Online distribution of HIV self-testing kits to promote HIV testing among men who have sex with men discontinuing pre-exposure prophylaxis after demonstration project completion in China: a multicentre open-label randomized controlled trial

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Summary

Background HIV self-testing (HIVST) offers potential solutions to challenges associated with site-based HIV testing (SBHT). However, the effectiveness of HIVST as an HIV prevention strategy for men who have sex with men (MSM) discontinuing pre-exposure prophylaxis (PrEP) after the completion of PrEP demonstration project has rarely been assessed.

Methods The China Real-world Study of Oral PrEP (CROPrEP) project was conducted in four cities in China. Participants were directed to community resources to continue their PrEP medication after the discontinuation of project-provided PrEP at the last CROPrEP visit. We conducted a multicentre open-label randomized controlled trial among MSM who had discontinued PrEP induced by the completion of CROPrEP. Eligible participants were randomly assigned to either the intervention group or the control group (1:1). Participants received regular health education and behavioural interventions throughout the trial. The intervention group was given a link to order free HIVST kits online, while the control group received information about free SBHT. Both groups completed internet-based follow-up surveys at three and six months. The primary outcome was the proportion of participants who underwent HIV testing during the six-month follow-up period. This trial was registered at chictr.org.cn (ChiCTR2000038416).

Findings Between November 2020 and January 2021, we recruited a total of 620 participants (300 in the intervention group and 320 in the control group). The follow-up completion rates were 99·0% and 95·0% in the intervention and control groups, respectively. At baseline, the median age of participants was 32 (interquartile range: 26–37), and 77·7% underwent HIV testing in the past three months. The proportion of participants who underwent HIV testing in the past three months was higher in the intervention group than in the control group at both the three-month (adjusted risk difference [RD]: 36·7, 95% confidence interval [CI]: 35·1–38·5, $p < 0·001$) and six-month (RD: 26·7, 95% CI: 24·6–28·7 $p < 0·001$) follow-up periods.

Interpretation Our study suggests that providing online distribution of HIVST kits for MSM with PrEP discontinuation induced by completion of the PrEP project effectively promoted HIV testing. This digital approach improves access to HIV testing for MSM and can be applicable to other settings where MSM turn to online public health services.

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Research in context

Evidence before this study

Discontinuing pre-exposure prophylaxis (PrEP) diminishes its protective effect, leaving individuals at risk of HIV seroconversion. Thus, regular HIV testing and behavioural monitoring is crucial. Previous studies have shown that providing HIV self-testing (HIVST) kits increased HIV testing rates and lowered sexual risk behaviours among individuals with high risk. We conducted a search on PubMed for English-language articles between January 1, 2012 and August 22, 2021, using the search terms "HIV", "HIV self-testing", "PrEP discontinuation", "PrEP cessation", "pre-exposure prophylaxis discontinuation", "HIV self-testing and PrEP discontinuation", and "HIV self-testing and PrEP cessation". No published studies were found on the impact of providing self-tests for men who have sex with men (MSM) after discontinuing PrEP due to the termination of PrEP demonstration project.

Added value of this study

Conducted among MSM who had discontinued PrEP induced by the China Real-world Study of Oral PrEP project, this multicentre open-label randomized controlled trial is the first study to evaluate the effects of providing HIVST kits to MSM after PrEP discontinuation induced by PrEP demonstration project. During the 6-month intervention period, HIV testing rates of intervention group were higher compared to the control group. Moreover, the prevalence of sexual risk behaviour was lower in the intervention group.

Implications of all the available evidence

This study provides evidence for HIVST use among MSM after discontinuing PrEP induced by PrEP demonstration project. Sexual risk behaviours remained high among participants who discontinued PrEP, highlighting the importance of regular HIV testing. HIVST serves as a complementary testing approach to promote HIV testing rates and safe sex practices. The online distribution of HIVST represents great potential to support HIV elimination goals.

Introduction

HIV disproportionately affects men who have sex with men (MSM), with MSM 25 times more vulnerable to HIV compared to the general population.[1] Pre-exposure prophylaxis (PrEP) has been shown to be effective in preventing HIV transmission when taken as prescribed by MSM.[2,3] Recently, the China Real-world Study of Oral PrEP (CROPrEP) demonstrated that PrEP use was associated with a lower incidence of HIV and a good safety profile.[4] However, inconsistent usage of PrEP has been frequently reported,[5] and HIV transmissions often occur after PrEP discontinuation.[6,7] Studies suggest that HIV incidence rates rise significantly to 2·1–3·9/100 person-years (PY) when PrEP is discontinued, vs. rates of 0·0–0·1/100 PY observed during PrEP usage.[8,9] Addressing HIV seroconversion after PrEP discontinuation is essential to combating the global HIV epidemic.

The discontinuation rate of PrEP within six months is considerably high at 41%.[5] After PrEP discontinuation, the HIV test service will also terminate which was offered every three months. Given the high risk of HIV infection among the population with PrEP discontinuation, it is vital to monitor their HIV testing and sexual behaviours. According to current recommendations in England, individuals are advised to undergo HIV testing at intervals of four and eight weeks following the discontinuation of PrEP.[10] However, little is known about the HIV testing rate of the PrEP discontinuation in other countries.

HIV testing is crucial for identifying HIV status and initiating the HIV treatment. Research has shown that frequent HIV testing can lower HIV transmission among MSM.[11] MSM face several challenges accessing site-based HIV testing (SBHT) in China due to privacy and stigma issues.[12] Additionally, COVID-19 has limited access to HIV prevention services and HIV testing.[13,14] Hence strategies that enhance HIV testing are necessary. HIV self-testing (HIVST) allows individuals to collect their sample, conduct the test, receive and interpret results privately. HIVST kits can be ordered online, making HIVST more convenient and confidential.[15] The World Health Organization has recommended HIVST as an option to expand the coverage of HIV testing in individuals with high risk.[16] Furthermore, HIVST has shown a favourable application effect on PrEP users, further emphasizing the importance of increased HIVST uptake and secondary distribution rates.[17,18] Despite its effectiveness, research on the application and secondary distribution of HIVST kits among MSM with PrEP discontinuation is limited, particularly resulting from the completion of PrEP project.

This study aims to investigate the effectiveness of distributing HIVST kits in promoting HIV testing and

reducing sexual risk behaviours among MSM with PrEP discontinuation following the completion of CROPrEP.

Methods

Study design and participant eligibility

To achieve the objectives of this study, we conducted a follow-up study based on the CROPrEP project. The CROPrEP study, conducted between 2018 and 2020 in China, was a nonrandomized controlled trial that assessed HIV incidence among MSM using PrEP.[4] Participants in the CROPrEP study were enrolled from four cities in China: Beijing, Shenyang, Chongqing, and Shenzhen. At the final visit of the CROPrEP study, the provision of study-provided PrEP was discontinued. During the final study visit, participants were provided with information about local PrEP providers but were responsible for self-initiating PrEP continuation.

This was a multicentre, open-label randomized controlled trial (RCT) involving MSM previously enrolled in the CROPrEP study. We conducted a combined online and offline recruitment from the four study cities of CROPrEP. The first participant was enrolled in the study on November 7, 2020, and the last completed the study on September 6, 2021. The recruited participants took HIV testing at the CROPrEP collaborating hospitals in their respective cities (Supplementary Material S1). Participants were eligible if they met the following criteria: (1) had taken PrEP for more than six months during the CROPrEP study; (2) did not take any PrEP for more than 3 months after the termination of CROPrEP; (3) self-reported having a stable residence, and (4) tested negative for HIV-1 on enrolment. The trial protocol was approved by the ethics committee of the First Affiliated Hospital of China Medical University in Shenyang, China (Supplementary Material S1). All participants provided online informed consent before undergoing the baseline survey. Confidentiality of personal information for all participants was strictly maintained throughout the study period. Participants were given the opportunity to withdraw from the study without facing any adverse consequences. To meet the needs of participants in the control group, we provided an additional complimentary HIVST kit to all participants in need after completing the study (data are not available). Study reporting follows CONSORT 2010 guidelines (Supplementary Material S2).

Randomization and masking

Randomization was performed using computer-generated codes with a random seed of 700. One staff performed randomization and divided codes (1:1) into two groups using SPSS software version 26·0 (IBM Inc). Another staff then placed the codes in opaque envelopes and assigned participants to either the intervention or control group based on the envelope they received during enrolment. Although participants and research staff were aware of group assignments due to the nature of the intervention, recruitment staff and participants did not discover their groups until the envelope was opened.

Procedures

Participants were instructed to add the dedicated WeChat account specifically created for this study. Eligible participants completed an online baseline survey, distributed by the study staff through the dedicated WeChat account. The survey collected sociodemographic information, past sexual behaviours, and HIV testing experiences within the three months before they discontinued PrEP (questionnaire platform: https://jinshuju.net/home). Sexual behaviours included frequency, types of partners (regular and casual), and condom usage. HIV testing experiences included whether participants underwent testing, the methods used (HIVST or SBHT), and the frequency of testing. Testing with partners was defined as simultaneous testing with a sexual partner in the same setting, with both partners aware of each other's test results. Participants in the intervention group received a link to order two free quadruplex self-testing kits produced by Wondfo Guangzhou, China. Each kit tested for HIV-1 antibody, *Treponema pallidum* antibody, Hepatitis B surface Antigen, and Hepatitis C virus antibody. The application link was provided once at the beginning of the study and remained active for the entire study period. Participants were informed that they could apply for the kits once a month using the provided link. These kits were discreetly delivered to individuals who ordered them online. Participants could use the kits individually or share them with their sexual partners. All distributed kits came with an operation manual that included a Quick Response code for result feedback and safety equipment (e.g., diluents, band-aids, safety lancets, and testing orifice plates. Supplementary Material S1, Supplementary Figures S2 and S3). Within two days of testing, participants shared a photo of their HIVST test result as proof. Participants in the control group were instructed to visit the designated testing facilities at the collaborating hospitals of the local CROPrEP project for laboratory testing. These hospitals served as the designated testing centres during the follow-up period of the CROPrEP. Since the participants have already undergone testing at these facilities, it was convenient for them to access testing services. Free condoms and lubricants were offered to all participants.

We followed up with participants at every three-month interval and conducted two online surveys on their HIV test experience and related risk behaviours during the past three months after PrEP was discontinued. Follow-up questionnaires were distributed to participants via the dedicated WeChat account (refer to Supplementary Material S1, Appendix B for detailed

questionnaire information). Participants had received unique identification numbers in the CROPrEP project to ensure identity uniqueness. They were required to upload a picture of their test result within 48 h using the Quick Response code for feedback. Reminder messages would be sent to participants who did not upload their results within one week. Participants who did not upload their results within two weeks would no longer be eligible to request additional kits. We paid each participant US$7·75 as financial compensation for completing each follow-up survey and an additional US$4·65 if he successfully uploaded a photo of his test results. Participants' partners could also earn US$4·65 by providing the correct index case identification numbers through a follow-up questionnaire via the dedicated WeChat account. Each partner could be compensated once, and repeat participation was prevented by registering phone numbers. For participants who had a reactive HIVST, we provided them with information about nearby confirmatory testing and link-to-care services.

Outcomes

The primary outcome was the proportion of participants who underwent HIV testing during the six-month follow-up period. Secondary outcomes include HIV testing frequency, the proportion of testing with partners (defined as simultaneous testing with a sexual partner in the same setting, while mutually aware of each other's test results), and the prevalence of sexual risk behaviours. Such behaviours include condomless anal intercourse (CAI) with regular partners, CAI with casual partners, CAI with partners of unknown HIV status, and CAI in group sex, reported at every follow-up stage. All outcomes were self-reported data collected from each follow-up survey.

Statistical analysis

Based on a previous HIVST intervention study conducted in China,[19] we assumed that 94·5% of participants in the intervention group and 86·6% of participants in the control group would undergo HIV testing during the study. We calculated sample sizes using PASS version 15.0 (NCSS, LLC., Kaysville, Utah, USA). Each group of 212 participants provided an 80% power to detect a difference between groups in HIV testing rates (two-tailed $\alpha = 0{\cdot}05$). Assuming a dropout rate of 15%, each group should contain at least 250 participants or a total of 500 participants.

We analysed data on an intention-to-treat basis, utilizing generalized estimating equations (GEE) to calculate odds ratios with 95% confidence interval (CI) for identifying behavioural characteristic differences between participants prior to and after discontinuation of PrEP. The Chi-square test was utilized for binary variables to analyse frequency distribution differences, while Wilcoxon-sum tests were utilized to compare continuous variables between the two groups.

For binary variables, we used the Chi-square test to identify differences in frequency distributions between groups at follow-up. Wilcoxon rank-sum tests were used to compare the two groups regarding continuous variables. We used the Cochran–Armitage trend test to determine trends in the behavioural characteristics of the two groups at follow-up. The risk difference (RD) and 95% confidence interval (CI) for both primary and secondary outcomes were adjusted for centre and baseline HIVST rates, and p-values were calculated using the Wald analysis. We used the GEE model to analyse factors related to the sharing of the HIVST kit with partners in the intervention group. A multifactorial GEE model adjusted for age, education degree, and income level. A two-tailed p-value of 0.05 was considered significant. All statistical analyses were conducted using SPSS version 26.0 (SPSS, IBM Inc.) and SAS version 9.4 (SAS Institute, Cary, NC). This trial has been registered at chictr.org.cn (ChiCTR2000038784).

Role of the funding source

The funders had no role in study design, data collection, analysis, interpretation, or paper writing. We made all the data collected available to the corresponding author, who had the ultimate responsibility for the decision to submit for publication.

Results

We randomly assigned 620 participants between November 2020 and January 2021: 300 to the intervention group and 320 to the control group. Among the 620 participants, 266 were from Shenyang, 222 were from Beijing, 69 were from Shenzhen, and 63 were from Chongqing. A total of 297 participants in the intervention group (99·0%) and 304 participants in the control group (95·0%) completed the six-month follow-up (Fig. 1). The baseline characteristics of participants are presented in Table 1, with a median age at 32 years old (interquartile range [IQR]: 26–37). 482 (77·7%) participants received HIV testing within the three months prior to enrolment. Significant differences were observed in the baseline HIVST testing rates between the two groups ($p < 0{\cdot}001$).

Following PrEP discontinuation, participants showed a lower rate of HIVST usage (57·3% vs. 67·6%, $p < 0{\cdot}001$, Supplementary Material S3, T1). A total of 1490 HIVST kits were mailed, with 1235 valid results collected, yielding a feedback rate of 82·9% (Supplementary Material S3, T2).

During the six-month intervention period, participants in the intervention group completed 597 questionnaires, and 245 of them reported sharing HIVST kits with their partners. Having CAI with regular partners (Adjusted Odds Ratio [AOR] = 1·8, 95% CI: 1·2–2·8, $p = 0{\cdot}005$) and depression (AOR = 1·9, 95% CI: 1·2–3·0,

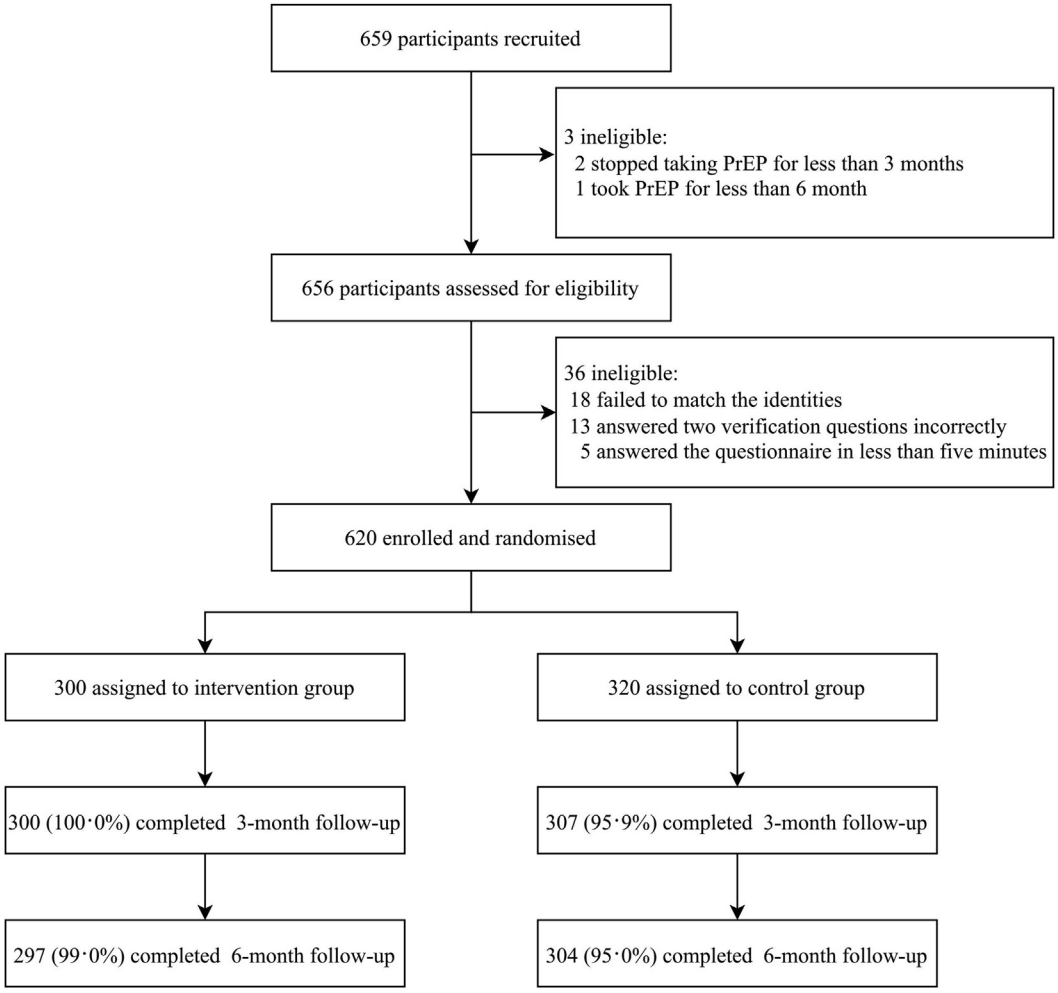

Fig. 1: **Trial profile.**

p = 0·008) were positively associated with HIVST kit sharing in the intervention group (Supplementary Material S3, T3). Six participants (three in each group) reported reactive HIV test results, with an overall HIV incidence of 1·85/100 PY (1·93/100 PY in the intervention group and 1·79/100 PY in the control group).

During the initial three months of follow-up, the intervention group had a higher rate of HIV testing than the control group (RD: 36·7, 95% CI: 35·1–38·5, p < 0·001). Moreover, the uptake rate of HIVST in the intervention group was twice that observed in the control group (RD: 45·2, 95% CI: 43·0–47·4, p < 0·001), with similar results observed during the second three months of follow-up (HIV testing rate: RD: 26·7, 95% CI: 24·6–28·7, p < 0·001; HIVST uptake rate: RD: 34·5, 95% CI: 32·0–37·6, p < 0·001). Compared to the control group, the frequency of HIV testing within the intervention group was significantly higher during the first three months (3·0 vs. 1·1, p < 0·001) and second three months (2·5 vs. 1·2, p < 0·001) of follow-up, with a similar pattern observed for the frequency of HIVST (the first three months: 2·5 vs. 0·9, p < 0·001; the second three months: 2·1 vs. 1·0, p < 0·001). The intervention group also exhibited a significantly higher rate of testing with partners during both periods (p < 0·001) (Table 2).

During the first and second three months of follow-up, the prevalence of engaging in CAI with regular partners was lower in the intervention group than in the control group (RD: −11·4, 95% CI: −12·5 to −10·3 and RD: −30·3, 95% CI: −31·1 to −29·4, respectively), as well as the prevalence of CAI in group sex (RD: −27·5, 95% CI: −27·5 to −26·5 and RD: −43·4, 95% CI: −43·9 to −42·8, respectively) (all p < 0·05). Furthermore, during the first three months of follow-up, the prevalence of CAI with casual partners (RD: −23·8, 95% CI: −24·2 to −23·3, p < 0·001) and partners of unknown HIV status (RD: −15·4, 95% CI: −15·4 to −15·3, p < 0·001) was lower in the intervention group.

Characteristic	Overall n (%)	Intervention group n (%)	Control group n (%)	p-value[a]
Total, n	620 (100·0)	300 (100·0)	320 (100·0)	
Demographics				
Age, median (IQR)	32 (26–37)	31 (26–35)	33 (26–38)	<0·005
Centre				<0·001
Shenyang	266 (42·9)	94 (31·3)	172 (53·8)	
Beijing	222 (35·8)	93 (31·0)	129 (40·3)	
Shenzhen	69 (11·1)	57 (19·0)	12 (3·8)	
Chongqing	63 (10·2)	56 (18·7)	7 (2·2)	
Educational degree				<0·001
High school and below	110 (17·7)	33 (11·0)	77 (24·1)	
College and above	510 (82·3)	267 (89·0)	243 (75·9)	
Monthly income, US$				0·058
≤888	365 (58·9)	165 (55·0)	200 (62·5)	
>888	255 (41·1)	135 (45·0)	120 (37·5)	
Marital status				0·073
Single	336 (54·2)	161 (53·7)	175 (53·4)	
In a relationship with a man	223 (36·0)	117 (39·0)	106 (35·3)	
Other[d]	61 (9·8)	22 (7·3)	39 (11·3)	
Main approach for seeking male partners in the past three months				0·992
Gay dating application[e]	340 (54·8)	167 (55·7)	173 (54·1)	
Regular sexual partner(s)	223 (36·0)	106 (35·3)	117 (36·6)	
Other[f]	57 (9·2)	27 (9·0)	30 (9·4)	
HIV testing type in the past three months				
HIVST	355 (57·3)	204 (68·0)	151 (47·2)	<0·001
SBHT	189 (30·5)	80 (26·7)	109 (34·1)	0·046
Any type of HIV testing	482 (77·7)	249 (83·0)	233 (72·8)	0·002
Testing with partner(s)	287 (46·3)	169 (56·3)	118 (36·9)	<0·001
Frequency of HIV tests in the past three months (mean, SD)[b]				
HIVST	1·4 (1·9)	1·7 (1·9)	1·1 (1·9)	<0·001
SBHT	0·5 (1·1)	0·5 (1·1)	0·6 (1·1)	0·074
Any type of HIV testing	1·9 (2·2)	2·2 (2·2)	1·6 (2·3)	<0·001
Sexual behaviours in the past three months				
Frequency of sexual behaviours[c]				0·179
Almost every day	8 (1·3)	3 (1·0)	5 (1·6)	
Every week	235 (37·9)	119 (39·7)	116 (36·3)	
Monthly or less	325 (52·4)	160 (53·3)	165 (51·6)	
No sexual behaviour	52 (8·4)	18 (6·0)	34 (10·6)	
Sexual role with man[f]				0·134
Top	220 (38·6)	105 (37·2)	115 (40·2)	
Bottom	172 (30·3)	82 (29·1)	90 (31·5)	
Versatile	149 (26·2)	85 (30·1)	64 (22·4)	
Oral only	27 (4·8)	10 (3·5)	17 (5·9)	
Has regular partner(s)[g]	381 (67·1)	194 (68·8)	187 (65·4)	0·387
Has casual partner(s)[g]	261 (46·0)	136 (48·2)	125 (43·7)	0·280
Has CAI with regular partner(s)[h]	217 (57·0)	105 (54·1)	112 (59·9)	0·256
Has CAI with casual partner(s)[h]	121 (46·4)	65 (47·8)	56 (44·8)	0·628
Has group sex	95 (17·6)	49 (18·0)	46 (17·1)	0·780
Has CAI in group sex[h]	34 (35·8)	16 (32·7)	18 (39·1)	0·510
Has CAI with partner(s) in unknown HIV status	78 (12·6)	37 (12·4)	41 (12·8)	0·857

IQR, interquartile range; HIVST, HIV self-testing; SBHT, site-based HIV testing, including facility-based site testing (such as the testing conducted at centre for disease control and prevention, hospitals, and clinics) as well as community-based testing conducted at gay voluntary agencies, community health centres, and through mobile outreach programs; CAI, condomless anal intercourse. [a]Analyze using chi-square test. [b]Analysed using Wilcoxon rank-sum tests. [c]Analysed using Fisher's exact test. The study focused exclusively on sexual behaviours with male partners. [d]Other refers to individuals who were either married or cohabiting with a woman, separated, divorced, or widowed. [e]Same-sex dating application refers to Blued, JACK, flip click, Jicco, cabinet, star gay friend, etc. [f]Other refers to different methods used to meet partners, such as common dating apps, introductions by friends, or meeting partners at parks, clubs, or baths. [g]The denominator excluded 52 subjects who reported no sexual behaviour. [h]The denominators correspond to the number of individuals who reported having regular sexual partner(s), casual sexual partner(s), and group sex, respectively.

Table 1: **Baseline characteristics.**

Characteristic	M3		Adjusted risk difference (95% CI)[a]	p-value	M6		Adjusted risk difference (95% CI)[a]	p-value
	Intervention group n (%)	Control group n (%)			Intervention group n (%)	Control group n (%)		
N	300 (100·0)	307 (100·0)			297 (100·0)	304 (100·0)		
HIV testing in the past three months (%)								
HIVST	272 (90·7)	140 (45·6)	45·2 (43·0, 47·4)	<0·001	240 (80·8)	141 (46·4)	34·5 (32·0, 37·6)	<0·001
SBHT	65 (21·7)	49 (16·0)	5·7 (5·0, 6·4)	0·021	64 (21·5)	54 (17·8)	3·8 (3·1, 4·4)	0·106
Any type of HIV testing	286 (95·3)	180 (58·6)	36·7 (35·1, 38·5)	<0·001	259 (87·2)	184 (60·5)	26·7 (24·6, 28·7)	<0·001
Testing with partner(s)	137 (45·7)	62 (20·2)	25·5 (35·1, 38·5)	<0·001	115 (38·7)	61 (20·1)	18·7 (17·4, 20·0)	<0·001
Frequency of HIV tests in the past three months (mean, SD)[b]								
HIVST	2·5 (2·0)	0·9 (1·5)		<0·001	2·1 (1·9)	1·0 (1·6)		<0·001
SBHT	0·5 (1·2)	0·3 (0·9)		0·060	0·5 (1·1)	0·3 (0·7)		0·162
Any type of HIV testing	3·0 (2·4)	1·1 (2·0)		<0·001	2·5 (2·3)	1·2 (1·9)		<0·001
Sexual behaviour in the past three months (%)								
Frequency of sexual behaviour[c]				<0·001				<0·001
Almost every day	3 (1·0)	25 (8·1)			3 (1·0)	25 (8·2)		
Every week	109 (36·3)	85 (27·7)			103 (34·7)	146 (48·0)		
Monthly or less	184 (61·3)	189 (61·6)			186 (62·6)	129 (42·5)		
No sexual behaviour	4 (1·3)	8 (2·6)			5 (1·7)	4 (1·3)		
Has regular partner(s)[d]	210 (70·9)	173 (57·9)	−3·2 (−3·5, −3·0)	0·002	197 (67·5)	182 (60·7)	6·5 (6·4, 6·5)	0·112
Has casual partner(s)[d]	132 (44·6)	143 (47·8)	−3·2 (−3·5, −3·0)	0·358	123 (42·1)	129 (43·0)	−1·0 (−1·5, −0·6)	0·599
Has CAI with regular partner(s)[e]	110 (52·4)	112 (64·7)	−11·4 (−12·5, −10·3)	0·008	116 (58·9)	162 (89·0)	−30·3 (−31·1, −29·4)	<0·001
Has CAI with casual partner(s)[e]	58 (43·9)	96 (67·1)	−23·8 (−24·2, −23·3)	<0·001	56 (45·5)	61 (47·3)	−1·9 (−2·2, −1·7)	0·671
Has group sex	43 (14·3)	44 (14·3)	−0·2 (−0·4, 0·0)	0·811	42 (14·1)	41 (13·5)	0·6 (0·4, 0·9)	0·886
Has CAI in group sex[e]	16 (37·2)	29 (65·9)	−27·5 (−27·5, −26·5)	0·037	15 (35·7)	32 (78·0)	−43·4 (−43·9, −42·8)	<0·001
Has CAI with partner(s) in unknown HIV status	32 (10·7)	80 (26·1)	−15·4 (−15·4, −15·3)	<0·001	29 (9·8)	37 (12·2)	−2·4 (−2·6, −2·2)	0·279

HIVST, HIV self-testing; SBHT, site-based HIV testing, including facility-based site testing (such as the testing conducted at centre for disease control and prevention, hospitals, and clinics) as well as community-based testing conducted at gay voluntary agencies, community health centres, and through mobile outreach programs; CAI, condomless anal intercourse. [a]Risk difference adjusted for centre and baseline rate of HIVST. [b]Analysed using Wilcoxon rank-sum tests. [c]Analyse using chi-square test. [d]The denominator excluded subjects who reported no sexual behaviour. [e]The denominators correspond to the number of individuals who reported having regular sexual partner(s), casual sexual partner(s), and group sex, respectively.

Table 2: **Effect of HIV self-testing intervention on primary and secondary outcomes.**

The trend analysis of the testing and sexual behaviours is presented in Fig. 2. Over the six-month intervention, the uptake rate of HIVST increased significantly in the intervention group, from 68·0% to 87·2% ($p < 0·001$ for trend). In contrast, the control group experienced a significant decrease in the rate of HIV testing (from 72·8% to 60·5%) and SBHT (from 34·1% to 17·8%), along with a significantly higher prevalence of CAI with regular partners (from 59·9% to 89·0%) and condomless group sex (from 39·1% to 78·0%), all $p < 0·001$ for trend.

Discussion

The results of this RCT indicate that providing HIVST to MSM after discontinuing PrEP upon completion of the PrEP project substantially improved HIV testing rates, increased the distribution of HIVST kits to partners, and reduced the prevalence of CAI and other high-risk sexual behaviours compared to control group. These findings suggest that HIVST may be considered the practicable testing strategy for the population with PrEP discontinuation.

Our study demonstrates that providing HIVST kits to MSM who discontinue PrEP after completion of the PrEP project significantly increased the frequency and experience of HIV testing, which is consistent with previous researches. Two RCTs conducted in the United States and Australia have shown that HIVST can increase the frequency of HIV testing among MSM,[20,21] while an RCT in China found that HIVST kit distribution increased the frequency of HIVST testing, and the frequency of SBHT in the intervention and control groups was comparable.[19] A meta-analysis also found that HIVST increased the mean number of HIV tests by 2·56 over follow-up,[15] which is higher than the value obtained in our study. The high baseline testing frequency resulting from the testing services of the PrEP project may have limited the effectiveness of our intervention in this regard.

Our findings indicate a decrease in the rate of SBHT during the study period, particularly in the control group. Two plausible explanations exist for this observed trend. Firstly, some participants appeared to have short-term discontinuation at the baseline survey. The testing

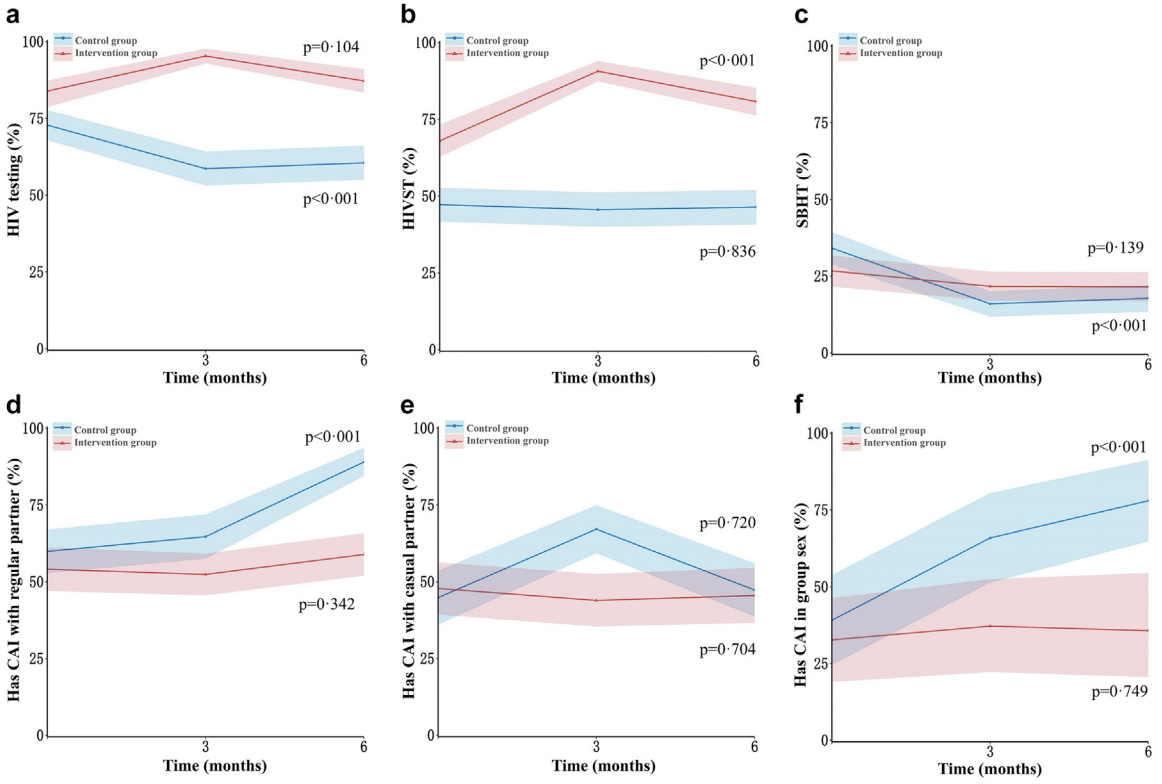

Fig. 2: **Cochran–Armitage test for trend of primary and secondary outcomes.** Cochran–Armitage test of the trend of HIV testing rate (a); HIVST rate (b); SBHT rate (c); the rate of CAI with regular partners (d); the rate of CAI with casual partners (e); the rate of CAI in group sex (f). HIVST, HIV self-testing; SBHT, site-based HIV testing, including facility-based site testing (such as the testing conducted at centre for disease control and prevention, hospitals, and clinics) as well as community-based testing conducted at gay voluntary agencies, community health centres, and through mobile outreach programs; CAI, condomless anal intercourse.

services offered by CROPrEP may have been a contributing factor to the elevated baseline rate of SBHT. Secondly, the COVID-19 epidemic in China was under good control during the baseline survey period which could have resulted in a rebound increase in SBHT. It is worth noting that the sensitivity of the self-test was variable,[22] and a positive result always requires confirmation through confirmatory laboratory testing. Therefore, further research is needed to explore methods for increasing the use of HIVST kits without impacting the SBHT rate.

Our study also found that sexual risk behaviours remained prevalent among individuals who discontinued PrEP. Previous research has primarily focused on risk compensation as a result of PrEP initiation and has shown that a decrease in perceived risk and sexual risk behaviour may contribute to the reason for discontinuation.[7,23,24] However, little evidence exists regarding actual changes in sexual behaviours after discontinuation. Our comparative analysis of sexual behaviours before and after discontinuation showed that the prevalence of sexual risk behaviours remained high in all participants and tended to increase in the control group after six months. These findings suggest that individuals who involuntarily discontinue PrEP induced by the completion of the PrEP project are more likely to maintain sexual risk behaviours. After six months of HIVST kit distribution, the prevalence of CAI was significantly lower in the intervention group than in the control group, implying that HIVST intervention can reduce the risk of HIV infection and should be considered a protective measure for the PrEP population with discontinuation.

During the study period, the self-reported HIV incidence was 1·85/100 PY, which was higher than during the CROPrEP period (0·90/100 PY) but lower than for PrEP nonusers (5·10/100 PY).[4] Six participants in the study were newly HIV infected, but these results were based on self-reporting. Individuals who test positive may not report their results to researchers due to stigma. Therefore, the HIV incidence in this study may be underestimated. Only one participant underwent laboratory testing for confirmation and was linked to care. The other five were not tracked, indicating that

tracking test results and ensuring positive cases linked to care present a significant challenge in the implementation of HIVST.[25] Future researches are needed to explore strategies for follow-up for newly tested HIV-positive users and linkage to care.

The distribution of HIVST kits not only increased the self-testing rate and reduced CAI but also expanded testing coverage. Moreover, secondary distribution of HIVST kits facilitates HIV testing with partners, as supported by existing research. Studies on Chinese MSM have shown that peer-driven secondary distribution of HIVST kits can increase the utilization rate of HIV testing kits.[26–28] Couple HIV testing can lead to safer sex and reduce the risk of HIV infection.[29,30] By engaging in couple HIV testing, individuals can understand the infection status and risk of themselves and their partners, which can help them make a better-informed sexual decision.[30,31]

This study has implications for future research and intervention. Firstly, this is the first RCT in China to provide HIVST kits to the population with project-induced discontinuation. It expands the evidence for HIVST interventions and provides a valuable reference for future PrEP-related HIVST studies. It is imperative to conduct larger-scale RCTs for this population in the future. Secondly, we combined digital media and mail intervention with RCT, which partially compensated for the shortcomings of traditional intervention methods that require a lot of manpower and resources. Thirdly, we, for the first time, explored the sexual behaviours of the MSM after PrEP discontinuation. Future studies should focus on behaviour tracking, especially for those who involuntarily discontinue PrEP. Fourthly, our study shows a decrease in sexual risk behaviour in MSM through HIVST intervention. Subsequent work will consider further qualitative research into the psychological factors influencing their behavioural change.

This study has several limitations. Firstly, regulatory restrictions on facility-based testing in China may have influenced the increased demand for self-testing. However, COVID-19 was effectively controlled in China during the study period, and the four study cities did not undergo strict lockdowns during the recruitment. Thus, we believe that the impact of COVID-19 on the study was minimal. Secondly, participants were only recruited from CROPrEP, which may have resulted in a lack of representativeness and generalizability. Thirdly, due to the initial setting of 700 seeds for random assignment, there was a slight difference in the number of participants in the two groups. Fourthly, the baseline HIV testing levels were imbalanced between the two groups, which could potentially compromise the reliability of the results. However, the adjusted analysis results provided evidence that the distribution of HIVST effectively increased HIV testing. Fifthly, the sample size was powered to detect differences in the primary outcome, thus the study might not have enough power to detect differences in other outcomes. Sixthly, the interpretation of the results was based on self-reported questionnaires, which may pose potential report and recall bias. Seventhly, we did not consider the PrEP usage and HIV status of participants' regular partners, which could have influenced the likelihood of HIV acquisition. Eighthly, blinding was not implemented in the data analysis of this study. However, the statistical analysis process was independently conducted by two researchers and followed by result verification. Lastly, our study had a duration of only six months, limiting the ability to observe the long-term effects of the intervention.

In conclusion, this study represents the first attempt to investigate the HIV testing rate among individuals following PrEP discontinuation resulting from the completion of the PrEP project in China. Our findings suggest that online distribution of HIVST represents an effective approach to increasing HIV testing and condom use. Digital network-based distribution of HIVST shows promise as a feasible strategy to reduce the risk of HIV exposure among individuals discontinuing PrEP.

Contributors

HS and QHH had the idea and designed the study. YYG, and ZXC recruited patients and collected the data. HZ and YYZ analysed and interpreted the data. ZXC, SC, ML, and YJJ had a check for the analysis. HZ and YYZ wrote the first draft of the article. HS and QHH revised the manuscript. All authors had unrestricted access to the data and participated in data interpretation. All the authors contributed to subsequent drafts and agreed to submit the article for publication.

Data sharing statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100922.

References

1 UNAIDS. *Global HIV & AIDS statistics — fact sheet*; 2022. https://www.unaids.org/en/resources/fact-sheet.
2 Mayer KH, Molina JM, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet*. 2020;396(10246):239–254.
3 Huang X, Hou J, Song A, et al. Efficacy and safety of oral TDF-based pre-exposure prophylaxis for men who have sex with men: a systematic review and meta-analysis. *Front Pharmacol*. 2018;9:799.

4 Wang H, Wang Z, Huang X, et al. Association of HIV preexposure prophylaxis use with HIV incidence among men who have sex with men in China: a nonrandomized controlled trial. *JAMA Netw Open*. 2022;5(2):e2148782.
5 Zhang J, Li C, Xu J, et al. Discontinuation, suboptimal adherence, and reinitiation of oral HIV pre-exposure prophylaxis: a global systematic review and meta-analysis. *Lancet HIV*. 2022;9(4):e254–e268.
6 Marcus JL, Hurley LB, Hare CB, et al. Preexposure prophylaxis for HIV prevention in a large integrated health care system: adherence, renal safety, and discontinuation. *J Acquir Immune Defic Syndr*. 2016;73(5):540–546.
7 Krakower D, Maloney KM, Powell VE, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc*. 2019;22(2):e25250.
8 Greenwald ZR, Maheu-Giroux M, Szabo J, et al. Cohort profile: l'Actuel pre-exposure prophylaxis (PrEP) cohort study in Montreal, Canada. *BMJ Open*. 2019;9(6):e028768.
9 Shover CL, Shoptaw S, Javanbakht M, et al. Mind the gaps: prescription coverage and HIV incidence among patients receiving pre-exposure prophylaxis from a large federally qualified health center in Los Angeles, California. *AIDS Behav*. 2019;23(10):2730–2740.
10 Brady M, Rodger A, Asboe D, et al. BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2018. *HIV Med*. 2019;20(Suppl 2):s2–s80.
11 Liu Y, Qian HZ, Ruan Y, et al. Frequent HIV testing: impact on HIV risk among Chinese men who have sex with men. *J Acquir Immune Defic Syndr*. 2016;72(4):452–461.
12 Liu Y, Sun X, Qian HZ, et al. Qualitative assessment of barriers and facilitators of access to HIV testing among men who have sex with men in China. *AIDS Patient Care STDS*. 2015;29(9):481–489.
13 Brown LB, Spinelli MA, Gandhi M. The interplay between HIV and COVID-19: summary of the data and responses to date. *Curr Opin HIV AIDS*. 2021;16(1):63–73.
14 Lagat H, Sharma M, Kariithi E, et al. Impact of the COVID-19 pandemic on HIV testing and assisted partner notification services, Western Kenya. *AIDS Behav*. 2020;24(11):3010–3013.
15 Witzel TC, Eshun-Wilson I, Jamil MS, et al. Comparing the effects of HIV self-testing to standard HIV testing for key populations: a systematic review and meta-analysis. *BMC Med*. 2020;18(1):381.
16 World Health Organization. *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach*; 2021. https://www.who.int/publications/i/item/9789240031593. Accessed July 16, 2021.
17 Zhang J, Tucker J, Tang W, et al. Internet-based HIV self-testing among men who have sex with men through pre-exposure prophylaxis: 3-month prospective cohort analysis from China. *J Med Internet Res*. 2021;23(8):e23978.
18 Ngure K, Ortblad KF, Mogere P, et al. Efficiency of 6-month PrEP dispensing with HIV self-testing in Kenya: an open-label, randomised, non-inferiority, implementation trial. *Lancet HIV*. 2022;9(7):e464–e473.
19 Zhang C, Koniak-Griffin D, Qian HZ, et al. Impact of providing free HIV self-testing kits on frequency of testing among men who have sex with men and their sexual partners in China: a randomized controlled trial. *PLoS Med*. 2020;17(10):e1003365.
20 MacGowan RJ, Chavez PR, Borkowf CB, et al. Effect of internet-distributed HIV self-tests on HIV diagnosis and behavioral outcomes in men who have sex with men: a randomized clinical trial. *JAMA Intern Med*. 2020;180(1):117–125.
21 Jamil MS, Prestage G, Fairley CK, et al. Effect of availability of HIV self-testing on HIV testing frequency in gay and bisexual men at high risk of infection (FORTH): a waiting-list randomised controlled trial. *Lancet HIV*. 2017;4(6):e241–e250.
22 Figueroa C, Johnson C, Ford N, et al. Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: a systematic review and meta-analysis. *Lancet HIV*. 2018;5(6):e277–e290.
23 Unger ZD, Golub SA, Borges C, Edelstein ZR, Hedberg T, Myers J. Reasons for PrEP discontinuation following navigation at sexual health clinics: interactions among systemic barriers, behavioral relevance, and medication concerns. *J Acquir Immune Defic Syndr*. 2022. https://doi.org/10.1097/QAI.0000000000002952.
24 Whitfield THF, John SA, Rendina HJ, Grov C, Parsons JT. Why I quit pre-exposure prophylaxis (PrEP)? A mixed-method study exploring reasons for PrEP discontinuation and potential re-initiation among gay and bisexual men. *AIDS Behav*. 2018;22(11):3566–3575.
25 Venter F, Majam M, Jankelowitz L, et al. South African HIV self-testing policy and guidance considerations. *South Afr J HIV Med*. 2017;18(1):775.
26 Zhao P, Zhou Y, Ni Y, et al. Testing together behaviors in secondary distribution of HIV/syphilis self-testing program among men who have sex with men in China. *AIDS Behav*. 2022;27(5):1430–1440.
27 Sha Y, Xiong Y, Ong JJ, et al. Comparing the effectiveness of secondary distribution of HIV/syphilis dual self-testing to testing card referral in promoting HIV testing among gay, bisexual, and other men who have sex with men in Guangzhou, China: a quasi-experimental study. *Sex Health*. 2022;19(4):357–366.
28 Xiao W, Yan L, Chen L, et al. Sexual network distribution of HIV self-testing kits: findings from the process evaluation of an intervention for men who have sex with men in China. *PLoS One*. 2020;15(4):e0232094.
29 Masters SH, Agot K, Obonyo B, Napierala Mavedzenge S, Maman S, Thirumurthy H. Promoting partner testing and couples testing through secondary distribution of HIV self-tests: a randomized clinical trial. *PLoS Med*. 2016;13(11):e1002166.
30 Thirumurthy H, Bair EF, Ochwal P, et al. The effect of providing women sustained access to HIV self-tests on male partner testing, couples testing, and HIV incidence in Kenya: a cluster-randomised trial. *Lancet HIV*. 2021;8(12):e736–e746.
31 Tiwari R, Wang J, Han H, et al. Sexual behaviour change following HIV testing services: a systematic review and meta-analysis. *J Int AIDS Soc*. 2020;23(11):e25635.