Pilot implementation of HIV self-testing delivery in private pharmacies combined to a Respondent Driven Sampling method to improve HIV testing for MSM and TGW in Phnom Penh – ANRS 0100s

Protocol version 1.1 – Date: 18th April 2022

Ethics committee approvals

Cambodia: Name of the committee: National Ethic Committee for Health Research (NECHR)

Date of approval:

Sponsor:

Institut national de la santé et de la recherche médicale-ANRS Maladies Infectieuses Emergentes **(Inserm - ANRS)**
2 rue Oradour-sur-Glane – 75015 Paris, France Tél. : 01 53 94 60 00 - Fax : 01 53 94 60 01

Coordinating investigators:

Cambodian coordinator	French coordinator
Pr. SAPHONN Vonthanak	Pr. Bruno SPIRE

MONITORING AND DATA MANAGEMENT CENTER (MDMC):

Prof. Mam Sovatha
University of Health Sciences
73 blvd Monivong, Sras Chak, Daun Penh, Phnom Penh Cambodia Phnom Penh, Cambodia

PAGE DE SIGNATURES

Pilot implementation of HIV self-testing delivery in private pharmacies combined to a Respondent Driven Sampling method to improve HIV testing for MSM and TGW in Phnom Penh

Protocol version 1.1 – Date 18th April 2022

Clinicaltrial.gov registration number N/A

Ethics committee approvals

Cambodia: Name of the committee: National Ethic Committee for Health Research (NECHR)

Date of approval:

Sponsor signature

Inserm-ANRS Maladies infectieuses Emergentes
Director: Prof. Yazdan Yazdanpanah
2 rue Oradour-sur-Glane
75015 Paris, France Tel: +33 153 94 60 46 / 60 00
Fax : +33 153 94 60 01

Paris, Date :

Name :

Signature

Coordinating investigators signature

Pr SAPHONN Vonthanak
University of Health Sciences (UHS)
73 Preah Monivong Bvd
Phnom Penh, Cambodia
Email: vonthanak@uhs.edu.kh

Date:

Name : Pr SAPHONN Vonthanak

Signature

Pr Bruno SPIRE
Sciences économiques et sociales de la santé et traitement de l'information médicale (SESSTIM)
Faculté de Médecine 27 Bd Jean Moulin 13385 Marseille Cedex 5, France
Email: bruno.spire@inserm.fr

Date : April, 8th, 2022

Name : Pr Bruno SPIRE

Signature 

Table of Contents

STUDY PROTOCOL VERSIONS 1.1

Version #	Date	Amendment #	Main modifications
1.0	15/03/2021	N/A	Initial protocol (submitted for grant approval)
1.1	18/04/2022	1	-Two main modifications have been made into the initial protocol version 1.0: external website (in place of smartphone application) and salivary HIV self-test (in place of fingerstick whole blood, venipuncture whole blood or serum/plasma).

LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ANRS|MIE	ANRS Maladie Infectieuses Emergentes
ART	Antiretroviral therapy
CBO	Community-based organisation
CEPED	Centre Population et Développement
CNIL	Commission nationale de l'informatique et des libertés
CRA	Clinical Research Assistant
e-CRF	Electronic case report form
DSMB	Data safety & monitoring board
FG	Focus Groups
GCP	Good clinical practice
GMO	Grant Management Office
HIV	Human immunodeficiency virus
HIVST	HIV Self-Test
MSM	Men who have sex with men
NCHADS	National Center for HIV/AIDS, Dermatology and STD
NECHR	National Ethics Committee for Health Research
RDS	Respondent-driven sampling
SAB	Scientific Advisory Board
SOPs	Standardized operating procedures
TGW	Transgender women
TMF	Trial Master File
TWG	Technical Working Group
WHO	World health organization

1. STUDY TEAM MEMBERS

SPONSOR
Inserm / ANRS | MIE 2 rue Oradour-sur-Glane – 75015 Paris, France. Phone: +33 1 53 94 60 00

COORDINATING INVESTIGATORS	
Pr SAPHONN Vonthanak University of Health Sciences (UHS) 73 Preah Monivong Bvd Phnom Penh, Cambodia Email: vonthanak@uhs.edu.kh	Pr Bruno SPIRE Sciences économiques et sociales de la santé et traitement de l'information médicale (SESSTIM) Faculté de Médecine 27 Bd Jean Moulin 13385 Marseille Cedex 5, France Email: bruno.spire@inserm.fr
STUDY COORDINATOR	
Dr. DARY Chhavarath University of Health Sciences Phone : +85517676953 Email : dr_chhavarath@uhs.edu.kh	
CO-INVESTIGATOR AND CLINICAL COORDINATOR	
Dr. Emilie Mosnier University of Health Sciences Phone : +85512479313 Email : oliseg@hotmail.com	
MONITORING AND DATA MANAGEMENT CENTER	
Monitoring / statistical analysis Methodology/Biostatistics	Dr. DARY Chhavarath Public Healht Unit, University of Health Sciences, Phnom Penh, Cambodia, 73 Preah Monivong Blvd, Phnom Penh, Cambodia
System development and data managing:	Mr. MAN Manith Head of IT Department, University of Health Sciences, Cambodia, 73 Preah Monivong Bvd Phnom Penh, Cambodia Mr. Un Vireak, Deput Head of IT Department, University of Health Sciences, Cambodia, 73 Preah Monivong Bvd Phnom Penh, Cambodia

COLLABORATIVE RESEARCH TEAMS	
Dr. OUK Vichea National Center for HIV/AIDS, Dermatology and STD (NCHADS) #245H, Sreet 6A, Phum Kean Khlang,12100 Phnom Penh, Cambodia.	Dr. Joseph LAMARANGE Institut de Recherche pour le Développement - UMR 196 IRD Centre Population et Développement (Ceped, UMR 196, Université Paris Cité, IRD, Inserm) 45 rue des Saints Pères 75006 Paris FRANCE

PARTNERS	
U-Care Pharmacy 29 Mao Tse Toung Blvd (245), Phnom Penh 12302, Cambodia.	Chhouk Sor Clinic Oknha Kleang Moeung St. (70), Phnom Penh, Cambodia.

1 STUDY SUMMARY

Clinicaltrial Id:

Title of Study: Pilot implementation of HIV self-testing delivery in private pharmacies combined to a Respondent Driven Sampling method to improve HIV testing for MSM and TGW in Phnom Penh

Short title – Sponsor N°: -ANRS 0100s

Sponsor: Institut national de la santé et de la recherche médicale - ANRS Emerging Infectious diseases **(Inserm-ANRS| MIE)**

Coordinating Investigator(s):
Pr. SAPHONN Vonthanak, University of Health Sciences, Cambodia
Pr. Bruno SPIRE, SESSTIM, France

Participating countries: CAMBODIA AND FRANCE

Primary objective:
Evaluate the feasibility of HIV self-testing (HIVST) delivery by a private pharmacy network among men who have sex with men (MSM) and transgender women (TGW) recruited through a classic and digital Respondent Driven Sampling method to improve HIV testing in Phnom Penh, Cambodia

Secondary objectives:

- Evaluate the acceptability and appropriateness of the strategy
- Identify barriers and facilitators
- Estimate the linkage to confirmatory testing for those with a reactive test and linkage to HIV care and ART for those with a positive confirmatory HIV test
- Estimate linkage to pre-exposure prophylaxis (PrEP) services for negative participants
- Estimate the characteristics of participants and compare to those reported in Integrated Biological and Behavioral Survey (IBBS 2019) for MSM and TGW in Cambodia
- Evaluate the adherence of participants to a 6-monthly repeated HIV testing

Methodology:

An interventional pilot study using a mixed qualitative and quantitative approach will be carried out in order to evaluate the feasibility, acceptability and appropriateness of the strategy and to identify barriers and facilitators.

The participant recruitment method will be designed as a Respondent Driven Sampling (RDS) by recruiting initial seeds both at hotspots and on social networks. Prior to seed recruitment, a consultative meeting will be conducted in order to optimise the selection criteria of the seeds. The seeds will then distribute electronic and paper coupons to their networks physically and via social media, messaging and calling applications such as Twitter, Whatapp and Telegram (e-coupons).

Each recruited participant will bring the coupon to be scanned at partner pharmacies to receive direct and free access to one HIVST kit. Partner pharmacies with a proper dedicated room/space securing privacy and secrecy in Phnom Penh are the study sites. There, trained community workers who get notified by partner at each visit of participant will do the study visit including information/consent (annexe 1 and 2), e-CRF filling (annexe 3) and give a link of an external website to send the HIV test results and receive information or advices. These recruited individuals will be considered as wave 1 of recruitment and will each receive 10 additional coupons to recruit the members of their networks. The next round of individuals recruited and enrolled will be considered as wave 2, and so on.

After 6 months, a qualitative assessment via focus groups will be conducted among MSM, TGW and pharmacists to evaluate feasibility, acceptability and appropriateness of the intervention and to identify barriers and facilitators.

Several ART sites/HIV clinics particularly in charge of key populations will be specifically selected as participating centers in order to collect information on linkage to care or prevention services for positive and negative participants, respectively.

Each participant will be followed during 18 months and encouraged to perform a 6-monthly HIV testing during this period.

Expected enrolment

A pragmatic approach is carried out in which the enrolment will be stopped at the end of the inclusion period or if the number of participants reaches a maximum of 1500.

Outcomes

With regard to the novel intervention, the outcomes will focus on its feasibility, adoption, acceptability and appropriateness.

The primary outcomes will be the HIV self-testing uptake defined as the number of HIV self-tests delivered / total number of coupons distributed

The secondary outcomes will be:

- Proportion of HIVST result's recorded / total number of HIVST delivered
- Proportion of paper and electronic coupons delivered and recorded
- Number of HIV tests realized / number of HIV tests results non recorded
- Proportion of MSM/TGW with positive HIV self-tests linked to an ART site
- Proportion of negative MSM/TGW linked to PrEP services
- Characteristics of participants recruited (sociodemographic, sexual behavior, utilization of dating application, substance use) in comparison with IBBS 2019 report
- Proportion of participants with 6-monthly repeated HIV testing during 18 months

Outcomes of acceptability and appropriateness will be explored during focus groups: comfort, usefulness, suitability, confidentiality, credibility, advantages and barriers.

Eligibility

Inclusion criteria

- To be aged from 18 years old (legal age in Cambodia)
- For MSM, to have at least one oral or anal intercourse with another man in the past 12 months
- For TGW, to be biologically a male at birth and self-identified as a woman or third gender and have at least one oral, anal or vaginal intercourse with another man in the past 12 months

Non-inclusion criteria

- Known HIV positive status

Statistical methods

We want to evaluate the feasibility of the intervention to improve HIV testing among MSM and TGW in Phnom Penh. We will use a pragmatic approach with the objective to recruit the maximum of MSM and TGW. According to the IBBS 2019, the estimated number of MSM in Phnom Penh is 6300 and the estimated number of TGW is 1400.
With 1500 participants (1000 MSM and 500 TGW), we will be able to estimate an HIV self-test uptake of 70% to within a 95% confidence interval of +/- 2 – 2.5% (width of the confidence interval (in %) = $1.96 \times \sqrt{(p \times (1-p) / n)}$).

Estimated planning or study timetable

- Protocol submission: December 2022
- Study implementation: February 2023 – July 2023
- Data collection: August 2023 – April 2025 (18 months)
- Duration of the study: 24 months

2 STUDY SYNOPSIS

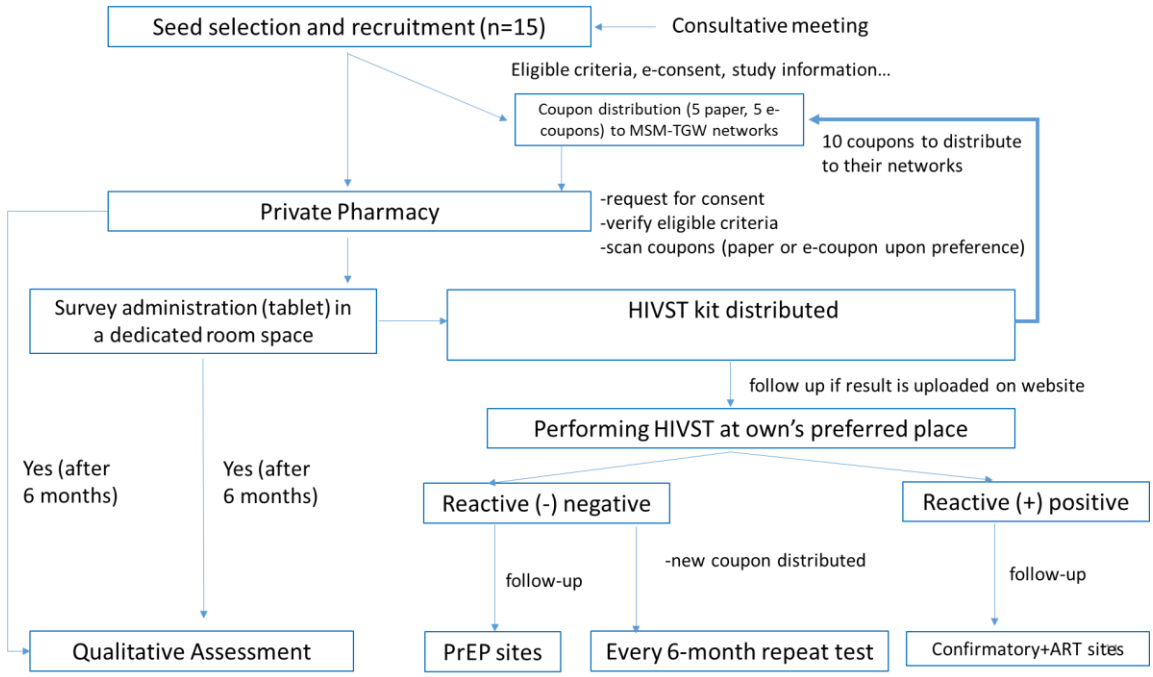

Figure 1: study flow and recruitment process by respondent-driven sampling

3 SCIENTIFIC RATIONALE

The sharp rise in the number of new HIV infections among MSM in Asia has continued, and sexual activity between men remains stigmatized and often hidden. HIV prevalence among MSM was 5% or higher in 10 of the 24 countries that reported these data to UNAIDS in 2019 (1). About 30% of all new infections in Asia are in MSM. In the region, HIV incidence is high among young (15-24 years old) MSM; a recent publication reported an HIV incidence of 7.4 per 100 person-years in Bangkok in this population (2).

Similar to MSM's HIV infection, in Asia and the Pacific, it is widely reported that most new HIV infections will be among men who have sex with men and transgender people by the year 2020. Limited studies have been reported regarding HIV surveillance, HIV and STI prevalence, population size estimations, or behavior patterns for either transgender women or transgender men in the region. The most current data documenting HIV infection rates amongst transgender people only include transgender women in urban settings. Nevertheless, the data shows disturbing HIV infection rates throughout the region: Delhi 49%, Mumbai 42%, Phnom Penh 37%, Jakarta 34%, Surabaya 25%, Bandung 14%, Chaing Mai 18%, Phuket 12%, Bangkok 11%, Lahore 0.5% (3).

Late diagnosis is a serious barrier to tackling HIV. Around 69% of people living with HIV in the Asia and the Pacific region were aware of their status in 2018, up from 58% in 2015. However, this means around 1.9 million people did not know they were HIV positive.

Progress on testing varies greatly between countries. In Thailand, 94% of people living with HIV were aware of their status in 2018, as were 86% of people living with HIV in Malaysia and 82% in Cambodia. At the other end of the spectrum, only 37% of people living with HIV in Bangladesh and 14% of people in Pakistan were aware of their status.

Stigma, discrimination and punitive legal environments prevent many people from key populations from accessing testing services (4). Indeed in Malaysia and Sri Lanka, the HIV testing and awarness among MSM account for 43.3% and 40.3%, respectively while the HIV testing and awarness for TG people are 43% and 36.9%, respectively (5).

Despite Cambodia's admirable achievements the 90-90-90 targets by 2020, the HIV epidemic among key populations and, as yet, unidentified priority populations is an abiding concern. The latest available key-population data show HIV prevalence is 2.3% among men who have sex with men (MSM) and 5.9% among transgender women (TGW) (6,7). Despite this high prevalence rate, remain low the uptake of HIV testing among men who have sex with men (MSM<50%) and transgender women (TGW=39%) and consistent condom use (69% in MSM during anal sex and 38% for TGW with non-commercial sexual partners) (8). The IBBS 2019 report highlighted that about half of MSM and one third of TGW did not report any HIV testing or since more than 12 months. This suggests that undiagnosed HIV infection may persist in hard-to-reach MSM and TGW and new modality of HIV-testing approaches are hence needed to improve the uptake of HIV testing among these key populations. In addition, of those who reported HIV testing, the majority of MSM and TGW were tested at Community-based organizations (CBO) facilities (23.5% for MSM and 36.2% for TGW) and by CBO outreach workers (53.4% for MSM and 53.8% for TGW) while private facilities are poorly used for HIV (9).

From the perspectives of some users not only among general population but also "hidden" or "marginalized populations" such as MSM and TGW, results of HIV self-tests should be interpreted in private settings in order to guarantee complete anonymity. HIVST is a process in which an individual performs an HIV rapid diagnostic test (RDT) and interprets the result in private. Lay users can perform HIVST reliably and accurately and achieve performance comparable to that of trained health-care workers (10). HIV self-testing has the potential to increase the number of people living with HIV who have access to testing, know their status, are diagnosed and initiate treatment. HIV self-testing shares many characteristics with current HIV testing and counselling approaches, including products, accuracy issues, linkage to care, potential benefits and risks and regulatory policies and frameworks (11). Of some key populations, HIV self-testing increased testing frequency among high-risk MSM and could increase HIV diagnose in the trans community (12,13). In 2016, WHO recommended HIV self-testing (HIVST) as a safe, accurate and effective way to reach people who may not test otherwise, including people from key populations, men and young people (10). Representatives from 13 countries across Asia and the Pacific gathered to develop road maps to implement and expand pre-exposure prophylaxis (PrEP) and HIV self-testing in the region (14).

In 2017, Cambodia developed national consolidated guidelines on HIV testing services in which many approaches including HIV self-testing (HIVST) are recommended to increase the HIV test

uptake, especially among hard-to-reach and key populations (15). Recent evaluation of the B-IACM in Cambodia revealed that 66.5% who received assisted HIVST want to confirm their HIV status (16). Even though MSM and TGW had not heard about HIVST, all of them expressed willingness to try it (17).

While HIVST kits are distributed primarily from public health facilities, the HIVST is also available through private ways and channels. Some studies including the one conducted in Cambodia by Pal et al. (2016) suggested that men who have sex with men, transgender women wish or prefer HIVST to be available over-the-counter at pharmacies and other locations or through the Internet (17,18). HIVST is already formally and informally available, and it will likely become increasingly available. Indeed, HIVST kits are authorised to be dispensed from pharmacies in some countries such as USA and France (19,20). In addition, HIVST were reported informally on sale through the Internet and in pharmacies in many countries – with specific reports on this from Australia, China, Namibia, Peru, South Africa, Philippines and Malaysia (21).

Respondent driven sampling (RDS), a form of peer referral-based sampling, has become a popular strategy to recruit "hidden" or "marginalized populations" such as MSM and TGW. RDS implementation resembles snowball sampling with several critical caveats. Initial participants are purposefully recruited to be "seeds" as long as they fit the study's eligibility criteria. After completing the study procedures, seeds are offered a limited number of vouchers to recruit their peers to participate. When vouchers are redeemed, eligible participants also complete the same study procedures and are asked to recruit their peers, and this continues until recruitment goals are met. Using specially formulated statistical programs, sampling weights are developed and applied to estimate population parameters. For the purpose of RDS, effective seeds generate large recruitment chains and samples, which has been shown to be associated with motivation and a commitment to the research goals (22).

To mitigate some of the challenges of implementing the methodology, notably slow recruitment rates, innovation around conventional RDS can be helpful (23). Indeed, since there has been rise of using the Internet and online communities of gay and bisexual men in a few decades to facilitate new connections for the purpose of information seeking, socializing and seeking sex, several studies have reported innovative internet- and application-based RDS strategies in different aspects of AIDS/HIV research such as improving uptake of HIV self-testing among MSM, providing technical support, counselling and referrals for further HIV testing services, HIV prevention, care and treatment and other services (24–28).

Study main hypothesis

- The main hypothesis is that private pharmacies could be able to deliver HIV self-testing kits giving the advantage of confidentiality, anonymity and time-saving, which could be an effective intervention to improve HIV testing coverage for MSM/TGW.
- The second hypothesis is that a RDS method with a diversity of seeds recruited at hotspots and on social networks could help to identify a new network of hidden key population.

4 OBJECTIVES OF THE STUDY

Primary objective:

- Evaluate the feasibility of HIV self-testing (HIVST) delivery by a private pharmacy network among men who have sex with men (MSM) and transgender women (TGW) recruited through a classic and digital Respondent Driven Sampling method to improve HIV testing in Phnom Penh, Cambodia

Secondary objectives:

- Evaluate the acceptability and appropriateness of the strategy
- Identify barriers and facilitators
- Estimate the linkage to confirmatory testing for those with a reactive test and linkage to HIV care and ART for those with a positive confirmatory HIV test
- Estimate linkage to pre-exposure prophylaxis (PrEP) services for negative participants
- Estimate the characteristics of participants and compare to those reported in Integrated Biological and Behavioral Survey (IBBS 2019) for MSM and TGW in Cambodia
- Evaluate the adherence of participants to a 6-monthly repeated HIV testing

5 METHODOLOGY

Study design

An interventional pilot study using a mixed qualitative and quantitative approach will be carried out in order to evaluate the feasibility, acceptability and appropriateness of the strategy and to identify barriers and facilitators.

The participant recruitment method will be designed as a Respondent Driven Sampling (RDS) by recruiting initial seeds both at hotspots and on social networks.

After 6 months, a qualitative assessment by focus groups discussion (FGD) will be conducted among MSM, TGW and pharmacists to evaluate feasibility, acceptability and appropriateness of the intervention and to identify barriers and facilitators.

Each participant will be followed during 18 months and encouraged to perform a 6-monthly HIV testing during this period.

Study overview

The intervention will be designed as a RDS by recruiting initial seeds both at hotspots and on social networks. 15 initial seeds will be recruited. Seeds will come to the study site for checking inclusion criteria and receiving information on self-testing, benefits of their participation and recruiting other participants in their networks along with the important details about the study. Once consent to the study, the seed is provided with two types of coupons for HIVST kit at partner pharmacy: 5 electronic coupons (e-coupons) consisting of a pictured unique anonymous QR code and identifier and address of partner pharmacies; 5 paper coupons consisting of a printed unique anonymous QR code, identifier and address of partner pharmacies. The seeds will then distribute

electronic and paper coupons to their networks physically and via social media, messaging and calling applications such as Twitter, Whatapp and Telegram (e-coupons).

Each recruited participant will bring the coupon to be scanned at partner pharmacies to receive direct and free access to one HIVST kit. Partner pharmacies with a proper dedicated room/space securing privacy and secrecy in Phnom Penh are the study sites. There, trained community worker/research team who get notified by partner at each visit of participant will do the study visit including information/consent, e-CRF filling and give a link of an external website to send the HIV test results and receive information or advices.

These recruited individuals will be considered as wave 1 of recruitment and will each receive 10 additional coupons to recruit the members of their networks. The next round of individuals recruited and enrolled will be considered as wave 2, and so on. The number of 10 coupons was selected to avoid a bias risk related to participation incentives.

To facilitate the return of HIVST kit results, participant will upload the picture of results labeled with their identifier directly using the link of the external website that they received from community worker/research team during their visits at pharmacy. In case of any question, they could reach community worker/research team by hotline number. According to the results, the participants will be proposed with a support for linkage to confirmatory test or to PrEP services. Each non-reactive participant will be provided another new coupon (paper or electronic format upon their preference) with a reminder to perform a 6-monthly HIV testing during 18 months. They will not be granted any token or incentives if they fail to return the result of HIVST kit taken at pharmacies. These incentives are also added upon the number of recruited members of their networks using common money transfer and payment services in Cambodia such as Wing, TrueMoney.

After 6 months, a qualitative assessment will be conducted to evaluate feasibility, acceptability and appropriateness of the intervention and to identify barriers and facilitators.

Several ART sites/HIV clinics particularly in charge of key populations will be specifically selected as participating centers in order to collect information on linkage to care or prevention services for positive and negative participants, respectively.

Tentative study agenda

- Protocol submission: December 2022
- Study implementation: February 2023 – July 2023
- Data collection: August 2023 – April 2025 (18 months)
- Duration of the study: 24 months

6 STUDY POPULATION

MSM and TGW who are residing in Phnom Penh at the time of enrollment and meet the eligible criteria below are the study population:

- To be aged from 18 years old (legal age in Cambodia)
- For MSM, to have at least one oral or anal intercourse with another man in the past 12 months
- For TGW, to be biologically a male at birth and self-identified as a woman or third gender and have at least one oral, anal or vaginal intercourse with another man in the past 12 months

7 STUDY ENDPOINTS

Primary endpoint

- HIV self-testing uptake defined as the number of HIV self-tests delivered / total number of coupons distributed

Secondary endpoints

- Proportion of HIVST result's recorded / total number of HIVST delivered
- Proportion of paper and electronic coupons delivered
- Number of HIV tests realized / number of HIV tests results non recorded
- Proportion of MSM/TGW with positive HIV self-tests linked to an ART site
- Proportion of negative MSM/TGW linked to PrEP services
- Characteristics of participants recruited (sociodemographic, sexual behavior, utilization of dating application, substance use) in comparison with IBBS 2019 report
- Proportion of participants with 6-monthly repeated HIV testing during 18 months

Outcomes of acceptability and appropriateness will be explored during focus groups: comfort, usefulness, suitability, confidentiality, credibility, advantages and barriers.

8 STRATEGIES AND TREATMENTS

Strategies and Treatments used in the study

The study does not involve with any direct medical treatment. However, intervention after delivering HIV test results will be proposed as follow:

- In case of reactive HIV test, the participant could join immediately one research team by hotline and messages on the website that will provide support and orientation. After 1 week, contact with the participant will be done by phone by the research team to confirm the linkage to one of the partner ART sites. The linkage between participants and HIV clinics will be done by the initial QR code.

If the linkage to confirmatory testing and/or care is not confirmed, we will propose to participant additional help of a community worker.

- In case of non-reactive test, the participant could download in the external website one electronic coupon (QR code) to repeat the HIV test every 6 month. Participants will be informed on the external website about the possibilities to join the pilot PrEP program in Chhouk Sar clinic in Phnom Penh.

9 STUDY IMPLEMENTATION

Patients participation in the study

Information

Patient participation in this study is voluntary. Each potential participant will be informed individually by research team of the purpose, scope of the study, procedures involved, duration of follow-up, potential risks and benefits and any discomfort it may entail. In addition to oral explanations, a written information sheet will be systematically provided in Cambodian language (see Appendix A).

Consent

If the patient accepts to be enrolled in the study, s/he will sign the paper and electronic consent forms including different consents: global participation, receiving funds, being recontacted by phone, participation in FGD. Informed consent must be obtained before any exam related to the study. Participants may be given, if they wish, a copy of the paper consent form after they sign.

Intervention

RDS intervention

The seeds will be recruited at hotspots, online applications and social media networks. Hotspots include steam sauna and spa and gay bars and clubs. Online applications and social media include Facebook groups, twitter, telegram, whatapps and other date applications such as Grindr, Planet Romeo, Hornet, Blued.

Prior to seed recruitment, a consultative meeting will be conducted among pimps (a person who controls sex workers, especially by finding customers for them, and takes some of the money that they earn), procurers (a person who finds sex workers for people who want to have sex with them), high class MSM & TGW, network organizers, social media group organizers in order to optimize the selection criteria of the seeds.

Selection criteria obtained from the meeting with pimps, procurers, high class MSM, network organizers, twitter groups organizer is applied to select the initial seeds that are very likely to lead us to reach a large diversity of MSM&TGW population.

A number of 15 seeds will be selected firstly to ensure the representation of gender, age group, sexual behaviors, and participation in sex work. If necessary, new seeds could be recruited later. Seeds will come to the study site for checking inclusion criteria and receiving information on self-testing, benefits of their participation and recruiting other participants in their networks along

with the important details about the study. Once consent to the study, the seed is provided with two types of coupons for HIVST kit at partner pharmacy: 1- 5 electronic coupons (e-coupons) consisting of a pictured unique anonymous QR code and identifier and address of partner pharmacies 2- 5 paper coupons consisting of a printed unique anonymous QR code, identifier and address of partner pharmacies. The seeds will provide paper- and e-coupons to their networks physically and via social media, messaging and calling applications such as Twitter, Whatapp and Telegram (e-coupons). For online application and social media, a peer could be reached by chat or call.

When the participant arrives in a partner pharmacy, the coupon (unique QR code with identifier) will be scanned by the pharmacist prior to the free delivery of HIV self-test. Community workers (CWs) will be then alerted by the pharmacist for study visits to participant directly at the dedicated space at the pharmacy. During the visit with CW, participant will :

- Receive the information about the study
- Receive an ID
- Check for eligibility criteria
- Be requested for his/her consent to participate in the study and to different specific consents as receiving funds, being recontacted by phone and participation in FGD
- Fill in the detailed e-CRF for sociodemographic status, sexual behaviors, utilization of dating application, substance use, knowledge about PrEP and willingness to pay for HIV self-testing by using Tablet with the eventual assistance from a community worker
- Receive the information on HIV self-testing instructions, list of partner pharmacies, helpline phone number, location of the 2 partners ART sites, location of the HIV clinics with prevention services and PrEP delivery availability
- Be provided one free HIV self-testing kit delivered
- Receive the link of the external website to performance HIV test, interpret and send the HIV test result, receive necessary information and in case of non-reactive, to receive another coupon for 6-monthly test during 18 months
- Receive 10 (paper or electronic) coupons to distribute to peers
- Be asked if the participant would agree to be recontacted for an eventual participation in a focus group

Incentives will be provided in two steps for participants to encourage them to return the results of HIVST and recruit their peers. In step one, each participant will receive 2 USD for returning the HIVST result successfully to the provided link. In step two, an amount of 1 USD will be provided for each recruited peer. This amount was decided as a balance between feasibility (encouragement) and sustainability of the strategy (not too high for possible scaling-up).

In case of any issue for tablet use or HIVST kit use, helpline phone number will be available. One dedicated community worker funded by the study will be in charge to manage helpline service.

Intervention after delivering HIV test result

In case of reactive HIV test, the participant could join immediately one research team by hotline or messages on the website that will provide support and orientation. After 1 week, contact with the participant will be done by phone by the research team (if the participant gave consent) to confirm the linkage to one of the partner ART sites. The linkage between participants and HIV clinics will be done by the initial QR code.

If the linkage to confirmatory testing and/or care is not confirmed, we will propose to participant additional help of a community worker.

In case of non-reactive test, the participant could download in the external website one electronic coupon (QR code) to repeat the HIV test 6 month later. Participants will be informed on the external website about the possibilities to join the pilot PrEP program in Chhouk Sar clinic in Phnom Penh.

Qualitative assessment

After 6 months, a qualitative assessment will be conducted to evaluate acceptability and appropriateness of the intervention. Qualitative assessment will be done by focus groups. Focus groups will be conducted in 3 specific populations: MSM, TGW and pharmacists. For each population of MSM and TGW, a qualitative sample will be selected in order to capture different profiles according to sex behaviors and demographic and socioeconomic characteristics.

Participation to focus groups will be anonymous and voluntary. Participants will be recruited via the interview in the pharmacy and by the external website. Focus groups will be conducted in a dedicated room, facilitated by a researcher in social and human sciences with the help of the project manager, trained to focus groups and using grids describing topics. Each focus group will be composed of 9-10 members for a 60-90 minutes discussion that will be recorded to facilitate retranscription and translation. Records will be deleted at the end of the study.

The topics included in grids for focus groups with MSM and TGW will be:

- Acceptability of the HIV test delivery: confidence and confidentiality, non-judgmental attitude, quality of explanations, location of pharmacies
- Acceptability of the HIV self-testing realization: quality of information and use-instructions, painful or stress experience, solitude feeling, orientation after testing
- Appropriateness of the strategy: usefulness, perception and improvement of the strategy, willingness to repeat the test in 6 months

The topics included in grids for focus groups with pharmacists will be:

- Satisfaction of the HIV test delivery: feeling at ease, time-consuming, contact with participants, logistical issues
- Willingness to sustain the strategy, perception and improvement of the strategy

Withdrawal of consent and loss to follow-up

Consent withdrawal

A participant will be considered to have withdrawn consent if s/he no longer wishes to remain in the study. In this case, a “withdrawal of consent form” could be filled in the external website.

When a participant who withdraws consent explicitly expresses the will that his/her data be removed from the database and his/her laboratory samples be destroyed, the study team will

carry out such will. When a patient who withdraws consent do not express such will, data and samples collected prior to the date of his/her consent withdrawal will be used for the analysis.

Loss to follow-up

When a participant who has not explicitly withdrawn consent does not return the HIVST result after one week, the research team will reach them by phone. Also, 1 week after returning positive HIVST results, if there is no information confirming the linkage to one of the partner ART sites or participant does not show up after receiving the reminder for 6-month HIVST, the research team will reach them by phone.

A participant who does not show up for a given schedule and the study team failed to reach by phone will be considered lost-to-follow-up.

10 LABORATORY EVALUATIONS

Samples collection and tests

The HIV Self-test used in the study is OraQuick® which is a private and rapid HIV tests using oral fluid with safe, accurate, and quick results.
The OraQuick ® HIV Self-Test uses oral fluid to check for HIV-1 and HIV-2 antibodies. It give you results in about 20 minutes, and can detect the virus in over 99% percent of people who are infected with HIV. Because the test is a "screening" test, it is always advised to have a second test to confirm the results and participants will be referred for that purpose in case of reactive HIVST.

Biobank

Not applicable.

11 ADVERSE EVENTS AND *IN UTERO* EXPOSURE

Not applicable.

12 SCIENTIFIC BOARDS AND COMMITTEES

a) Scientific Advisory Board (SAB)

Composition

The SAB will consist of: (i) the investigators, the study, clinical coordinators and statisticians/methodologists of the study; (ii) representative members of the community-based organizations; (iii) a representative of the NCHADS; (iv) a representative of partner pharmacies (v) other external experts; and (vi) sponsor representatives.

Meeting agenda

The SAB will meet before the beginning of the inclusion phase, as well as once or twice per year until the end of the study. The sponsor or one or several board members may also request a special meeting at any time.

Role

The role of the SAB is to ensure that the study is carried out appropriately, not only scientifically but also clinically and ethically. The members of the SAB report directly to the sponsor.

- They will ensure that the study personnel carry out the study properly, adhere to the protocol and maintain patient safety;
- They will guarantee that the study remains scientifically relevant by ensuring the relevancy of the study questions and that the methods used are valid and appropriate;
- They will make all decisions regarding necessary and relevant protocol modifications, such as:
  - Actions needed to facilitate patient recruitment;
  - Decisions to open or close participating study sites.
- They will enforce the rules pertaining to access to the study data as well as reports and publications of the results;
- They will remain in contact with the sponsor, and the coordinating investigators, and will make sure investigators and other personnel have access to up-to-date information.

At the end of each meeting, a report containing the meeting minutes, signed by the SAB Chair will be sent to the members of the SAB, and the director of ANRS EID.

13COORDINATION, MONITORING, DATA MANAGEMENT

Coordination

The Grant Management Office (GMO) of the UHS is the referent for the study's methodology and management. The GMO is responsible, in coordination with the clinical and administrative coordinators, for the overall study management (preparation and organisation of the study, monitoring, data management and analysis). Research activities will be coordinated and monitored by a Project Manager who will work in close collaboration with the 2 coordinating investigators and the clinical coordinator. These activities include notably:

- Recruitment, training and management of the clinical research assistants (CRAs) and of the community workers;
- Organising and supporting inclusion and follow-up of patient on site;
- Coordinating Monitoring and data-management activities;

The Project Manager will hold regular meetings with the CRAs and the community workers, from the first pre-inclusion until the end of the study.

The goals of these meetings will be:

- To verify that the study is being carried out in accordance with the protocol, SOP and Good Clinical Practice

- To verify that all inform consent forms are valid
- To verify that confidentiality of data is fully respected
- To discuss difficult patient files, and facilitate patient care in case of positive HIVST, in collaboration with the Clinical Coordinators
- To discuss any file that the research team estimate as problematic after having reviewed the trial database.

The sponsor mandates the GMO to coordinate the research. The delegation of tasks between GMO members, coordinating investigators, sponsor and study site teams is specified in a signed agreement under the supervision of the Sponsor. This document can be revised as often as necessary. The GMO works in close coordination with the Clinical Research Department of the ANRS. The GMO is responsible for the preparation of the research including training, logistic, patient monitoring, data collection and analysis. The GMO is responsible for monitoring the compliance with the protocol, the GCP-ICH and the study procedures.

- **Preparation and organisation of the study**: the UHS team will finalize and review the study documents (including; protocol, information sheet and consent form, electronic Case Report Forms (e-CRF), table grids for FG (annexe 4&5), and all the Standard Operating Procedures), prepare the recruitment procedures, and organize the training for the CRAs and the community workers.
- **Website and Database**: will be developed and managed by IT office at UHS.
- **Data analysis and analysis report**: will be coordinated at the UHS coordinating centre.
- **Reporting**: the operational team will be responsible for finalizing:
  - the necessary reports and presentations for the Scientific Advisory Board;
  - the study yearly progress reports; The operational team will bring its support in preparing any communications on the research study (poster, oral presentation, papers).

Study documents

Essential study documents (protocol, case report forms, SOPs, etc) and regulatory (ethical clearance, task delegation, agreements, curriculum vitae, etc..) will constitute the Trial Master File (TMF). The TMF will be held at the GMO located at the UHS and will be retained for 15 years.

Each investigator will keep a hard copy of relevant TMF documents in an Investigator Site File (ISF). The Clinical Research Assistants (CRAs) will be responsible for checking that the documents contained in the ISF of each study site are up-to-date.

Data management

The UHS Team will be responsible, on behalf of the sponsor, for implementation of procedures for data collection, storage, protection, retention and destruction. The team has implemented a data safety and security concept according to the requirements. All related procedures will be developed in cooperation with the data security engineer of the UHS team and have to be approved by the official data protection officer of the University of Health Sciences prior to implementation.

Data collection

Data from participants will be collected in partner pharmacies, after signature of Informed consent, in tablets on electronic case report forms (e-CRF). The community workers will be responsible for filling out data into the e-CRF. A unique e-CRF will be assigned for each participant. The participant will only be registered through a unique confidential code.
A Standard Operating Procedure (SOP) will be provided to guide the community workers to fill out the e-CRF. All information required by the protocol should be provided and any omission would require explanation.
The CRAs are responsible for ensuring that all sections in the e-CRF are completed correctly and that number of entries can be verified with the number of HIVST delivered in each pharmacy. The results of the HIVST will be recorded by the participants on the external website with the unique ID.

Data entry and checking

Data will be entered on a regular basis at the GMO from tablets to the database. After data entry, the database will be checked for consistency. The data manager will implement data management programs to ensure completeness, consistency and reliability of data. All consistency test will be designed according to the proposition of a team constituted of the Coordinating Investigators, the project manager and the data Manager. If any inconsistency or question related to the collected data, the CRAs will go back to the community workers for clarification during the monitoring visit. The corrections will be entered and followed in the database with traceability of the corrections.
Methods to ensure restricted access to the database; and the data management procedures, including the procedures to verify the completeness, accuracy, quality and validity of the data, will be described in specific trial SOPs.

Data storage

All data and software will be physically stored in dedicated data centers. Data will be physically stored in a MySQL Server.
All software are hosted on certified virtual servers running Linux Enterprise in a VMWare environment. There are several dedicated servers for each system, ensuring separation between the testing / pre-production environment and the production environment. System updates are applied only after validation in the pre-production environment.
For security reasons, the application tiers and the database management systems run independently in separate servers.
All exploitation, monitoring and backups operations are performed by UHS Team, in accordance with UHS policies.
All systems and applications are continuously monitored. Appropriate measures are automatically taken whenever an alert is issued.

Data protection

Data Access

An access concept for the database will be implemented, based on the roles and permissions. Thus, data access will be limited to authorized persons only, and unauthorized access to anonymized data will be prevented.
Any change of data (e.g. error correction during query management) will be recorded automatically via an audit trail within the database.
At the end of the study, once the database has been declared complete and accurate, the database will be locked.

Data Tracking

All modifications during the study conduct will be tracked. Data will be electronically and systematically revalidated after each major change, and corrections/completeness applied whenever necessary.
All system log-ins, interventions, modifications and form status changes will be thoroughly recorded in an Audit Trail log system.

Data Export

Data and metadata will be exported in due time in plain text CSV or STATA formats. These exports might be post-processed programmatically by UHS team to facilitate data analysis and data visualisation.

Data Security

Physical access to the data centers is logged and limited to authorized personnel using badge authentication. On a regular basis, vulnerability testing is performed to reduce potential exposure.
Remote access to servers is limited to authorized personnel. Connections to servers are encrypted using SSH. System logs are stored in a dedicated centralized system for audit purposes. The internal network is protected by multiple firewalls, proxy, reverse-proxy and anti-virus solutions.
Web servers operate under SSL (HTTPS) certifications, ensuring Web connections are encrypted and secure.
At the Database level, only people part of the investigation team, the sponsor team, the affiliated reviewers or auditors, as well as inspection authorities are given access to data. Personal accounts are granted individually for each person. Identification is made by a personnel ID and a password. Failure to provide the correct password after a limited number of attempts automatically deactivates the faulty account (protection against non-authorized attacks).

Data Safety

Backups operations are performed by the UHS Team service at UHS, in accordance with UHS policies.
Backup strategy compromises an optimized daily, monthly and yearly retention plan:
For Website and Study Database

- Server backups :1x differential per day (24 days retention), 1x full every 24 days (retention 12 months), annual (preserved infinitely)

- Database backups : every day, with 2 full backups twice per week (double copies, 2 months retention for Sunday backups, and 14 days for the others), log backups every hour (2 months retention)
- For Database Management System and Administrative Database
- Server backups : 1x differential per day (14 days retention, with mirroring), 1x full every month (retention 12 months), annual (preserved infinitely)
- Database backups : every day, with 2 full backups twice per week (double copies, 2 months retention for Sunday backups, and 14 days for the others), log backups every hour (2 months retention)

Monitoring

Monitoring will be conducted according to the Good Clinical Practice (ICH Harmonized Tripartite Guidelines for Good Clinical Practice 1996) to guarantee the good quality of the research and safeguard the health and the rights of the participants.
The monitoring plan is established by the GMO with the Sponsor and the Coordinating Investigators before the beginning of the study.
The CRAs will come on a regular basis at the partner pharmacies to check for completeness, accuracy and legibility of data reported on the e-CRF. They will check the consistency between the e-CRF filled and the number of HIVST delivered. The pharmacist shall give to the CRA access to relevant pharmacy stock records, to confirm their consistency with the CRF entries. No information about the identity of the subjects should appear on the CRF. All CRF must be signed by the community workers in charge of the participant inclusion and/or follow-up. E-CRF will be considered as a source document for all the study sites regarding all the information it contains.

Monitoring activities will be coordinated by the GMO. The CRA(s) will visit the site regularly during the study, including during set up, implementation, and at the end of the trial:

- To establish and maintain up-to-date the Investigator's site Files (ISF) and Trial Master File (TMF)
- To verify that all inform consents are valid
- Check the adherence to the protocol, SOPs and to Good Clinical Practice (patient informed consent, eligibility criteria, e-CRF filling, HIVST storage and dispensation …);
- To check the study organisation and management on site (communication between participants, pharmacists and community workers, confidentiality during e-CRF filling, HIVST availability);
- Evaluate the progress of enrolment;
- Check the completeness and the accuracy of patient data on the e-CRF;
- To verify that confidentiality is fully respected
- Check that the storage and dispensation of HIVST respect the study protocol and dedicated SOP

14 STATISTICAL ANALYSES

Calculation of number of participants needed

We will use a pragmatic approach with the objective to recruit the maximum of MSM and TGW. According to the IBBS 2019, the estimated number of MSM in Phnom Penh is 6300 and the

estimated number of TGW is 1400.
With 1500 participants (1000 MSM and 500 TGW), we will be able to estimate an HIV self-test uptake of 70% to within a 95% confidence interval of +/- 2 – 2.5% (width of the confidence interval (in %) = 1.96 x √(p x (1-p) / n).

Analysis plan

Description of the characteristics at inclusion.

These variables will be described by their median, interquartile range, mean, standard deviation, or frequencies (%), as appropriate. These variables will be compared to those reported in the IBBS 2019 for MSM and TGW.

Primary outcome

The percentage, and its 95% confidence interval of HIV self-tests delivered among the total number of coupons distributed will be given and stratified by gender (MSM or TGW) and by type of coupons (paper or electronic).

Secondary outcomes

- The percentage and its 95% confidence interval of HIVST result's recorded among the total number of HIVST delivered will be given and stratified by gender (MSM or TGW)
- For those accepting to be contacted by phone, the percentage and its 95% confidence interval of HIVST realized among the number of HIV tests results non recorded will be given
- The percentage and its 95% confidence interval of participants with positive HIV self-tests linked to an ART site will be given and stratified by gender (MSM or TGW)
- The percentage and its 95% confidence interval of participants with negative HIV self-tests linked to PrEP services will be given and stratified by gender (MSM or TGW)
- The percentage and its 95% confidence interval of participants with 6-monthly repeated HIV testing during the 18 months (so 4 HIVSTs during the total duration of the study) will be given
- The probability of discontinuation of HIV testing and its 95% confidence interval, as well as the median time to the occurrence of HIV testing discontinuation, will be determined using a Kaplan Meier analysis, to take into account censored data due to lost of follow-up.

For qualitative assessment, bilingual research staff transcribed all interviews verbatim and translated them into English. We used both inductive and deductive approaches when analysing the data. Inductive analysis was used in the early stage to explore the ideas and meanings contained in the raw data and to identify concepts, patterns and themes. Similar codes were collated to form initial themes. Once patterns, themes and subthemes were established by open coding, deductive content analysis was used to validate these in an iterative process. We reported the results in participant-based, and provider-based issues. QSR NVivo V.12 for Windows was used to manage the data.

15 SCIENTIFIC COMMUNICATION

All written or oral communications of the study's results must receive the approval of the coordinating investigators and of the SAB of the study.

The GMO will realize data analysis. This analysis will lead to a report, submitted to the SAB for approval. This report will help to prepare scientific publications whose final draft must be approved by the SAB .

All publications will include the name of sponsor as follows ("ANRS-MIE. The French National Agency for Research in HIV/AIDS, Viral Hepatitis and Emerging Infectious Diseases is the sponsor of the project") followed by the ANRS study number (ANRS 0100s + Acronym).

In case of ancillary studies, results will be published after approval by SAB. In addition, these results will be published only after the publication of the main results obtained during the research project. Results obtained through ancillary studies will be also transmitted to ANRS-MIE for information.

16 ETHICS AND LEGAL CONSIDERATIONS

- **16.1. Ethics**

This research project will be conducted with regard to fundamental ethical principles that are described in the updated version of the Declaration of Helsinki (64th World Medical Association [WMA] General Assembly, Fortaleza, Brazil, October 2013), and in the ANRS ethics charter for research in developing countries (July 2017) (http://www.anrs.fr/Ressources-et-publications/Publications/Publications-ANRS/Charte-d-ethique-de-la-recherche-dans-les-pays-en-developpement).

- **16.2. Policies and legal aspects**

This study will be conducted in conformity with the French Public Health Code, as modified, notably, by Public Health Low no 2004-806 of August 9, 2004 and its subsequent texts, and the Law n° 2012-300 of March 05th 2012 on research involving the human person ('Jardé Law') and its subsequent texts.
This research project will be also conducted in accordance with national regulations and laws in Cambodia, and according to E6 Good Clinical Practice (GCP).
The protocol, information sheet, and informed consent (**appendix 1 and 2**) will receive the approval from the National Ethics Committee for Health Research (NECHR). The written NECHR approval must be made available to the legal sponsor before the study can start. The sponsor or its delegate is, together with the investigator, responsible for submission to and communication with the NECHR as well as for obtaining approval of all subsequent major changes, in compliance with local law.

The research will be performed according to the present protocol. All researchers and investigators participating to this project will respect the protocol, especially in obtaining informed consent (see below).

- **16.3. Information and consent**

Participation in the study is voluntary. The consent of each potential participant is a prerequisite before starting any sampling or before obtaining any specific information related to the research project. The informed consent must be signed by each participant after giving full research description:

- What is being studied?
- What is the procedure/protocol?
- Who is sponsoring the study?
- What are the risks and burdens?
- What are the benefits?
- Whom to contact with questions/concerns

The person in charge of informed consent process at the trial site will read out and explain the information notice to the patient in his/her language, and will answer any questions that may arise. Each potential participant will be given time to think about the information before making a decision.
Each subject must fully understand that they have the full freedom to accept or refuse to participate in the study. Once one subject is included in the research project, he has to understand that he can also withdraw from it whenever he wants without any problems/consequences and he will continue to benefit from the regular medical care and check-up.
When one person gives his/her consent for participating to the study, he (she) will write his (her) last name and first name, date and sign the informed consent.
Each signed informed consent will be kept in a safe manner and in a safe place for a total duration of 15 years after the end of the research project.

- **16.4. Data confidentiality**

All information collected from enrolled subjects will be strictly confidential and coded. Investigators will make individual data available upon request by representatives of the sponsor and representatives of the ethical and regulatory health authorities, for monitoring purposes or in the event of external audit or inspection. Disclosure to other third parties is strictly prohibited. All persons having access to the data, including the investigator, are subject to the obligation of professional secrecy.
During the implementation and by the end of the research, information collected among participants must be de-identified and names, personal addresses must not be indicated in any document brought back to the GMO.
For this purpose, each participant will receive a unique identification number. This code will be the only patient identifier on any document related to the study, as well as in the electronic study database. There will be no link between the name of the patient and his/her personal identifier in the database.

- **16.5. Data processing**

All data obtained through this research project will be recorded in a database at GMO (UHS). The Sponsor Inserm-ANRS |MIE in collaboration with GMO, study coordinator and investigators will prepare all the necessary documentations in the purpose to obtain the required authorization from the French National Commission of Informatic and Liberty (CNIL).

- **16.6. Final report**

The official date for the end of the study is the date of the last visit of the last participant.

The sponsor or its representative will notify the end of the study to the NECHR within 90 days. A premature end may be decided by the sponsor, following the advice of the SAB, or the ethical authority. In case the study is ended prematurely, the sponsor or its representative will notify the ethical authority within 15 days, and clarify the reasons for such a premature termination. In this case, the sponsor and the investigators, in close collaboration with the country health authority, will take appropriate decision to ensure that patients have access to the best available care and treatment according to the country condition.

GMO will write the final report, in partnership with principal investigators, as well as summary report, one year after the end of the research and will transmitted them to ANRS. Within one year after the end of the study, the sponsor or its representative will release to the ethical authority the final study report and/or summary including the results of the study and the scientific publications or communications related to these results available at this time.

The report and its summary are established according to ICH recommendations (International Conference for Harmonisation – ICH Topic E3 – Structure and Content of Clinical Study Reports CPMP/ICH/137/95. Accessible at: https://database.ich.org/sites/default/files/E3_Guideline.pdf).

- **16.7. Archiving system**

Forms and data related to the research project are key documents. They can be useful to demonstrate that researchers and investigators respect GCP and current laws/legislation. Consequently, all these documents will be archived by GMO and ANRS during 15 years after the end of the research program.
Informed consents will be kept in a safe manner at GMO in sealed envelopes on which ID numbers of the participants will be indicated, as well as name and signature of the coordinating investigators.
No documents must be destroyed without prior authorization from ANRS.

17 ACCESS TO DATA AND SPECIMENS

All collected data related to the study protocol will be under the GMO's responsibility from the beginning to the end of the trial. After the end of the trial, the GMO will remain responsible for the database, until otherwise decided by the sponsor.

Data will be utilized according to this protocol. Any utilization for analysis not listed in the protocol should be approved by the trial coordinating investigators and either the SAB (if the study is still ongoing) or the sponsor (if the study is terminated).

After the analysis and publication of the study results, the data will be made available to investigators and external researchers to maximize the impact of the data by encouraging secondary analysis to address other research questions. The clear process for data access will be developed with the sponsor in the dissemination and exploitation plan to ensure transparency and accountability of data requestors, and the data release decision making process. Policies will be developed to assure that those who re-use data duly credit those who produced the data. The requestor should be explicit about the proposed research use of data, including the justification for the specific datasets requested. The shared data will be formatted to the required standards for sharing once defined by the SAB.

18 DUTIES OF INVESTIGATORS

According to GCP aimed to achieve high quality of the research, each investigator must:

- To respect participants' rights and to ensure subjects' welfare,
- To ensure his availability as well as availability of his team,
- To ensure that enrollment will be feasible according to the research protocol,
- To organize technical infrastructures for the implementation of sampling, filling in of questionnaires and archiving of documents/records during the research study and 15 years after the end of the research,
- To collect and archive in a safe way signed informed consents,
- To ensure that researchers are following the protocol and to allow completed questionnaires to be regularly sent to GMO,
- To accept a possible audit of the research project carried out by ANRS itself or by other agencies if necessary.

19 REFERENCES

1. UNAIDS DATA 2019 [Internet]. Disponible sur: https://www.unaids.org/en/resources/documents/2019/2019-UNAIDS-data
2. Griensven F van, Guadamuz TE, Wijngaarden JW de L van, Phanuphak N, Solomon SS, Lo Y-R. Challenges and emerging opportunities for the HIV prevention, treatment and care cascade in men who have sex with men in Asia Pacific. Sex Transm Infect. 1 août 2017;93(5):356-62.
3. 2013 Annual Update [Internet]. Asia Pacific Coalition on Male Sexual Health; Disponible sur: https://www.apcom.org/wp-content/uploads/2016/01/2013-APCOM-Annual-Update.pdf
4. HIV and AIDS in Asia & the Pacific regional overview [Internet]. Avert. 2015 [cité 23 nov 2021]. Disponible sur: https://www.avert.org/professionals/hiv-around-world/asia-pacific/overview
5. UNAIDS - KEY POPULATIONS ATLAS [Internet]. [cité 24 nov 2021]. Disponible sur: https://kpatlas.unaids.org/dashboard
6. Chhim S, Ngin C, Chhoun P, Tuot S, Ly C, Mun P, et al. HIV prevalence and factors associated with HIV infection among transgender women in Cambodia: results from a national Integrated Biological and Behavioral Survey. BMJ Open. août 2017;7(8):e015390.

7. Yi S, Chhim S, Chhoun P, Tuot S, Ly C, Mun P, et al. Men Who Have Sex with Men in Cambodia: Population Size, HIV Risky Behaviors, and HIV Prevalence. American Journal of Epidemiology and Infectious Disease. 2016;4(5):10.
8. Yi S, Ngin C, Tuot S, Chhoun P, Chhim S, Pal K, et al. HIV prevalence, risky behaviors, and discrimination experiences among transgender women in Cambodia: descriptive findings from a national integrated biological and behavioral survey. BMC Int Health Hum Rights. déc 2017;17(1):14.
9. NCHADS and FHI-360. Integrated Biological and Behavioural Survey among Men Who Have Sex with Men and Transgender Women in Cambodia 2019. NCHADS and FHI-360;
10. World Health Organization. WHO RECOMMENDS HIV SELFTESTING – EVIDENCE UPDATE AND CONSIDERATIONS FOR SUCCESS [Internet]. World Health Organization; 2019. Disponible sur: file:///C:/Users/Sovanthida/Downloads/WHO-CDS-HIV-19.36-eng.pdf
11. WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection - recommendations for a public health approach. 2nd éd. World Health Organization; 2016.
12. Katz DA, Golden MR, Hughes JP, Farquhar C, Stekler JD. HIV Self-Testing Increases HIV Testing Frequency in High-Risk Men Who Have Sex With Men: A Randomized Controlled Trial. JAIDS Journal of Acquired Immune Deficiency Syndromes. 15 août 2018;78(5):505-12.
13. Saul H, Gursul D. Self-testing for HIV could increase diagnoses in the trans community. BMJ. 10 nov 2021;375:n2633.
14. Thirteen countries from Asia and the Pacific plan scale-up of PrEP and HIV self-testing [Internet]. Unitaid. [cité 24 nov 2021]. Disponible sur: https://unitaid.org/news-blog/thirteen-countries-from-asia-and-the-pacific-plan-scale-up-of-prep-and-hiv-self-testing/
15. NCHADS. National Consolidated Guidelines on HIV Testing Services in Cambodia. 2017.
16. Evaluation of the Boosted- Integrated Active Case Management (B-IACM) in Cambodia. 2017 oct.
17. Pal K, Ngin C, Tuot S, Chhoun P, Ly C, Chhim S, et al. Acceptability Study on HIV Self-Testing among Transgender Women, Men who Have Sex with Men, and Female Entertainment Workers in Cambodia: A Qualitative Analysis. Andrei G, éditeur. PLoS ONE. 9 nov 2016;11(11):e0166129.
18. World Health Organization. HIV self-testing: key questions, answers and messages for community organizations [Internet]. World Health Organization; 2018 [cité 24 nov 2021]. Report No.: WHO/CDS/HIV/18.23. Disponible sur: https://apps.who.int/iris/handle/10665/273771
19. Self-Testing: a convenient and private option [Internet]. 2021 [cité 24 nov 2021]. Disponible sur: https://www.cdc.gov/hiv/basics/hiv-testing/hiv-self-tests.html
20. Autotests de dépistage de l'infection par le VIH [Internet]. 2015 [cité 23 nov 2021]. Disponible sur: https://www.has-sante.fr/jcms/c_1768844/fr/autotests-de-depistage-du-vih
21. GUIDELINES ON HIV TESTING SERVICES HIV SELF-TESTING AND PARTNER NOTIFICATION SUPPLEMENT TO CONSOLIDATED GUIDELINES ON HIV TESTING SERVICES. World Health Organization; 2016.
22. Bryant J. Using respondent-driven sampling with 'hard to reach' marginalised young people: problems with slow recruitment and small network size. International Journal of Social Research Methodology. 2 nov 2014;17(6):599-611.
23. Lachowsky NJ, Lal A, Forrest JI, Card KG, Cui Z, Sereda P, et al. Including Online-Recruited Seeds: A Respondent-Driven Sample of Men Who Have Sex With Men. J Med Internet Res. 15 mars 2016;18(3):e51.

24. Weiss KM, Jonas KJ, Guadamuz TE. Playing and Never Testing: Human Immunodeficiency Virus and Sexually Transmitted Infection Testing Among App-Using MSM in Southeast Asia. Sexual Trans Dis. juill 2017;44(7):406-11.
25. De Boni RB, Veloso VG, Fernandes NM, Lessa F, Corrêa RG, Lima RDS, et al. An Internet-Based HIV Self-Testing Program to Increase HIV Testing Uptake Among Men Who Have Sex With Men in Brazil: Descriptive Cross-Sectional Analysis. J Med Internet Res. 1 août 2019;21(8):e14145.
26. Strömdahl S, Lu X, Bengtsson L, Liljeros F, Thorson A. Implementation of Web-Based Respondent Driven Sampling among Men Who Have Sex with Men in Sweden. PLoS One. 2015;10(10):e0138599.
27. Bengtsson L, Lu X, Nguyen QC, Camitz M, Hoang NL, Nguyen TA, et al. Implementation of web-based respondent-driven sampling among men who have sex with men in Vietnam. PLoS One. 2012;7(11):e49417.
28. Huang E, Marlin RW, Young SD, Medline A, Klausner JD. Using Grindr, a Smartphone Social-Networking Application, to Increase HIV Self-Testing Among Black and Latino Men Who Have Sex With Men in Los Angeles, 2014. AIDS Educ Prev. août 2016;28(4):341-50.