and ≥600 USD), primary sex position during AI (top, bottom, and versatile), and HIV-prevention knowledge (inadequate and adequate).

Due to technical limitations, Table 2 has been placed in the supplementary files section.

Table 3a. HIV prevalence and BED-CEIA-based HIV incidence among MSM participants (N = 4496)

| | Total | HIV infection | HIV recent infection | HIV established infection | HIV prevalence (%) (95%CI) ^b | HIV incidence/100 PY (95%CI) ^c |
|----------------------------|-------|---------------|----------------------|---------------------------|---|---|
| Subgroups of RD use | 4496 | 444 | 186 | 250 | 9.9 (9.0–10.8) | 8.9 (7.6–10.2) |
| 0DUs | 3221 | 282 | 116 | 161 | 8.8 (7.8–9.8) | 7.7 (6.3–9.1) |
| 1DUs | 1050 | 144 | 62 | 79 | 13.7 (11.7–15.9) | 13.1 (9.8–16.3) |
| 2DUs | 155 | 13 | 7 | 6 | 8.4 (4.5–13.9) | 9.7 (2.5–16.9) |
| 3DUs | 70 | 5 | 1 | 4 | 7.1 (2.4–15.9) | 2.4 (–2.3 to 7.0) |

Table 3b. Association between recent or established HIV infection and subgroup of RD use (N = 4488)^a

| Subgroups of RD use | Total | Recent HIV infection (N=186) | | | Established HIV infection (N=250) | | |
|---------------------|-------|------------------------------|--|----------|-----------------------------------|--|----------|
| | | n (%) | Adjusted model ^d aOR (95%CI) | <i>P</i> | n (%) | Adjusted model ^d aOR (95%CI) | <i>P</i> |
| 0DUs | 3216 | 116 (3.6) | 1 | – | 161 (5.0) | 1 | – |
| 1DUs | 1047 | 62 (5.9) | 2.2 (1.5–3.0) | <0.001 | 79 (7.5) | 2.1 (1.5–2.8) | <0.001 |
| 2DUs | 155 | 7 (4.5) | 2.3 (1.0–5.2) | 0.054 | 6 (3.9) | 1.4 (0.6–3.4) | 0.433 |
| 3DUs | 70 | 1 (1.4) | 0.8 (0.1–5.8) | 0.809 | 4 (5.7) | 1.9 (0.6–5.4) | 0.247 |

0DUs: No RDs used in the past 6 months; 1DUs: One type of RD (one-type-RD-users) used in the past 6 months; 2DUs: Two types of RDs used in the past 6 months; 3DUs: Three or more types of RDs used in the past 6 months. a. Recent and established infections were determined using the BED-CEIA. Because of insufficient numbers of blood specimens, the BED-CEIA could not be conducted on samples from eight HIV antibody-positive participants. b. HIV prevalence was calculated from all HIV infections (i.e., recent and established) diagnosed through the study. c. The HIV incidence determined using the BED-CEIA was then adjusted using the sensitivity and specificity adjustment formula and parameters recommended by the Chinese Centers for Disease Control and Prevention. d. Adjusted odds ratios (AORs) and the corresponding 95%CI were derived through multivariate logistic regression analysis with adjustment for the following social demographics: study site (Shanghai, Nanjing, Changsha, Zhengzhou, Ji'nan, Shenyang, and Kunming), age (18–25, 26–30, and >30 years), residence (local cities and non-local cities), education (junior school

or below, high school, and college or above), marital status (never married and married), occupation (student and non-student), monthly income (no income, 1-599, and ≥ 600 USD), primary position during AI (top, bottom, and variable), and HIV-prevention knowledge (inadequate and adequate).

Figures

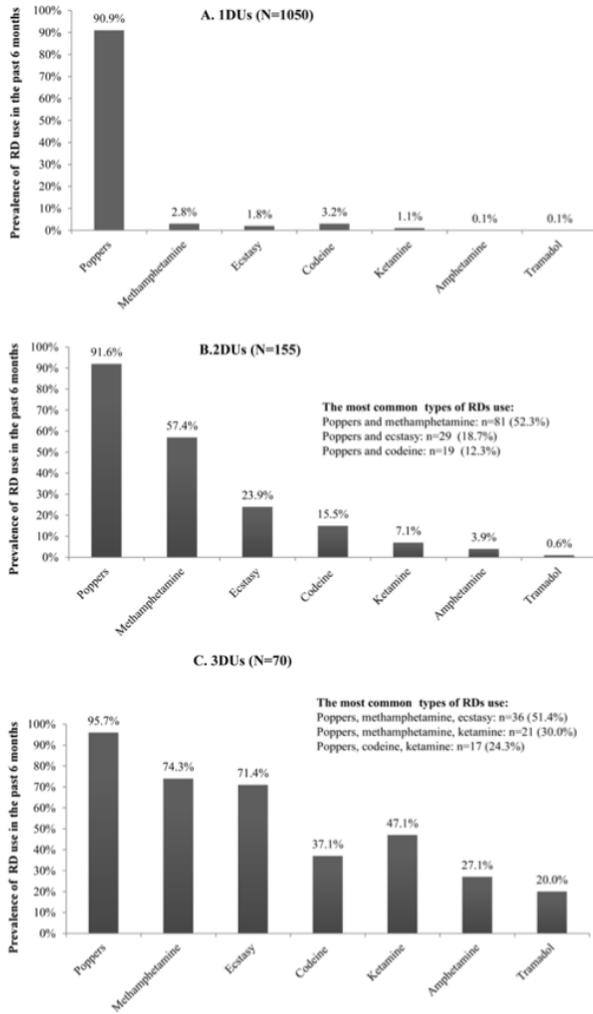


Figure 1

Prevalence of specific RD use in the past 6 months among different subgroups of RD use (N=4496) 1DUs: One type of RD (one-type-RD-users) used in the past 6 months; 2DUs: Two types of RDs used in the past 6 months; 3DUs: Three or more types of RDs used in the past 6 months. Out of the 4496 MSM participants, 1050 participants used a one type of RD in the past 6 months (Panel A), 155 used two types of RDs in the past 6 months (Panel B), and 70 used three or more types of RDs in the past 6 months (Panel C). The prevalence of the types of most common used RDs are also listed above.

Figure A. Recent HIV infection

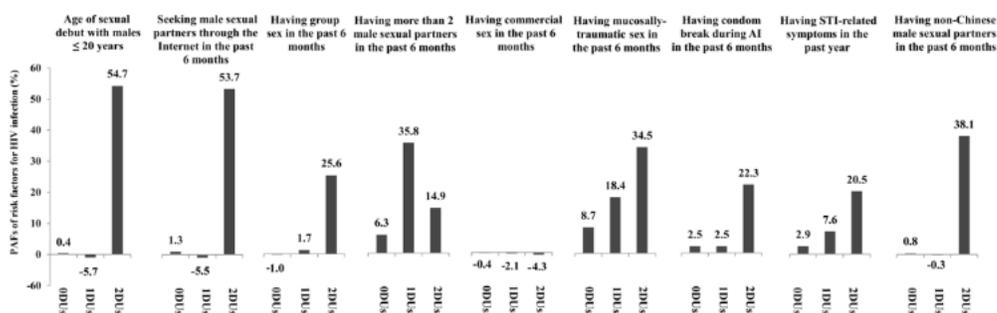


Figure B. Established HIV infection

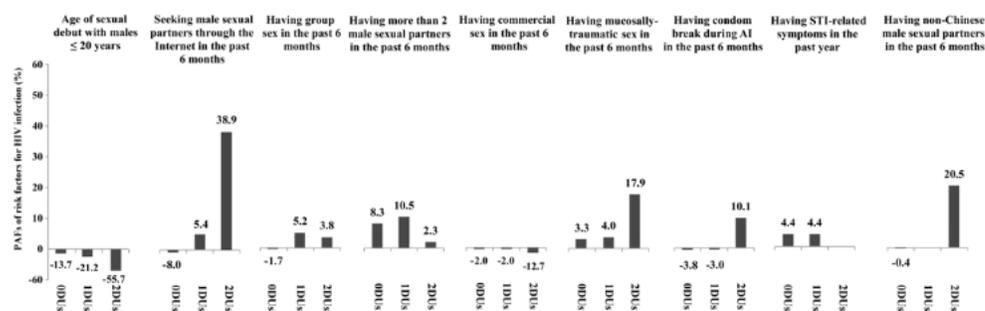


Figure 2

Population Attributable Fractions (PAFs) of HIV high-risk behaviors for recent and established HIV infections based on polydrug categories (N=4488) a 0DU: No RDs used in the past 6 months; 1DU: One type of RD (one-type-RD-users) used in the past 6 months; 2DU: Two or more types of RDs (polydrug-users) used in the past 6 months. AI: anal intercourse; Commercial sex: buying or selling sex services, including anal intercourse or oral intercourse; STI-related symptoms: abnormal pain or burning sensation upon micturition, urethra secretion, genital/anal skin damage or hyperplasia; Mucosally-traumatic sex: Mucosally-traumatic sex means sexual intercourse especially anal intercourse sometimes may be rougher or last for longer and caused vagina, anus, or rectum mucosal trauma, which could facilitate HIV/STIs transmission. a. Recent and established infections were determined using the BED-CEIA. Because of insufficient numbers of blood specimens, the BED-CEIA could not be conducted on samples from eight HIV antibody-positive participants. The figure includes information only for participants who answered a specific question, so sample sizes may differ because of missing data. Because PAFs could not be calculated in two subgroups (two types of RDs used and three or more types of RDs used), they were combined to make a “multiple RDs used in the past 6 months” subgroup. Because of limited participants in “Had STI-related symptoms in the past year” and “Had non-Chinese male sexual partners in the past 6 months” subgroups, the PAFs to established HIV infection could not be calculated.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table2.tif](#)