Preplanned Studies

Association Between Incorrect Use of Pre- and Post-Exposure Prophylaxis and HIV infection Among Men Who Have Sex with Men — Shenzhen City, Guangdong Province, China, 2021–2023

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Summary

What is already known about this topic?

Preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) have been proven effective in preventing human immunodeficiency virus (HIV) transmission.

What is added by this report?

Men who have sex with men (MSM) who incorrectly used PrEP/PEP demonstrated higher HIV positivity rates compared to both correct users and non-users. Since PrEP/PEP users are more likely to engage in unprotected anal intercourse (UAI), incorrect use of these prophylactic measures may constitute a significant risk factor for HIV transmission among MSM.

What are the implications for public health practice?

It is crucial to implement strategies that guide MSM toward correct PrEP/PEP utilization while emphasizing that these prophylactic measures should not be considered substitutes for condom use.

ABSTRACT

Introduction: Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) are promising interventions to curb HIV transmission among men who have sex with men (MSM). However, incorrect use may elevate HIV risk. This study investigated the impact of improper PrEP/PEP use on HIV infection among MSM.

Methods: A cross-sectional survey was conducted in Shenzhen (2021–2023) using time-location sampling and respondent-driven sampling. χ^2 tests and Poisson regression with robust error variance were employed for univariate and multivariate analyses.

Results: Compared to PrEP/PEP non-users, MSM who incorrectly used PrEP [adjusted odds ratio (a*OR*)=2.17, 95% confidence interval (*CI*): 1.05, 4.49] and PEP (a*OR*=3.76, 95% *CI*: 1.40, 10.15) were more likely to be HIV-positive. No HIV-positive cases were reported among MSM who correctly used PrEP. Correct PEP users showed no significant difference in HIV prevalence compared to non-users.

Conclusions: Correct PrEP/PEP use is an effective HIV prevention strategy for MSM, but incorrect use may increase infection risk. Public health efforts must prioritize interventions promoting adherence to PrEP/PEP guidelines, emphasizing that PrEP/PEP should complement — not replace — consistent condom use.

Men who have sex with men (MSM) constitute one of the populations at highest risk for human immunodeficiency virus (HIV) infection. In 2022, MSM accounted for approximately 25% of newly diagnosed HIV cases in China, with this proportion exceeding 60% in developed urban areas (*1*). A significant disconnect exists between knowledge and behavioral practices among MSM, creating substantial challenges for HIV risk reduction interventions. Post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) have emerged as the most promising strategies for preventing HIV transmission in the MSM population. However, incorrect implementation of PrEP/PEP may increase HIV infection risk among MSM and potentially contribute to HIV drug resistance (*2*), thereby accelerating viral transmission. Our findings indicate that MSM who incorrectly used PrEP/PEP were more likely to test HIV-positive compared to both correct users and non-users. This observation highlights the critical importance of proper PrEP/PEP utilization, particularly given that PrEP/PEP users demonstrate

higher rates of unprotected anal intercourse (UAI), which may explain why incorrect PrEP/PEP usage represents a significant risk factor for HIV infection among MSM.

This cross-sectional study investigated PEP and PrEP utilization and HIV infection status among MSM in Shenzhen City, Guangdong Province, China, from 2021–2023. Participants were recruited through time-location sampling (TLS) and respondent-driven sampling (RDS), following previously described methodologies (*3*). The inclusion criteria for study participation were as follows: Biologically male, aged 16 years or older and had engaged in sexual activity with men within the past 12 months. Data collection was conducted via tablet-based self-administered questionnaires, capturing demographic information and HIV risk behaviors. Blood samples were collected for laboratory HIV testing to determine infection status. Correct PEP use was defined as medication obtained from healthcare facilities with proper medical prescription, accompanied by HIV testing both before initiation and after completion of the treatment course. Correct PrEP use was defined as medication obtained from healthcare facilities and taken according to medical professionals' prescriptions. Incorrect PrEP/PEP use encompassed any medications obtained through non-healthcare facilities or those obtained from healthcare facilities but not taken as prescribed.

Statistical analyses were performed using SPSS (version 20.0, IBM Corp, State of New York, America). Univariate analyses employed chi-square tests, with factors showing $P<0.1$ included in multivariate analyses. Multivariate regression analyses utilized Poisson regression with robust error variance through generalized linear models. Results are presented as number (%), means ± standard deviations, adjusted odds ratios (a*OR*s), and 95% confidence intervals (*CI*s). Statistical significance was set at 0.05.

This study surveyed 3,723 MSM with a mean age of 33.65±8.81 years, yielding an HIV prevalence of 2.67% (99/3,723). Significant differences in HIV infection status were observed across ethnicity, educational level, sexual role, syphilis infection status, engagement in UAI, PEP use, and PrEP use ($P<0.05$, Table 1). Poisson regression analysis revealed that, compared to HIV-negative MSM, HIV-positive individuals were more likely to be of other ethnicities (a*OR*=2.94, 95% *CI*: 1.49, 5.81), have receptive sexual roles (a*OR*=3.11, 95% *CI*: 1.64, 5.87) or versatile roles (a*OR*=2.34, 95% *CI*: 1.33, 4.10), be infected with syphilis (a*OR*=2.59, 95% *CI*: 1.12, 5.97), and engage in UAI (a*OR*=3.03, 95% *CI*: 1.93, 4.76). Notably, compared to PrEP/PEP non-users, MSM who incorrectly used PrEP (a*OR*=2.17, 95% *CI*: 1.05, 4.49) and PEP (a*OR*=3.76, 95% *CI*: 1.40, 10.15) were more likely to report HIV-positive status. Furthermore, no HIV-positive cases were reported among MSM who correctly used PrEP, and no significant difference in HIV prevalence was observed between correct PEP users and non-users (Table 1).

Among the study participants, 8.5% (316/3,723) reported PrEP/PEP usage. Significant differences were observed in the distribution of PrEP/PEP users across education level, duration of residence, monthly income, sexual role, HIV testing history, and UAI engagement ($P<0.05$, Table 2). Poisson regression analysis revealed that MSM who used PrEP/PEP were more likely to have college or higher education (a*OR*=1.49, 95% *CI*: 1.03, 2.15), recent HIV testing within 6 months (a*OR*=1.49, 95% *CI*: 1.03, 2.15), and engagement in UAI (a*OR*=1.95, 95% *CI*: 1.54, 2.47). These individuals were also more likely to report both insertive and receptive sexual roles (a*OR*=0.74, 95% *CI*: 0.57, 0.97) but were less likely to have resided in Shenzhen for more than 6 months (a*OR*=0.60, 95% *CI*: 0.44, 0.82) (Table 2).

DISCUSSION

The adoption rate of PrEP/PEP among MSM in Shenzhen remains relatively low at 8.5%, considerably below the approximately 20% utilization rate reported in a recent multicenter study across China from 2019–2022 (*4*). This disparity highlights an urgent need for enhanced implementation strategies. Our analysis revealed that while 81.71% (143/175) of PEP users adhered to correct usage protocols, only 22.16% (37/167) of PrEP users demonstrated proper adherence. Notably, the study found complete protection against HIV transmission among MSM who correctly used PrEP, with zero HIV-positive cases in this group. Conversely, MSM who reported HIV-positive status were significantly more likely to have used PrEP/PEP incorrectly compared to HIV-negative individuals, suggesting a potential association between incorrect prophylaxis use and increased HIV acquisition risk, though causal relationships require further investigation. These findings emphasize the critical importance of ensuring proper PrEP/PEP utilization when recommending these interventions to MSM.

Our findings indicate that MSM utilizing PrEP/PEP

TABLE 1. Factors associated with HIV infection among MSM in Shenzhen city in 2021–2023 (*N*=3,718).

Variables	HIV-negative, no. (%)	HIV-positive, no. (%)	χ^2	*P*	a*OR*	95% *CI*
Year			3.63	0.06		
2021–2022	2,333 (96.96)	73 (3.03)				
2023	1,286 (98.01)	26 (1.98)			0.58	0.36, 0.93
Ethnicity			9.37	0.00		
Han	3,498 (97.46)	91 (2.54)				
Other	101 (92.66)	8 (7.34)			2.94	1.49, 5.81
Educational level			6.81	0.03		
Junior high school and below	517 (95.91)	22 (4.08)				
High middle school	893 (96.95)	28 (3.04)			0.78	0.44, 1.36
College and above	2,209 (97.82)	49 (2.17)			0.66	0.40, 1.11
Length of residence			1.43	0.23		
0–6 months	422 (96.56)	15 (3.43)				
≥7 months	3,008 (97.53)	76 (2.46)				
Income (CNY)			3.50	0.17		
≤3,000	350 (97.49)	9 (2.51)				
3,001–7,000	433 (96.00)	18 (3.99)				
≥7,001	2,836 (97.52)	72 (2.48)				
Marital status			0.53	0.77		
Unmarried	2,924 (97.30)	81 (2.70)				
Cohabiting/married	367 (97.86)	8 (2.13)				
Separated/divorced/widowed	328 (97.04)	10 (2.96)				
Sexual roles			14.42	0.00		
Inserters	1,282 (98.61)	18 (1.38)				
Receptive	583 (95.88)	25 (4.11)			3.11	1.64, 5.87
Both	1,754 (96.90)	56 (3.09)			2.34	1.33, 4.10
Sexual orientation			0.51	0.92		
Homosexual	2,596 (97.22)	74 (2.77)				
Heterosexual	31 (96.87)	1 (3.13)				
Bisexual	711 (97.66)	17 (2.34)				
Unsure	281 (97.56)	7 (2.43)				
Syphilis infection			9.87	0.00		
No	3,556 (97.45)	93 (2.55)				
Yes	63 (91.30)	6 (8.70)			2.59	1.12, 5.97
HIV test			1.73	0.20		
No	2,026 (97.03)	62 (2.97)				
Yes	1,593 (97.73)	37 (2.27)				
UAI			30.34	<0.001		
Yes	1,320 (95.30)	65 (4.69)			3.03	1.93, 4.76
No	1,835 (98.54)	27 (1.45)				
PEP			12.18	0.00		
Unused	3,451 (97.40)	92 (2.60)				
Incorrect use	28 (87.50)	4 (12.50)			3.76	1.40, 10.15
Correct use	140 (97.90)	3 (2.10)			0.69	0.25, 1.93

Continued

Variables	HIV-negative, no. (%)	HIV-positive, no. (%)	χ^2	*P*	a*OR*	95% *CI*
PrEP			10.34	0.01		
Unused	3,461 (97.46)	90 (2.53)				
Incorrect use	121 (93.07)	9 (6.92)			2.17	1.05, 4.49
Correct use	37 (100.00)	0 (0)			0	0, 0

Abbreviation: a*OR*=adjusted odds ratio; *CI*=confidence intervals; HIV=human immunodeficiency virus; MSM=men who have sex with men; PEP=postexposure prophylaxis; PrEP=preexposure prophylaxis; UAI=unprotected anal intercourse; CNY=Chinese yuan.

were 1.9 times more likely to engage in UAI compared to non-users, suggesting that some individuals may view prophylaxis as a replacement for consistent condom use (*5*). The HIV yield was significantly higher among PrEP/PEP users compared to non-users (14.1% *vs.* 8.3%, *P*=0.041). This elevated infection rate likely stems from the combination of incorrect prophylaxis use and increased UAI, which collectively amplify HIV transmission risk among non-compliant MSM.

Previous research has indicated that Chinese MSM demonstrate a preference for event-driven PrEP over daily PrEP (*6*). Our findings reveal that more than 60% of MSM transitioned from daily to event-driven PrEP regimens. However, we observed that the HIV yield among MSM using event-driven PrEP was 6.1% (7/114), exceeding that of daily PrEP users (3.8%, 2/53). This disparity may be attributed to the inherent complexity of event-driven PrEP protocols, which increases the likelihood of incorrect usage among MSM, potentially leading to HIV infection. Therefore, while previous studies have demonstrated the effectiveness of event-driven PrEP in reducing HIV infection risk among MSM (*7*), additional real-world studies in China are essential to evaluate its efficacy and develop appropriate implementation guidelines.

Moreover, improper PrEP/PEP usage may contribute to HIV drug resistance (*2*,*8*), potentially catalyzing new epidemic waves. Our unpublished data indicates that the prevalence of nucleotide reverse transcriptase inhibitor resistance among HIV-infected individuals with PrEP/PEP exposure was significantly higher compared to those without exposure (12.5% versus 1.7%, *P*=0.025). Research has shown that PrEP/PEP-related HIV drug resistance can develop when these interventions are administered during undetected acute infection, emphasizing the critical importance of HIV testing prior to PrEP/PEP initiation (*9*). Furthermore, the increasing use of PrEP during acute HIV infection may result in false-negative HIV test results (*10*). Consequently, current HIV testing protocols may be insufficient for PrEP/PEP users, particularly regarding the recommended quarterly testing schedule for event-driven PrEP users. To prevent continued PrEP/PEP use among HIV-infected MSM, we recommend that individuals who use these interventions incorrectly or cannot ensure proper adherence undergo HIV testing before each subsequent use.

This study has two main limitations. First, this study was a cross-sectional study that could not establish the causality between incorrect PrEP/PEP use and HIV infection. In the future, we plan to undertake a longitudinal observational follow-up study to investigate the reasons for incorrect PrEP/PEP use among MSM and assess its causal association with HIV infection in this population. Second, as the study was conducted in a developed Chinese city characterized by a predominantly migratory population and where MSM constitute most newly diagnosed HIV-positive cases, the findings may have limited generalizability to other urban settings.

In conclusion, while correct PrEP/PEP usage among MSM represents a promising strategy for HIV prevention, incorrect usage may paradoxically increase HIV infection risk, particularly given that PrEP/PEP users demonstrate higher rates of UAI. The current priority lies in developing and implementing effective strategies to promote proper PrEP/PEP adherence while emphasizing that these preventive medications should complement, rather than replace, consistent condom use.

Conflicts of interest: No conflicts of interest.

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TABLE 2. Factors associated with PrEP/PEP use among MSM in Shenzhen city in 2021–2023 (*N*=3,723).

Variables	Unuse PrEP/PEP, no. (%)	Use PrEP/PEP, no. (%)	χ^2	*P*	a*OR*	95% *CI*
Year			1.13	0.29		
2021–2022	2,215 (91.87)	196 (8.13)				
2023	1,192 (90.85)	120 (9.15)				
Ethnicity			0.08	0.78		
Han	3,291 (91.56)	303 (8.43)				
Other	99 (90.82)	10 (9.17)				
Educational level			19.15	<0.001		
Junior high school and below	494 (91.48)	46 (8.52)				
High school	875 (94.90)	47 (5.10)			0.72	0.46, 1.14
College and above	2,038 (90.13)	223 (9.86)			1.49	1.03, 2.15
Length of residence			3.95	0.05		
0–6 months	391 (89.26)	47 (10.73)				
≥7 months	2,843 (92.06)	245 (7.93)			0.60	0.44, 0.82
Income (CNY)			9.32	0.01		
≤3,000	315 (87.50)	45 (12.50)				
3,001–7,000	409 (90.68)	42 (9.31)			0.94	0.59, 1.51
≥7,001	2,683 (92.13)	229 (7.86)			0.77	0.53, 1.14
Marital status			1.86	0.39		
Unmarried	2,744 (91.22)	264 (8.78)				
Cohabiting/married	348 (92.30)	29 (7.69)				
Separated/divorced/widowed	315 (93.19)	23 (6.80)				
Sexual roles			18.02	<0.001		
Inserter	1,176 (90.39)	125 (9.61)				
receptive	539 (88.36)	71 (11.63)			1.14	0.84, 1.56
Both	1,692 (93.37)	120 (6.62)			0.74	0.57, 0.97
Sexual orientation			1.10	0.78		
Homosexual	2,439 (91.24)	234 (8.75)				
Heterosexual	29 (90.62)	3 (9.38)				
Bisexual	671 (92.04)	58 (7.96)				
Unsure	268 (92.73)	21 (7.27)				
Syphilis infection			0.21	0.65		
No	3,344 (91.54)	309 (8.46)				
Yes	63 (90.00)	7 (10.00)				
HIV test			9.18	0.00		
No	1,940 (92.73)	152 (7.27)				
Yes	1,467 (89.94)	164 (10.05)			1.48	1.17, 1.88
UAI			34.07	<0.001		
Yes	1,224 (88.31)	162 (11.68)			1.95	1.54, 2.47
No	1,755 (94.05)	111 (5.95)				

Abbreviation: a*OR*=adjusted odds ratios; *CI*=confidence intervals; HIV=human immunodeficiency virus; MSM=men who have sex with men; PEP=postexposure prophylaxis; PrEP=preexposure prophylaxis; UAI=unprotected anal intercourse; CNY=Chinese yuan.

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