BMJ Open

HIV and other STIs self-testing to reduce risk compensation among men who have sex with men who use oral pre-exposure prophylaxis in China: protocol for a randomised waitlist-controlled trial

Jing Zhang,[1,2,3,4] Xiaojie Huang,[5,6] Yaokai Chen,[7] Hui Wang,[8] Yonghui Zhang,[1,2,3,4] Hongyi Wang,[1,2,3,4] Zhu Mei,[1,2,3,4] Yueru Jia,[1,2,3,4] ZhenXing Chu,[1,2,3,4] Qing-Hai Hu,[1,2,3,4] Xiaoqing He ,[7] Lukun Zhang,[8] Zhili Hu,[1,2,3,4] Rantong Bao,[1,2,3,4] Shangcao Li,[1,2,3,4] Haibo Ding,[1,2,3,4] Yongjun Jiang,[1,2,3,4] Wenqing Geng,[1,2,3,4] Weiming Tang ,[9] Junjie Xu ,[1,2,3,4] The CROPrEP Group

To cite: Zhang J, Huang X, Chen Y, *et al*. HIV and other STIs self-testing to reduce risk compensation among men who have sex with men who use oral pre-exposure prophylaxis in China: protocol for a randomised waitlist-controlled trial. *BMJ Open* 2020;**10**:e036231. doi:10.1136/bmjopen-2019-036231

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-036231).

Received 06 December 2019
Revised 27 April 2020
Accepted 28 April 2020

For numbered affiliations see end of article.

Correspondence to
Dr Junjie Xu; xjjcmu@163.com

ABSTRACT

Introduction Pre-exposure prophylaxis (PrEP) reduces the risk of HIV infection among men who have sex with men by up to 99%. However, in real-world settings, PrEP users may exhibit risk compensation after uptake of PrEP, including more condomless anal intercourse (CAI) and increased sexually transmitted infection (STI) acquisition. HIV self-testing (HIVST) decreases CAI among men who have sex with men (MSM) by providing awareness of the HIV status of oneself and one's sexual partners. Here, we describe the rationale and design of a randomised waitlist-controlled trial to examine the impact of HIVST on risk compensation among PrEP users.

Methods and analysis The study is a two-arm randomised waitlist-controlled trial with 1000 HIV-negative MSM in four major cities in China who will be taking oral PrEP (involving tenofovir disoproxil fumarate/emtricitabine) either daily (n=500) or in an event-driven regimen (n=500). The participants will be randomised (1:1) to either the immediate HIVST intervention arm (HIVST plus standard facility-based counselling and testing from 0 to 12 months) or the waitlist arm (standard facility-based counselling and testing from 0 to 6 months, then crossover to receive the HIVST intervention in months 7–12). Participants will provide blood samples to assess the incidence of syphilis and herpes simplex virus type 2 (HSV-2) during a follow-up. The primary outcomes will be the occurrence of CAI, number of sexual partners and incidence of syphilis and HSV-2 during a follow-up. The secondary outcomes will be the HIV and STI testing frequency and STI treatment adherence during a follow-up. The planned start and end dates for the study is 26 December 2018 and 31 December 2020.

Ethics and dissemination The Medical Science Research Ethics Committee of The First Affiliated Hospital of China Medical University has approved the study (IRB(2018)273).

Trial registration number ChiCTR1800020374

Strengths and limitations of this study

- This study will objectively evaluate the impact of HIV and sexually transmitted infections (STIs) self-testing on the incidence of STIs and HIV-related risk behaviour among men who have sex with men (MSM) who are using pre-exposure prophylaxis (PrEP).
- This study will explore the impact of HIV and STIs self-testing on the frequency of both HIV and other STIs and the adherence to STI treatment among MSM using PrEP.
- The randomised waitlist-controlled design of this study enables understanding of the outcomes by different timing of HIV self-testing provision during PrEP.
- This prospective study may be subjected to lost to follow-up bias and attrition bias.
- Due to limited resources, this study only exams limited types of STIs other than HIV, including syphilis, herpes simplex virus type 2, hepatitis B, hepatitis C.

INTRODUCTION

Men who have sex with men (MSM) are one of the key populations at risk of HIV infection and a target population for pre-exposure prophylaxis (PrEP). PrEP has been shown to be effective at reducing HIV infection among MSM at risk of HIV by up to 99%.[1 2] PrEP involving tenofovir disoproxil fumarate/emtricitabine was approved for HIV prevention among adults in 51 countries and regions worldwide in April 2019.[3] There are currently at least 381 580 people who have initiated PrEP in 68 countries.[4]

There is high frequent HIV testing accompanied with PrEP programmes, which always include facility-based HIV testing performed every 3 months.[5] As exposure to antiretroviral drugs in individuals with undiagnosed HIV is the main risk factor for drug resistance associated with PrEP,[6] it is imperative to exclude HIV-positive individuals from PrEP programmes and to ensure consistent and frequent HIV testing. However, adherence to clinical visit during PrEP is low in a real-world setting, only 68% of PrEP users (MSM, transgender and heterosexual women and men) in a large urban academic medical centre in the USA attended their first clinic visit, and only 35% attended their third clinic visit.[7]

Recent studies have shown that HIV self-testing (HIVST) can not only double the uptake of HIV testing among MSM,[8–10] but also have highly acceptability and feasibility among PrEP users.[11] It can reduce the clinical burden associated with PrEP among female sex workers.[12] An ongoing study is assessing whether delivery of HIVST with PrEP can replace facility-based HIV testing among heterosexual male and female receiving PrEP.[13]

Risk compensation of sexually transmitted infections (STIs) other than HIV is another concern with PrEP initiation in real-world setting.[14–16] Several studies have reported slightly increased condomless anal intercourse (CAI) and considerably increased STIs among PrEP users in real-world settings.[14 17] Currently, physicians and public health professionals mainly depend on risk-reduction counselling to reduce high-risk sexual behaviour among PrEP users, and there is a lack of effective interventions to reduce risk compensation among PrEP users.

Recently, studies have reported heightened awareness of risk and risk reduction behaviour following HIVST uptake.[18–20] For example, if a potential partner had a positive HIVST result or refused HIVST, condoms might be used or the sexual encounter might be ended.[18–20] To our knowledge, there are no previous studies on the effect of HIVST on risk compensation among PrEP users.

PrEP decreases users' risk of HIV infection but has no effect on the transmission of other STIs, such as syphilis, herpes simplex virus type 2 (HSV-2), hepatitis B virus (HBV) and hepatitis C virus (HCV), which are highly prevalent among MSM in China. Syphilis is almost twice as prevalent as HIV among MSM in China,[21] and remains pandemic at the prevalence of 13.5%[22] and incidence at 9.6/100 person-years.[23] The prevalence of HSV-2, HBV and HCV among MSM in China is 10.6%, 8.9% and 1.2%, respectively.[22] Furthermore, 65.3% of the MSM in China with suspected STI-infections did not seek diagnosis and treatment in STI clinics.[24] According to the previous studies, the incidence of syphilis among MSM taking PrEP is 44.6 times higher than MSM not taking PrEP.[25] Study measuring treatment for STIs during PrEP is urgently in need and still scarce.[26]

Recent studies found that STIs self-testing may be an efficient way to identify STIs,[27] may increase the rate of first-time STI testing, and could be integrated into HIVST services.[28] However, the study of self-testing combined with HIV and other STIs is lacking. The effects of STI self-testing on STI treatment initiation and adherence after a positive STI self-test result has not been explored among PrEP users.

China has an estimated 2 467 800 MSM who are at high risk of HIV infection, but there are currently no related guidelines in China and the PrEP programmes in China are still in a demonstration stage.[29] We designed this randomised waitlist-controlled trial of combined self-testing kits of HIV and other STIs among MSM using PrEP in China to explore the effects of self-testing on CAI and STI incidence.

METHODS

Study aims

The primary aims of this randomised waitlist-controlled trial are to determine whether HIV and other STIs self-testing kits can decrease high-risk sexual behaviours (self-reported CAI and number of male sexual partners) and the incidence of syphilis and HSV-2 in PrEP users. The secondary aim of this study is to examine the impact of combined HIV and STI self-testing kits on HIV and STI testing frequency and adherence to appropriate treatment of STI among PrEP users.

Study settings

We are currently conducting an ongoing real-world study of PrEP in four major cities in China (named China Real-world study of Oral PrEP (CROPrEP)), with the support of the 'Action Plan for the 13th Five-Year Plan of the Mega Programme' of the China National Health and Family Planning Commission. The CROPrEP trial, along with the current trial, is conducted in the following four major cities: Beijing, Shenyang, Chongqing and Shenzhen (the four study sites are The Youan Hospital of Capital Medical University in Beijing, The First Affiliated Hospital of China Medical University in Shenyang, The Chongqing Public Health Medical Center of Southwest University in Chongqing, and The Third People's Hospital of Shenzhen). These four cities are major cities located in the middle, northeast, southwest and southeast parts of China. These study sites meet the following requirements: (1) class A hospitals that provide HIV voluntary counselling and testing rooms and have an HIV treatment clinic with physicians specialised in infectious disease; (2) have previously successfully built and maintained a large cohort of MSM and (3) associated with a local community-based organisation (CBO) that has the capacity to improve MSM participation retention and intervention implementation.[30 31]

Participants

The participants will be HIV-negative MSM using PrEP in the CROPrEP trial, including both daily and event-driven PrEP users. Participants are currently being recruited for the CROPrEP trial using online postings, posters and

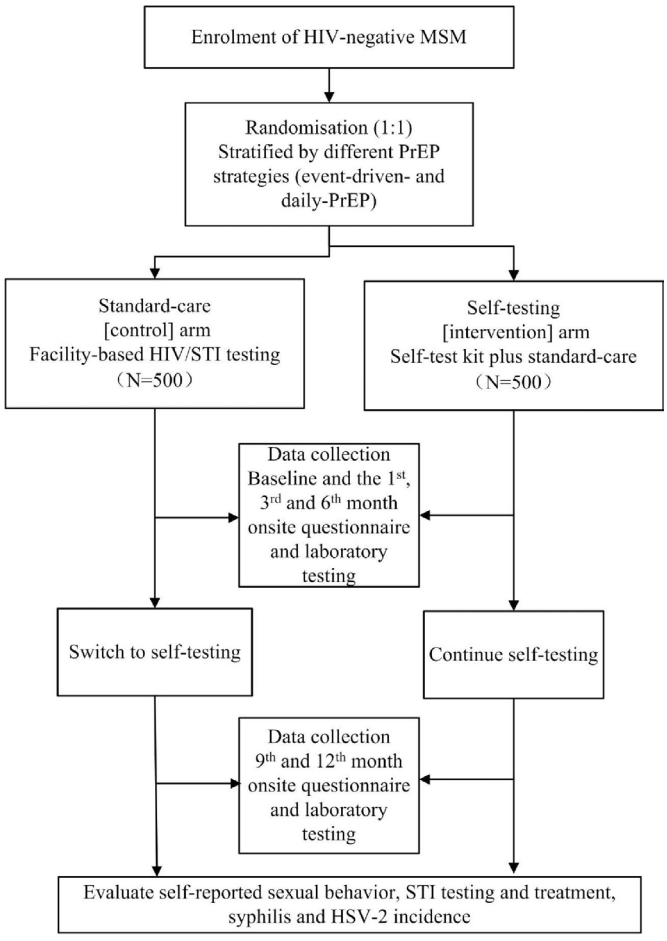

Figure 1 Study flow chart. MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; STIs, sexually transmitted infections.

brochures, outreach events run by the CBOs and MSM peer referral.

Inclusion criteria

Participants are eligible for this study if they: (1) were designated male at birth; (2) have sex with male partners; (3) are aged 18–65 years old; (4) report having one or more of the following risk factors in the last 6 months: (A) had condomless receptive anal sex with a male partner, (B) had more than two male sexual partners, (C) had self-reported STIs such as syphilis, gonorrhoea, chlamydia, chancroid or lymphogranuloma venereum or (D) have ever used postexposure prophylaxis (PEP) medication, but have not received PEP in the previous month; (5) have a non-reactive fourth-generation HIV ELISA at baseline screening, and undetectable HIV-1 RNA; (6) have no evidence of severe liver or kidney dysfunction based on a comprehensive evaluation (including physical examination, urine test and blood biochemical examination) and (7) indicate willingness to participate and sign an informed consent form.

Exclusion criteria

Individuals will be excluded if they: (1) are found to be ineligible in the eligibility evaluation to join the CROPrEP trial; (2) refuse to accept or use the HIVST kits (with reasons recorded) or (3) refuse to sign the informed consent form. The main exclusion criteria for CROPrEP are HIV infected, allergic to the ingredients of the study drug, having serious chronic disease, having serious chronic disease.[32]

Study design

The study is a randomised waitlist-controlled trial with blinded outcome assessment and blinded data analysis. MSM using PrEP will be randomised in a 1:1 ratio into one of the two study arms: an immediate HIV and STI self-testing arm and a waitlist-control arm. The immediate HIV and STI self-testing arm will immediately receive free HIV from pick-up at the study site (postal service is also available if necessary), syphilis, HBV, and HCV self-testing kits for 12 months, in addition to standard quarterly clinic visits (for facility-based counselling and testing). The waitlist-control arm will receive the standard quarterly clinic visits for 6 months, after which they will crossover and receive the intervention (HIV and STI self-testing kits) for 6 months (figure 1).

Recruitment and retention strategies

Participants began being recruited to the CROPrEP trial from December 2018 using (1) posters and brochures in the HIV testing and treatment clinics and waiting areas at the four study sites for MSM who come for counselling and testing, (2) postings in MSM chat groups and on the study sites' official WeChat and Tencent QQ accounts (two of the most widely used social media applications in China) and (3) outreach events run by the CBOs in hotspots (bars, public baths and parks) that provide study information, (4) MSM peer referral. Any potential participants who express interest in CROPrEP trial will be contacted by CBO and study site staff to schedule a screening appointment.

During the follow-up period, participants will have access to supports for adherence from both physicians and leaders of CBOs, providing routine reminders of follow-up visits and survey via shot message, face-to-face appointment and live chat.

Randomisation and blinding

Computer-generated randomisation numbers, stratified by PrEP strategy (daily or event-driven PrEP use), will be produced and sealed in envelopes (to ensure allocation concealment) by a research assistant not associated with the trial. All study site staff and CBO staff will be blinded to the randomisation numbers during the recruitment, informed consent procedure and enrolment. The randomisation numbers will then be made into drawing straws in two separate boxes (one for daily and one for event-driven PrEP users). After signing the informed consent form, each participant will draw a randomisation number from one of the boxes (according to their PrEP strategy) and hand it to a staff member. The staff member will reveal the randomisation result to the participant immediately.

Throughout the study, outcome assessors and data analysts will be blinded to the group assignments.

Intervention group

Participants in the intervention group will have access to two HIVST kits per month in addition to facility-based HIV testing services. The HIVST kits will be distributed at every clinic visit and can also be mailed to the participants if required. The participants will be encouraged to test themselves and their sexual partners using the kits.

Self-testing kits and testing procedure

The kits used will be finger stick-based the quadruplex detection reagents (Wondlfo Guangzhou, China) of HIV-*Treponema pallidum* (TP)-HBV-HCV, which have been approved by the Food and Drug Administration in China. The kit can detect HIV-1 antibodies in blood specimens at 6 weeks postinfection, and antibodies related to syphilis, HCV and HBV surface antigen. The kits will be packaged with all the consumables required for the collection of a finger blood sample (a disposable retractable blood needle, an ethylenediaminetetraacetic acid) capillary tube, Wondlfo solution, a sealed cotton alcohol swab and a sealed bandage). The results can be read in 15–20 min. Each kit will be accompanied by instructions and a link to a demonstration video of the procedure for testing, interpreting the results and uploading the image of the results. We have successfully conducted a large study of MSM who were using HIVST for the first time, which demonstrated widespread acceptance.[33]

After randomisation, doctors will provide the participants in the intervention group face-to-face and paper-based HIVST instructions. All information and demonstration videos will be available on study sites' WeChat and Tencent QQ account. We will also provide a link to the study database in Jinshuju (China) for participants to upload images of the test results. Each kit will be packaged with a card with the participant's patient identification number (PID). Participants will be asked to take an image of each test result with the card, and then to upload the image. Participants will be compensated for their time and effort with ¥5 (US$0.7) if they upload an image of the test result. Participants and partners with a positive screening results of STIs will be contacted and referral by staff of this study for confirmation testing and treatment at STIs clinic in the study sites.

Online and telephone-based support

Participants will be able to contact staff via WeChat and a telephone support line for consultation regarding HIVST administration and side effects (such as bruising and infection) caused by blood collection. The WeChat account is set up with the automatic response menu with frequently asked questions, which is 24 hours, 7 days. The telephone support line works from 8:00 am to 0:00 hours.

Control group

Participants in the control group will receive the standard HIV consultation and testing services provided at the study clinics. After completion of an initial 6 months of follow-up, these participants will be provided with a free supply of HIVST kits for the remaining 6 months (ie, the same intervention provided to the intervention group will be provided to the control group during this period).

HIV diagnostic tests

Participants will be asked to upload all their HIVST results to the study database and to inform the study staff of any positive or indeterminate HIV results. Participants and their partners with these results will be contacted by the study site staff and CBOs to undergo confirmatory laboratory testing and post-test counselling at the study clinics. If they prefer to go to a Center for Disease Control and Prevention (CDC) other than the study clinics, they will be offered assistance in arranging an appointment. The participant's PrEP study involvement will cease if the diagnostic results are positive.

Outcome measures

The primary study outcomes will be to determine whether HIV and other STIs self-testing kits will affect the frequency of self-reported prevalence of high-risk sexual behaviours (self-reported CAI and number of male sexual partners) in each group, and incidence of syphilis and HSV-2 during follow-up. The secondary study outcomes will be the HIV and STI testing frequency STI treatment adherence, and existing problems of STIs referral and treatment during the follow-up.

Monitoring and quality control

All health professionals and staffs work at four study sites of this research will be trained about the protocol and rationale of this trial before they started. As the coordinating centre, the First Affiliated Hospital of China Medical University will perform quality control every 3 months on data of all four study sites to evaluate the compliance of protocol. A data inspection company are employed to independently audit the conduct of the trial and quality of the data. Both the coordinating centre and the data inspection company will have access to the final trial dataset. Any adverse events will be recorded by clinical physicians of this study. Severe adverse events will be reported to the ethics committee within 72 hours. The causal association and severity assessment will be independently evaluated by two physicians. Any reported adverse events will be clinically tracked until they are restored or stabilised. Although according to guidelines of HIVST by WHO,[34] instances of harms following voluntary HIVST have been few, we will adapt the medical resources to monitor adverse events during follow-up when it occurs. The assessment of adverse effects of PrEP was described in previous published article.[32] If there are any important protocol modifications, it has to be reported to the Institutional Review Board (IRBs) at the First Affiliated Hospital of China Medical University.

Primary and secondary outcomes will be evaluated by researchers in order to monitor risk compensation

before crossover of the control participants to the HIVST intervention at the 6-month follow-up. If there is significant risk compensation in the intervention group at the 6-month follow-up, the HIVST intervention will be stopped for both the intervention and control groups to avoid further risk compensation.

Data collection

We will collect data using an anonymous online data collection system named Jinshuju (www.jinshuju.com), which is an online survey system operated by a company that has a confidentiality contract with the study team to encrypt the data and ensure the safety and privacy of participants' information. Four accounts with Jinshuju will be set up (one for each study site), and the passwords will only be known by designated staff. Participants in both the intervention and control groups will visit the clinics for five times (at the baseline visit and the follow-up visits at 1, 3, 6, 9 and 12 months after initiation of PrEP). The online data collection platform has a built-in quality control system, which will remind the participants and staff for missing data and cross check for logical mistakes once the questionnaire is submitted.

The baseline questionnaire was validated based on expert review and implementation in a large MSM cohort in China.[35] Data to be collected will include sociodemographic information, HIV testing history (including both HIVST and facility-based testing) in the past 12 months, history of syphilis, HSV-2 and any other STIs, and high-risk sexual behaviour (number of male sexual partners, frequency of CAI and number of male sexual partners with CAI) in the past 12 months.

The onsite follow-up questionnaire data will include the HIVST times and results in the past 3 months, the use of HIVST by male sexual partners (involving the number of HIVST kits used, the place, time and results of HIVST use), HIV facility-based testing in the past 3 months, testing and treatment for syphilis, HSV-2 and any other STIs in the past 3 months (STI testing, screen test positive, diagnosis, treatment start date, treatment finish date and retest result) and sexual behaviour (number of male sexual partners, frequency of CAI, and number of male sexual partners with CAI) in the past 3 months, and the participants' HIVST use and sharing of HIVST kits with sexual partners.

Laboratory testing

Other than HIV and STIs self-testing kits provided to and used by participants in the intervention group, laboratory testing will be performed at every clinical visit for all participants. At every follow-up visit, blood will be drawn to test for HIV, syphilis and HSV-2 in the facility-based laboratories of the four study sites. HIV-1 antibody screening will be conducted using a fourth-generation ELISA (Vironostika HIV-1/2 Microelisa System; BioMerieux, Holland). Cases deemed to be HIV positive based on the ELISA will be asked to return to the clinic to consent to further confirmatory testing using an HIV-1/2 western blot (WB) test (HIV Blot 2.2 WB; Genelabs Diagnostics, Singapore). If the WB test is positive, we will conclude that the participant is infected with HIV. For participants who do not return or do not consent to the WB test, we will conclude that they are infected based on two positive ELISAs based on the same blood sample.[36] The laboratory-confirmed HIV diagnoses will be based on the standard HIV testing protocols in China.[37] Laboratory syphilis screening will be conducted using a TP particle agglutination assay (TPPA; Fujirebio, Tokyo, Japan) and those with a positive result in TPPA will go through the rapid plasma reagin (RPR) test (Shanghai Kehua Bio-engineering, China). Participants with positive results for both TPPA and RPR will be considered to have syphilis. HSV-2 infection was determined by HSV-2-specific IgG and IgM antibody testing using an ELISA (Beier Bioengineering, Beijing, China). Quality control and reference for each test will be performed at each of the four study sites before participant enrolment and during the study. The test results will be marked with each participant's PID and collected from the patient management system at each study site. And diagnosis and treatment seeking behaviour after screened positive for STIs will be collected through questionnaires of follow-ups.

Patient and public involvement

Although we did not involve patients or the public in the design of the study, the large sample size MSM cohorts maintained for years in the study sites and close cooperation with local CBOs were useful during the study design phase. The study and questionnaire were presented to the leaders from local CBOs and staff from the CDC for comments before it was submitted to IRBs for ethics approval. The results of the study will be disseminated to the study participants via study account on social media and community dialogues. As for the burden of the intervention, the previous rate of usage of HIVST and willingness to accept HIVST during PrEP were collected among all participants at enrolment before randomisation, which was 74.5% and 96.9%, respectively. All participants were informed consent before randomisation, and take part in the study voluntarily.

Statistical analysis plan

Analysis plan

All data from the questionnaires, facility-based testing and self-testing results will be downloaded from Jinshuju database to avoid data reinput errors. Downloaded data will be exam for distribution and range before analysis. These data will be imported to and analysed using SPSS V.24.0 (IBM). Baseline characteristics and HIV testing history will be compared between the intervention and control groups. The primary analysis will be a between-group comparison of the rates of self-reported high-risk sexual behaviour and the laboratory testing-based incidence of syphilis and HSV-2 at months 3, 6, 9 and 12 using the χ^2 test. The secondary analysis will be a between-group comparison of the mean self-reported STI testing

frequency and STI treatment adherence during follow-up using t-tests and χ^2 tests. The associations of HIVST use by the HIVST group with HIV-related high-risk behaviours, STI testing and treatment adherence will be analysed by time-dependent Cox regression analysis.

Sample size

The required sample size was calculated using PASS V.11 software (NCSS, 2019) based on an inferiority trial design, a two-sided alpha of 0.05, 80% power, and the assumption of 20% lost to follow-up. We assumed that the HIVST group would be superior to the waitlist group for reducing HIV high-risk behaviours among PrEP users. Based on a previous study on risk compensation among MSM who use PrEP, the estimated increase in CAI from baseline was 30%.[14] Thus, to calculate the required sample size, we assumed a decrease of 30.0% in high-risk behaviour in the HIVST group compared with the waitlist PrEP group. The sample size was calculated to be 762 men, with 381 in each arm. Based on the estimated 20% lost to follow-up, the total sample size was calculated to be 914 men. We rounded up the final sample size to 1000 men.

Study schedule

The study requires 28 months (from 1 December 2018 to 1 February 2020), including 10 months of recruitment, 12 months of follow-up and 6 months of data analysis and reporting.

Ethics and dissemination

The study protocol and informed consent forms were reviewed and approved by the IRB of the First Affiliated Hospital of China Medical University (IRB (2018) 273). Written informed consent will be obtained from each participant before collecting any study information or blood samples. Participants will take part in the study voluntarily and will have the right to refuse to answer any of the questions. Participants will have the right to withdraw from the study without penalty. The online survey data will be kept strictly confidential according to the non-disclosure agreement.[32]

DISCUSSION

PrEP is an effective biomedical strategy for HIV prevention with several concerns while in implementation in real-world setting, including high frequent facility-based HIV testing during usage, increased CAI and incidence of STIs, and low adherence to treatment of STIs among PrEP users. This study is innovative in terms of design, intervention and study aims, and will therefore add value to the current understanding of implementation of PrEP in real-world setting.

We plan to use a randomised waitlist-controlled trial design for several reasons. The waitlist-controlled design ensures that all participants will eventually have access to the HIVST kits, to ensure equity and ethics compliance. This design not only allows comparison between the intervention and control groups, but it also allows the effectiveness to be assessed after different intervention durations. The major challenge of the study is the need to follow participants for 12 months and the associated expected lost to follow-up. To address this challenge, we will cooperate closely with local CBOs to improve participant outreach. We will use WeChat, the most popular social media application in China, to provide 24 hours online HIVST support.

As a major limitation, this study only detects limited types of STIs other than HIV, which not including *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (CT/NG) and other STIs. Previous studies show that the infection rate of CT/NG among the general MSM population in China is low,[38 39] compared with syphilis. However, the detection for CT/NG is relatively expensive. To accurately assess the infection rate of CT/NT, each MSM needs to be sampled and tested for three anatomical sites, including the oropharyngeal site, urethral and anorectal site.[40] The average cost of sample and testing of CT/NG at each anatomical site is more than US$15. This project group could not afford this cost. Therefore, no CT/NG testing was carried out in this study. It is strongly recommended to perform relevant STI testing in the future study.

Author affiliations
[1]NHC Key Laboratory of AIDS Immunology (China Medical University), National Clinical Research Center for Laboratory Medicine, The First Affiliated Hospital of China Medical University, Shenyang, China
[2]Key Laboratory of AIDS Immunology, Chinese Academy of Medical Sciences, Shenyang, China
[3]Key Laboratory of AIDS Immunology of Liaoning Province, Shenyang, China
[4]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, China
[5]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China
[6]Beijing Youan Hospital, Capital Medical University, Beijing, China
[7]Chongqing Public Health Medical Center, Chongqing, China
[8]Department of Infectious Diseases, Shenzhen Third People's Hospital, Shenzhen, China
[9]University of North Carolina at Chapel Hill Project-China, Guangzhou, China

Collaborators CROPrEP Study TeamChina Medical University: Jing Zhang, Jun-jie Xu, Hong Shang, Hong-yi Wang, Zhen-xing Chu, Qing-hai Hu, Hai-bo Ding, Yong-jun Jiang, Wen-qing Geng, Zhi-li Hu, Ran-tong Bao, Shang-cao Li, Hang Li, Xiaoyun Shi, Rui Li, Yangyang Gao, Yanni Ma. Beijing Youan Hospital: Xiao-jie Huang, Yi Duan, Guanghui Zhang. Chongqing Public Health Medical Center: Yao-kai Chen, Xiao-qing He, Yao Li. Shenzhen Third People's Hospital: Hui Wang, Lu-kun Zhang, Fang Zhao.

Contributors Conceived and designed the experiment: JZ, WT and JX; performed the study and experiments: JZ, XH, YC, HuW, YZ, HoW, ZM, YJ, ZC, Q-HH, XH, LZ, ZH, RB, SL, HD, YJ and WG; drafted the study report: JZ and JX. All authors reviewed and approved the final report.

Funding This work was supported by the Mega-Projects of national science research (13rd Five-Year Plan [2017Z×10201101–002–007]), the Mega-Projects of national science research (12th Five-Year Plan [2012Z×10001006–001–010]), National Natural Science Foundation of China (81872674), the Mega-Projects of national science research (2018Z×10101001–001–003).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Xiaoqing He http://orcid.org/0000-0002-2134-3809
Weiming Tang http://orcid.org/0000-0002-9026-707X
Junjie Xu http://orcid.org/0000-0003-4303-7295

REFERENCES

1 CBS News. CDC recommends pill to protect against HIV. Available: https://www.cbsnews.com/news/cdc-recommends-pill-to-protect-against-hiv/ [Accessed 3 Sep 2019].
2 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.
3 AVAC: Global Advocacy for HIV Prevention. Resources. Available: https://www.avac.org/resources/infographics. [Accessed 23 Jul 2019].
4 NAM. 380,000 people on PreP globally, mostly in the USA and Africa, 2018. Available: http://www.aidsmap.com/news/oct-2018/380000-people-prep-globally-mostly-usa-and-africa-updated [Accessed 14 Sep 2019].
5 AVAC: Global Advocacy for HIV Prevention. *Pre-exposure prophylaxis for the prevention of HIV in the United States*, 2017.
6 Parikh UM, Mellors JW. Should we fear resistance from tenofovir/emtricitabine preexposure prophylaxis? *Curr Opin HIV AIDS* 2016;11:49–55.
7 Zucker J, Carnevale C, Richards P, *et al*. Predictors of disengagement in care for individuals receiving pre-exposure prophylaxis (PrEP). *J Acquir Immune Defic Syndr* 2019;81:e104–8.
8 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:e241–50.
9 Zhang C, Li X, Brecht M-L, *et al*. Can self-testing increase HIV testing among men who have sex with men: a systematic review and meta-analysis. *PLoS One* 2017;12:e0188890.
10 Johnson CC, Kennedy C, Fonner V, *et al*. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. *J Int AIDS Soc* 2017;20:21594.
11 Ngure K, Heffron R, Mugo N, *et al*. Feasibility and acceptability of HIV self-testing among pre-exposure prophylaxis users in Kenya. *J Int AIDS Soc* 2017;20:21234.
12 Ortblad KF, Chanda MM, Musoke DK, *et al*. Acceptability of HIV self-testing to support pre-exposure prophylaxis among female sex workers in Uganda and Zambia: results from two randomized controlled trials. *BMC Infect Dis* 2018;18:503.
13 Ortblad KF, Kearney JE, Mugwanya K, *et al*. HIV-1 self-testing to improve the efficiency of pre-exposure prophylaxis delivery: a randomized trial in Kenya. *Trials* 2019;20:396.
14 Hoornenborg E, Coyer L, Achterbergh RCA, *et al*. Sexual behaviour and incidence of HIV and sexually transmitted infections among men who have sex with men using daily and event-driven pre-exposure prophylaxis in AMPrEP: 2 year results from a demonstration study. *Lancet HIV* 2019;6:e447–55.
15 Holt M, Murphy DA. Individual versus community-level risk compensation following preexposure prophylaxis of HIV. *Am J Public Health* 2017;107:1568–71.
16 Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. *J Int AIDS Soc* 2019;22 Suppl 6:e25355.
17 Traeger MW, Schroeder SE, Wright EJ, *et al*. Effects of pre-exposure prophylaxis for the prevention of human immunodeficiency virus infection on sexual risk behavior in men who have sex with men: a systematic review and meta-analysis. *Clin Infect Dis* 2018;67:676–86.
18 Martinez O, Carballo-Diéguez A, Ibitoye M, *et al*. Anticipated and actual reactions to receiving HIV positive results through self-testing among gay and bisexual men. *AIDS Behav* 2014;18:2485–95.
19 Balán IC, Carballo-Diéguez A, Frasca T, *et al*. The impact of rapid HIV home test use with sexual partners on subsequent sexual behavior among men who have sex with men. *AIDS Behav* 2014;18:254–62.
20 Frasca T, Balan I, Ibitoye M, *et al*. Attitude and behavior changes among gay and bisexual men after use of rapid home HIV tests to screen sexual partners. *AIDS Behav* 2014;18:950–7.
21 Zhou Y, Li D, Lu D, *et al*. Prevalence of HIV and syphilis infection among men who have sex with men in China: a meta-analysis. *Biomed Res Int* 2014;2014:1–12.
22 Chow EPF, Tucker JD, Wong FY, *et al*. Disparities and risks of sexually transmissible infections among men who have sex with men in China: a meta-analysis and data synthesis. *PLoS One* 2014;9:e89959.
23 Chen G, Cao Y, Yao Y, *et al*. Syphilis incidence among men who have sex with men in China: results from a meta-analysis. *Int J STD AIDS* 2017;28:170–8.
24 Xu J-J, Yu Y-Q, Hu Q-H, *et al*. Treatment-seeking behaviour and barriers to service access for sexually transmitted diseases among men who have sex with men in China: a multicentre cross-sectional survey. *Infect Dis Poverty* 2017;6:15.
25 Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS* 2016;30:2251–2.
26 Traeger MW, Cornelisse VJ, Asselin J, *et al*. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. *JAMA* 2019;321:1380–90.
27 Habel MA, Brookmeyer KA, Oliver-Veronesi R, *et al*. Creating innovative sexually transmitted infection testing options for university students: the impact of an STI self-testing program. *Sex Transm Dis* 2018;45:272–7.
28 Wang C, Cheng W, Li C, *et al*. Syphilis self-testing: a nationwide pragmatic study among men who have sex with men in China. *Clin Infect Dis* 2020;70:2178–86.
29 Xu J, Tang W, Zhang F, *et al*. PrEP in China: choices are ahead. *Lancet HIV* 2020;7:e155-e157.
30 Jia Z, Huang X, Wu H, *et al*. HIV burden in men who have sex with men: a prospective cohort study 2007-2012. *Sci Rep* 2015;5:11205.
31 Xu J-J, Zhang M, Brown K, *et al*. Syphilis and HIV seroconversion among a 12-month prospective cohort of men who have sex with men in Shenyang, China. *Sex Transm Dis* 2010;37:432–9.
32 Wang H, Zhang Y, Mei Z, *et al*. Protocol for a multicenter, real-world study of HIV pre-exposure prophylaxis among men who have sex with men in China (CROPrEP). *BMC Infect Dis* 2019;19:721.
33 Jin X, Xu J, Smith MK, *et al*. An Internet-based self-testing model (easy test): cross-sectional survey targeting men who have sex with men who never tested for HIV in 14 provinces of China. *J Med Internet Res* 2019;21:e11854.
34 WHO. Guidelines on HIV self-testing and partner notification supplement to consolidated guidelines on HIV testing services, 2016. Available: https://www.who.int/hiv/pub/vct/hiv-self-testing-guidelines/en/. [Accessed 13 Jan 2020].
35 Chu Z-X, Xu J-J, Zhang Y-H, *et al*. Poppers use and sexual partner concurrency increase the HIV incidence of MSM: a 24-month prospective cohort survey in Shenyang, China. *Sci Rep* 2018;8:24.
36 Liu M-Q, Zhu Z-R, Kong W-H, *et al*. High rate of missed HIV infections in individuals with indeterminate or negative HIV western blots based on current HIV testing algorithm in China. *J Med Virol* 2016;88:1462–6.
37 National AIDS Control Organisation. *National guideline for detection of HIV/AIDS*, 2015.
38 Zhang X, Jia M, Chen M, *et al*. Prevalence and the associated risk factors of HIV, STIs and HBV among men who have sex with men in Kunming, China. *Int J STD AIDS* 2017;28:1115–23.
39 Fu G-F, Jiang N, Hu H-Y, GF F, HY H, *et al*. The epidemic of HIV, syphilis, Chlamydia and gonorrhea and the correlates of sexual transmitted infections among men who have sex with men in Jiangsu, China, 2009. *PLoS One* 2015;10:e0118863.
40 Zhou Y, Cai Y-M, Li S-L, *et al*. Anatomical site prevalence and genotypes of Chlamydia trachomatis infections among men who have sex with men: a multi-site study in China. *BMC Infect Dis* 2019;19:1041.