BMJ Open

PrEP15-19 Choices: an implementation study protocol of HIV prevention with oral and long-acting injectable cabotegravir PrEP in real-word settings among sexual and gender minority adolescents in Brazil

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To cite: Dourado I, Dezanet L, Magno L, *et al*. PrEP15-19 Choices: an implementation study protocol of HIV prevention with oral and long-acting injectable cabotegravir PrEP in real-word settings among sexual and gender minority adolescents in Brazil. *BMJ Open* 2025;**15**:e083146. doi:10.1136/bmjopen-2023-083146

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2023-083146).

Received 14 December 2023
Accepted 04 December 2024

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ABSTRACT

Introduction Long-acting injectable (LAI) cabotegravir is a promising new method for preventing HIV. Safe and effective long-acting agents for pre-exposure prophylaxis (PrEP) for HIV infection are needed to increase preventive options among sexual and gender minority adolescents.

Methods and analysis This is a multisite, prospective implementation study of three PrEP modalities (LAI-PrEP, event-driven (ED) and daily oral), using a mixed-method design with quantitative and qualitative approaches. The study will include a sample of 550 HIV-negative adolescent men who have sex with men, non-binary individuals assigned male at birth, transgender men and women, aged 15–19 years, in three Brazilian capital cities. Participants will be allocated into two arms, according to their choice of PrEP modalities, and followed up to 36 months. Switching between oral and LAI-PrEP will be allowed, according to the participants' needs and preferences. The qualitative studies will focus on investigating the processes involved in linkage and retention in care, switching between PrEP modalities and strategies of the implementation process of LAI-PrEP in the current PrEP programming and acceptability from health providers, policymakers and stakeholders' perspectives.

Ethics and dissemination The adolescent's autonomy for consenting to their participation and understanding of PrEP will be assessed by the project team before any care is given and will be recorded in their medical record. Adolescents aged 15–17 years will sign an informed assent form, waiving the need for the approval of a legal guardian, except in cases where the adolescent is found not to have the necessary autonomy. The study was approved by the WHO Ethics Review Committee and by the local IRBs from the universities coordinating the study, the University of São Paulo, the Federal University of Bahia and the Federal University of Minas Gerais. This project is part of an effort to expedite the inclusion of new modalities in the Brazilian PrEP Programme, based on the development of studies to evaluate the implementation of LAI-PrEP and ED-PrEP as a choice. The results will be published in peer-reviewed journals and presented to the study participants and communities.

Trial registration number https://ensaiosclinicos.gov.br/rg/RBR-104736f4. The trial registration number: RBR-104736f4

INTRODUCTION

Despite the decreasing trend in the overall incidence of HIV in Brazil, young and adolescent men continue to show an increase in the number of cases in the 2000s.[1 2] The national HIV/AIDS response through the Brazilian National Health System (in Portuguese, *Sistema Único de Saúde - SUS*) expanded the oral pre-exposure prophylaxis (PrEP) prescription to include adolescents aged 15 or older and included the event-driven oral PrEP (ED-PrEP) in the guidelines in 2022.[3 4]

Daily oral PrEP with Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was previously demonstrated to be effective, safe and feasible among adolescents in real-world settings.[5] Although ED-PrEP has been shown effective among adults, there needs to be more evidence on the use of this regimen among adolescents.[6] Both of these oral PrEP modalities are challenging for adolescents and young people because of the high discontinuation rate and adherence issues.[7] Moreover, social factors such as parental consent,[8]

stigma and discrimination can negatively affect oral PrEP engagement.[9–14]

In this context, long-acting injectable (LAI) cabotegravir (CAB) PrEP is considered as a practical and safe new method for HIV prevention because it is based on a unique bimonthly injection that does not depend on daily pill adherence. Furthermore, it was considered more effective among men who have sex with men (MSM) and transgender women (TGW) than oral PrEP.[15 16] Nevertheless, LAI-PrEP knowledge, acceptability and service implementation to key populations are still scarce globally, especially in low- and-middle-income countries (LMIC). In Latin America, one study on awareness and acceptability of LAI-PrEP showed that 15.3% and 18.0% of sexual and gender minority adolescents (SGMA) were aware of the ED-PrEP and LAI-PrEP options, respectively. In this study, 56.4% and 81.5% reported intention to use ED-PrEP and LAI-PrEP, respectively, and the intention to use LAI-PrEP was high among those who reported three or more casual partners in the previous 3 months.[17]

Despite the availability of knowledge about the efficacy, awareness and acceptability of LAI-PrEP and ED-PrEP, more data are needed on the feasibility of protocols that offer the three modalities of PrEP for SGMA in LMIC. Therefore, the main objective of this study is to evaluate the implementation of a PrEP protocol with three modalities (ie, LAI, ED and daily oral) for SGMA, aged 15–19 years in Brazil, to understand the processes of choosing the methods, linking to services and retention on PrEP, as well as to evaluate strategies that will more effectively integrate sexually transmitted infections (STIs) care into the provision of PrEP.

METHODS AND ANALYSIS

Study design

The PrEP15-19 Choices (figure 1) is a multisite (3), prospective and implementation study based on the reach, effectiveness, safety, adoption, implementation and maintenance (RE-AIM) framework,[18] using a mixed-method design with quantitative and qualitative approaches. The objectives and outcomes are presented in the supplementary material (online supplemental appendix 1).

Study population

SGMA, among them, adolescent men who have sex with men (AMSM), adolescent transgender women (ATGW) and adolescent transgender men (ATGM), non-binary assigned as male at birth, aged 15–19 years, in three Brazilian capitals (Salvador, Belo Horizonte and São Paulo) will be included (online supplemental appendix 2). Eligibility criteria is described in table 1. The full list of exclusion criteria is described in the supplementary material (online supplemental appendix 3). In Salvador, the PrEP clinic is located at the Diversity Centre (in Portuguese, *Casarão da Diversidade*), a space for promoting human rights among the LGBTQIA+population. In Belo Horizonte, the PrEP clinic is located at a Youth Reference Centre (in Portuguese, *Centro de Referência das Juventudes*), which is a public space located in the city centre with intense youth gatherings, especially those in social vulnerability, which are the main target population for the project. In São Paulo, the PrEP clinic is located in two sites, at CASA 1 in the central region, which offers PrEP as an extramural activity performed by nurses and peer educators, linked to the second one, a primary care health service (in Portuguese, *Centro de Saúde Escola Butantã*) in the west region.[19]

Figure 1 PrEP15-19 Choices's logo.

Study procedures

Recruitment and follow-up

According to the choice of PrEP modalities, participants will be recruited in 12 months and will be allocated into two arms: LAI-PrEP arm and oral PrEP arm (ie, ED and daily oral) (figure 2). They will be prospectively followed up in month 1 and, thereafter, every 2 or 4 months for LAI-PrEP or oral PrEP users, respectively. Then, they will be followed up to 36 months, the end of the study, or until HIV infection, loss of follow-up or withdrawal from the project. Those who discontinue PrEP during the study period will be followed up until the project closure. In all PrEP initiation and follow-up visits, participants will be counselled regarding the management of the risk of acquiring HIV infection. In addition to HIV testing, participants will be tested for STIs, safety exams (ie, liver and renal function), assessment of adverse events, sexual risk compensation evaluation and will have access to a range of differentiated services and other HIV prevention methods (online supplemental appendix 4 and 5 in the online supplemental material). The inclusion of participants in the LAI-PrEP arm started in April 2024 and we estimate that it will be completed by October 2025, allowing for a minimum of 12 months of follow-up.

Table 1 Eligibility criteria of participants in the pre-exposure prophylaxis (PrEP)15-19 Choices study

Inclusion criteria	Self-identified AMSM, ATGW, ATGM and non-binary assigned as male at birth; Age between 15 and 19 years; In contexts of increased vulnerability or risk of acquiring HIV infection presenting at least one of the following criteria: condomless receptive or insertive anal intercourse in the 6 months prior to screening/enrollment; condomless vaginal intercourse in the last 6 months; any STI episode in the last 6 months; use of post-exposure prophylaxis (PEP) at least once in the last 6 months; frequent use of alcohol or drugs before or during sexual intercourse; transactional or commercial sex in the last 6 months; PrEP request by the participant who shows vulnerability and/or increased risk of HIV infection, based on risk management counselling and vulnerability context assessment by the research team.
Exclusion criteria for any PrEP choice (LAI-PrEP or oral PrEP)	HIV-positive status at screening/enrollment; Weight under 35 Kg; Currently participating in another interventional trial of PrEP agents, experimental medication or HIV vaccine trial; Participant shows, according to a specialised psychological assessment, mental and/or intellectual impairment that do not allow PrEP use.

AMSM, adolescent men who have sex with men; ATGM, adolescent transgender men; ATGW, adolescent transgender women; LAI-PrEP, long-acting injectable pre-exposure prophylaxis; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis.

Between October and December 2026, participants will be transitioned and linked to SUS services for the use of oral and/or injectable PrEP (if available).

Participants' choices will be based on their needs, preferences and sexual behaviour, considering the offered modalities and other existing HIV prevention methods. The healthcare team will counsel the participants on PrEP modalities, including risk assessment and benefits. Clinical and socio-behavioural questionnaires (online supplemental material), covering information on the use of the PrEP modality, other preventive methods and sexual practice, will be administered at enrolment and every 4 months on a regular visit. The health team will apply the questionnaires during in-person or telehealth visits.

All participants will receive virtual contact from peer navigators aiming to promote engagement in the first month and retention and adherence during the follow-up. Assessment of the risk of discontinuation and non-adherence will be carried out at the beginning of follow-up, and psychosocial healthcare professionals and peer navigators will offer support with a singular care plan to those with a high probability of interrupting PrEP, as well as for those non-adherents to PrEP. The definitions of PrEP retention, engagement and adherence are presented in online supplemental appendix 6 of the supplementary material.

PrEP modalities

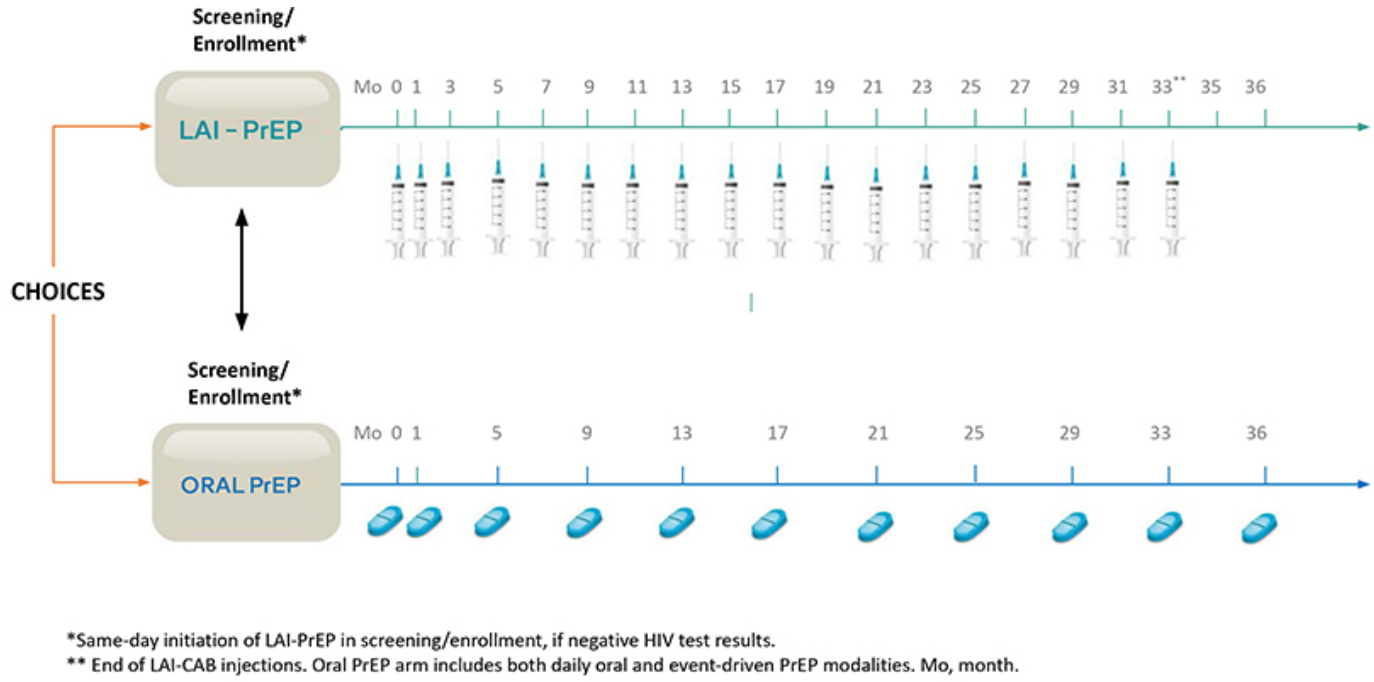
LAI-PrEP

If the initial PrEP choice is for LAI-PrEP, participants will receive the first injection of LAI-CAB 600 mg (3 mL) on the same day of enrolment (initiation visit 1, at month 0), another loading dose 1 month apart (initiation visit 2, at month 1) and then every 2 months (reinjection visits) thereafter until month 33. Clinical information on every visit will be registered in the online clinical research forms.

Participants who discontinue using LAI-PrEP throughout the study period will follow a discontinuation protocol, which provides for the use of daily oral PrEP for 1 year (online supplemental appendix 7). In month 33, participants receiving their last injection of LAI-CAB will be referred to the Ministry of Health (MoH) standard of care (SOC) PrEP services, including LAI-PrEP, if available, to continue the use or tail phase monitoring, according to the individual's choice. Between the months 34 and 36, participants will be followed in the project until connected to SOC services.

HIV screening and blood sample storage

To identify HIV early infections in participants who choose to receive LAI-PrEP, individuals will be screened for HIV using a fourth-generation HIV-rapid test and a point of care (POC) qualitative NAT HIV test (GeneXpert HIV-1) in the study entry (initiation visit 1) and in each visit of LAI-CAB restart or discontinuation (online supplemental appendix 8). The first injection of LAI-CAB (initiation visit 1) and those at reinitiating will be applied based on the result of a negative POC qualitative NAT HIV test performed on the same day. Subsequent injections (reinjection visits) will take place based on a negative fourth-generation HIV-rapid test performed at each visit. HIV test results will be interpreted together with information on signs and/or symptoms of acute HIV infection, reports of condom use during sex, occurrence of STI episodes and LAI-PrEP adherence for those already on PrEP in order to guide clinical decisions. If



*Same-day initiation of LAI-PrEP in screening/enrollment, if negative HIV test results.
** End of LAI-CAB injections. Oral PrEP arm includes both daily oral and event-driven PrEP modalities. Mo, month.

Figure 2 Study design according to pre-exposure prophylaxis (PrEP) choices. LAI-PrEP.

the result is positive, confirmatory HIV testing in a new blood sample will be conducted according to the current Brazilian guidelines for laboratory diagnosis of HIV infection.[20] A comprehensive description of the study strategies to prevent and timely diagnose acute HIV infection in participants using LAI-PrEP is presented in the supplementary material (online supplemental appendix 9).

Missed doses and oral bridging

Oral bridging with TDF/FTC will be offered to participants who anticipate being unable to attend their scheduled injections (planned missed injections). Individuals who plan to delay the scheduled injection visit by more than 7 days will be counselled to take oral PrEP (TDF/FTC) until a new dose of LAI-CAB is applied. Oral bridging should be used between the visit of the delayed injection and the application of the next injection. In addition, post-exposure prophylaxis (PEP) will be indicated using the Brazilian recommended SOC regimen (tenofovir disoproxil fumarate/lamivudine/dolutegravir) in case of high-risk condomless sex and for participants who have an injection delay of more than 7 days and who have not started oral bridging. There is no limit to the number of times the participant can choose to use oral bridging. Whenever there is a delay of more than 30 days from the scheduled application date, a qualitative NAT HIV test will be carried out during the visit of LAI-PrEP restart.

Participants using LAI-PreP with detectable HIV viral load

During the study period, participants with a detectable HIV viral load during LAI-PrEP use will proceed to the steps described in the supplementary material (online supplemental appendix 7), regardless of their HIV-rapid test result.

Test performance for the identification of acute HIV infection in the use of LAI-PrEP

At study entry sensitivity and specificity of rapid tests (ie, third-generation and fourth-generation), POC qualitative NAT HIV test, HIV fourth-generation laboratory-based enzyme immunoassay, quantitative HIV viral load (VL) and HIV self-test in the oral fluid will be assessed by comparing them with the gold standard, the HIV-VL test, using the Hologic Aptima HIV-1 RNA qualitative assay (Hologic, San Diego, California, USA) at study entry. These tests will be retrospectively conducted by the laboratory for all cases of HIV infection identified after the first LAI-CAB injection, except for the HIV self-test in oral fluid. For this test, participants will be invited to perform it and report the results at every visit that

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The protocol covers different types of services (primary health care, community services and and specialized healthcare) and care approaches (clinical, social support and mental health), better reflecting the diversity of the pre-exposure prophylaxis (PrEP) implementation.
⇒ It includes interventions at various stages of the PrEP continuum (demand, linkage, adherence and retention), allowing for the assessment of specific effects and their interrelationships.
⇒ The use of mixed methods and the participation of diverse populations and key actors strengthen the analysis of the feasibility of implementing a choice-based PrEP protocol.
⇒ The sample will not be sufficient to assess effectiveness results considering the modalities of PrEP provision.
⇒ The low participation rate of trans people may hinder the production of specific knowledge for this population.

involves LAI-CAB injection. Additionally, in all visits in the LAI-PrEP arm, blood samples will be collected and stored (one tube containing 2 mL of serum preferably or plasma for HIV serology and one tube containing plasma for HIV viral load test), and laboratory-based tests will be conducted retrospectively to investigate HIV breakthrough infections (online supplemental appendix 10). Furthermore, the samples will be stored at minus 70°C in the laboratories of each site for 2 years after the end of the study. An aliquot sample of serum or plasma will also be collected and stored for all participants at screening/enrolment and will be processed for genotyping in case of an HIV infection.

Switching between PrEP modalities

Participants will be informed on the possibility of switching between oral PrEP and LAI-PrEP throughout the study, according to their needs and preferences, that is, as many times as they want to change the PrEP regimen until the first 21 months of the study. This will provide knowledge of switching rates, as well as a minimum of 12 months of administration of LAI-PrEP for all participants who initiate this modality. The prescription of oral PrEP for users who switch from LAI-PrEP will be carried out in accordance with the current Brazilian guidelines for oral PrEP.[3]

Protection against HIV infection during the first days of LAI-PrEP use

Considering that adequate pharmacological levels of LAI-CAB in the anal and vaginal mucosa are not accomplished in the first 7 days following the first LAI-CAB injection,[21] participants will be counselled to use or continue to use barrier prevention methods for HIV infection and condoms will be delivered to participants. Additional guidance on the other HIV prevention methods will be based on the information on the current use of oral PrEP and the clinical judgement of the participant's adherence to it and is stated in online supplemental appendix 11.

Oral PrEP: daily oral and event-driven PrEP

We will offer daily oral and ED-PrEP. The '2+1+1' regimen[22] : (1) start use, by ingesting two pills between 2 and 24 hours before each sexual intercourse, (2) take one pill every new day in which there is sexual intercourse and (3) end the regimen by taking 1 pill 24 hours later and another 48 hours after the last day of sexual intercourse. Participants will be counselled on how to switch between the ED and daily regimens of oral PrEP, according to their sexual needs and practices. They will also be counselled on strategies they can adopt to correctly initiate and complete the use of ED-modality. This includes providing illustrated material, using reminders and having medications in hand to initiate and complete the regimen. ED-PrEP will not be recommended for TGW using estradiol-based hormones and transgender men, according to Brazilian regulations. Clinical follow-up will include the protocol for daily oral PrEP adopted by the SOC of the Brazilian MoH.[3] This protocol provides consultations every 4 months, including clinical exams, safety laboratory tests and anti-HIV and STI screening. Clinical information on every visit will be registered in the clinical research forms. The minimum laboratory tests included for the PrEP initiation and follow-up are fourth-generation HIV-rapid test, creatinine, syphilis, hepatitis A, B and C serologies, preferably by rapid test, and urine pregnancy test for transgender men.

HIV screening in oral prep

HIV screening among oral PrEP users will include fourth-generation HIV-rapid tests using whole blood sample (see the supplementary material – online supplemental appendix 9 for a comprehensive approach to HIV screening in the oral PrEP arm). If tested positive, HIV confirmatory exams in a new blood sample will be conducted according to current Brazilian guidelines for laboratory diagnosis of HIV infection.[20]

Providing oral prep by Telehealth

For the purpose of evaluating a protocol for simplifying the clinical follow-up and avoiding discontinuation for those on oral PrEP, participants will be able to choose to perform clinical follow-up using telehealth, which will allow for remote assessments every 4 months and an annual in-person visit (online supplemental appendix 12). The use of telehealth will be at the discretion of the participant, as this follow-up method may not be appropriate or desired by some participants. It will be allowed for those participants showing the ability to manage routine telehealth and exams. Remote consultations may take place using video calls or asynchronously, which will be performed using an online clinical form, self-filled by the user. Fourth-generation HIV-rapid tests or laboratory-based third-generation or fourth-generation laboratory-based HIV enzyme immunoassays will be performed at PrEP clinics or at a location of the participant's choice. However, there is also the possibility of performing the HIV self-test in oral fluid if the participant does not want to perform an HIV laboratory-based test. Remote assessments will be performed by a healthcare worker qualified to prescribe PrEP in accordance with national standards, who at their discretion will decide to renew the PrEP prescription remotely or schedule an in-person consultation for clinical assessment or at the participant's request. PrEP refill will be picked up at the service pharmacy or sent by mail. An online platform will be developed, accessible by smartphone, computer or tablet, which will allow participants to receive reminders for clinical evaluations, links to fill in the clinical form, exam requests and PrEP prescriptions. Healthcare workers will be trained in the telehealth protocol. Data collection forms for asynchronous assessment will contain selected clinical and laboratory information that support decisions on prescribing PrEP or clinical investigation of STIs and acute HIV infection. It includes information on signs and symptoms, adherence and adverse events. When necessary, an

intercurrence visit will be offered in the form of a face-to-face visit or a real-time teleconsultation with audio and/or video, using video call, phone call or WhatsApp, according to the participant's choice.

Management of adverse events

The management of any adverse event for LAI-PrEP or oral PrEP, clinical or laboratory, will be carried out according to the intensity/severity grading provided in the DAIDS table for grading the severity adult and paediatric adverse events.[23] Online supplemental appendix 13 summarises the general management of adverse events, the extent of the work-up in laboratory changes of the safety tests for each arm and the specific hepatic criteria for interruption of LAI-PrEP. A Clinical Management Committee, composed of the clinical coordinating team of each site and one external member, will be responsible for monitoring the progress of the study and the safety of the study participants, aiming to guide clinical conduct for investigation and resolution of possible cases of adverse events and standardise their reporting.

STI incidence assessment

Addressing STIs in the context of PrEP integrates the provision of differentiated service delivery for SGMA and is an important component of this proposal. A comprehensive approach to STI prevention will comprise screening testing and provision of services delivery that include friendly environments, counselling, follow-up and linkage to health services. All STI tests are described in online supplemental appendix 4 and 5 for the LAI-PrEP and oral PrEP arms, respectively. During the clinical consultation, a health professional from the research team will communicate all STI results at the time of the syndromic and/or etiological diagnosis. All participants diagnosed with a bacterial STI will be offered antimicrobial treatment (etiological or syndromic) in accordance with Brazilian guidelines as a POC,[24] and cases of hepatitis B and C will be referred to specialised SUS services. Vaccines against HPV, hepatitis A and B will also be offered and encouraged for participants and their sexual partners coming to PrEP clinics or receiving any STI treatment and it will depend on the availability of SUS in each of the cities.

Qualitative investigations

The qualitative studies will investigate the processes involved in: (1) linkage and retention in care and switching between PrEP modalities and (2) the possible strategies of the implementation process of LAI-CAB in the current PrEP programming. A comprehensive approach will be adopted to enable a deeper understanding of the intersection between personal, social, structural and programmatic aspects underlying adolescents' preferences and decision-making on HIV prevention and retention in care across time. The analysis of the potential implementation process of LAI-PrEP in the current PrEP programming in Brazil aims to characterise the acceptability of healthcare providers and stakeholders. Data collection will consist of in-depth interviews with adolescents, health providers, stakeholders, policymakers and members of community-based organisations (CBO). Ethnographic observations with notes in a field diary will be carried out as a complementary technique to the interview production processes and implementation committee meeting sessions.[25]

Patient and public involvement

We recognise the significance of incorporating Patient and Public Involvement (PPI) in our research. We will actively strive to engage study participants at different stages of our research process and involve them in the dissemination of the study's findings.

Analysis

Quantitative investigations

Descriptive statistical analyses will be performed to describe the choice of PrEP regimen by HIV risk behaviour, sociodemographic characteristics and barriers and motives of choice at study entry. The frequency distribution of the participant's characteristics in choosing injectable and oral PrEP will be compared using χ^2 test or Fisher's exact test for categorical variables and the Kruskal-Wallis test for continuous variables. PrEP choice at study entry will be further examined by using multivariable logistic regression analyses to investigate the association between PrEP choice and associated factors (sociodemographic variables, HIV risk behaviour, barriers to PrEP use and reasons of PrEP choice at study entry). A multivariable model will be developed by adding all covariables with a p value of less than 0.20 in univariate analysis and removing nonsignificant variables in backward-stepwise fashion. Variables will only be kept in the final multivariable model if they have a p-value of less than 0.05.

Data on sexual behaviour and the pattern of use (non-use) of PrEP modalities over time will be analysed longitudinally by using transition matrix techniques, the Herfindahl-Hirschman index and multivariable models considering the dependency structure of the data.

A characterisation of HIV infections among LAI-PrEP users will be described according to age (15–17 and 18–19 years), sub-population (AMSM, ATGW and ATGM), HIV viral load, HIV drug resistance test and drug (CAB or TDF) blood levels.

Adherence, retention and PrEP engagement are defined previously and all analyses will be performed separately for each PrEP modality. Optimal adherence to PrEP will be examined by using univariate and multivariable Cox regression models to investigate the association between adherence to PrEP and associated factors (sociodemographic variables, HIV risk behaviour and barriers to PrEP use). Hazard ratios with 95% confidence intervals (CI) will be estimated.

Descriptive statistical analyses will be performed to describe the occurrence of adverse events and STIs. These analyses will be conducted within the two study arms, separately.

We will estimate the sensitivity, specificity and concordance of the HIV diagnostic tests at study entry (including third-generation and fourth-generation HIV-rapid tests, HIV fourth-generation enzyme immunoassay and HIV self-test in oral fluid) with the HIV-VL test, using the Aptima HIV-1 qualitative RNA assay as the gold standard to detect HIV infection at study entry among persons on LAI-PrEP.

Qualitative investigations

Iterative thematic analysis will be used to analyse data from interviews. Such categorisation will help systematically order and sort coded data by prioritising codes that will help identify reiteration, complementarity and discrepancy between codes.[26] A codebook will be developed according to the following steps: reading of transcriptions to ensure familiarisation with their content and establish initial codes to raw data (inductive approach), development of new codes as additional themes emerge in the data (deductive approach) until code saturation is achieved and labelling, description, definition and illustration of codes by raw data.[27] NVivo software will be used to assist coding and analytical processes.[28 29]

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Acknowledgements The authors acknowledge the Ministry of Health of Brazil for their support. The authors would like to thank Heather Ingold, Rachel Baggaley and Robin Schaefer for their contribution in the research protocol.

Collaborators The contributors associated with PrEP 15-19 Choices Brazil Study Group are as follows: Salvador site: Beo Leite, Joilson Nascimento Paim, Guilherme Barreto Campos, Lucas Miranda Marques, Nathalia Suzart, Suilan Pedreira; São Paulo site: Dulce Aurélia de Souza Ferraz, Dyemison Pinheiro, Eduardo Oliveira, Eliane Sala, Maria Mercedes Escuder, Raphaella Goulart; Belo Horizonte site: Ana Paula Silva, Erica Dumont Pena, Gabriella Jomara da Silva, Marília Greco, Matheus de Paula Alves.

Contributors ID was involved in the study conceptualisation, funding acquisition, investigation, methodology, writing—original draft, writing—review and editing methodology. ID is the guarantor. LD was involved in the study conceptualisation, methodology, review and final version approval. LM was involved in the study conceptualisation, investigation, methodology, writing—original draft, writing—review and editing methodology. MW was involved in the final version's methodology and review. FS was involved in the final version's methodology and review. PM was involved in the final version's methodology and review. EMZ was involved in the study conceptualisation, investigation, methodology and review and editing methodology. PC was involved in the final version's methodology and review. RdPV, MTC and TRAR were involved in the study conceptualisation and review and editing methodology. UT was involved in the final version's methodology and review. DG was involved in the study conceptualisation, funding acquisition, investigation, methodology, review and editing. ADG was involved in the study conceptualisation, funding acquisition, methodology, writing—original draft, writing—review and editing methodology. All of the authors have approved the manuscript and agree with its submission.

Funding This work was made possible thanks to Unitaid's funding and support (Grant number UNITAID #2017-15-FIOTECPrEP). Unitaid accelerates access to innovative health products and lays the foundation for their scale-up by countries and partners. Unitaid is a hosted partnership of the World Health Organization. ViiV Healthcare will donate the study medication.

Competing interests None declared.

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

Patient consent for publication Not applicable.

Ethics and dissemination This study will be conducted in accordance with the principles of the Resolution 466/2012 of the Brazilian Research Ethics Commission (CONEP), which complies with all Brazilian laws on rights of adolescents and the Declaration of Helsinki. The research protocol and informed consent and assent forms were reviewed and approved by the WHO Ethics Review Committee (29 May 2023; ERC 0003789), and by the local IRBs from the universities coordinating the study: University of São Paulo (26 May 2023; #CAAE 67076822.6.1001.0068), Federal University of Bahia (4 August 2023; #CAAE 67076822.6.2002.5030) and Federal University of Minas Gerais (11 September 2023; #CAAE 67076822.6.2001.5149). Any important protocol modifications will be communicated to relevant parties (eg, WHO ERC, local IRBs and participants). The local research ethics committee or the study's principal investigator may pause or stop this study at any time. An informed consent and assent form explaining the research aims and procedures and participants' rights will be presented to each participant by a team member before they decide to participate in this study (Appendix 14). It is noteworthy to mention that the Research Ethics Committees have waived the need for the approval of a legal guardian for adolescents aged 15 to 17 years, who will sign an informed assent form if they are found to have the necessary autonomy.The PrEP15-19 Choices study is an implementation study of a protocol with three PrEP modalities for high-risk SGMA in Brazil, aiming at helping expedite the inclusion of new PrEP methods in the Brazilian National Health System. In this way, executive summaries will be produced with study results to ensure the rapid dissemination of knowledge to managers and communities. Social media and community radios will also contribute to the dissemination of study results. We will also include LAI-PrEP and ED-PrEP content in the online training, to be developed by the project team for healthcare professionals. The results will be published in peer-reviewed journals of great relevance. The findings will also be presented to the study patients and communities. Specifically, for the scientific community, at the end of the study, we plan to organise a meeting to discuss general findings, divide themes/subjects among researchers according to their interest and expertise, and develop a final technical report. This study will contribute to reducing HIV incidence among vulnerable adolescents at high risk of HIV infection.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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