Enrolment Participant Information Leaflet and Informed Consent Form

Evaluation of stepped PrEP adherence support for young South African Women using a SMART Design: PrEP SMART

FINAL VERSION 2.0, 26 August 2020

SPONSOR: University of Washington, USA; US National Institute of Mental Health, US National Institutes of Health.

PRINCIPAL INVESTIGATOR: Sinead Delany-Moretlwe, MBBCh PhD DTM&H

INSTITUTION: Wits RHI, University of the Witwatersrand

SITE TELEPHONE NUMBER: 011 358 5447 or 060 815 9640 (24-hour emergency line)

To the Potential Participant: This consent form might contain some words that are unfamiliar to you. Please ask the study staff about anything you do not understand or anything you want to learn more about. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. Once you understand the study, and if you agree to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy to keep.

Introduction and study summary

Hi, my name is _____ *(INSERT NAME)*, and I am a _____ *(INSERT DESIGNATION)* at Wits RHI. Wits RHI is a part of the University of the Witwatersrand, Johannesburg and we conduct research on sexual and reproductive health problems, including HIV, which affect many people living in South Africa.

We would like to invite you to participate in a research study called PrEP SMART. Your participation in this study is voluntary. Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

This study is for young women aged 18-25 who may be at risk for getting HIV. Taking a medication to prevent becoming HIV-infected is called "pre-exposure prophylaxis" or "PrEP". Women who take PrEP daily have a much lower chance of getting infected with the HIV virus, but it can be hard to take PrEP. The purpose of this study is to understand what kind of support makes it easier to young women to take PrEP.

If you decide to be in this study, you will be in it for up to 9 months. At study visits:

- We will ask you to answer personal questions about yourself;
- We will conduct medical tests, including testing for HIV and other infections you can get during sex; and
- We will assign you to different types of support, including participating in WhatsApp groups or receiving SMS messages and receiving different types of counseling

If you decide to participate in the study, you may be uncomfortable answering some of the questions or having some of the procedures done. You may choose not to answer any question you do not want to and you may choose not to have other procedures conducted, including medical testing. You may also

find the WhatsApp group or SMS messages inconvenient or have concerns about confidentiality of receiving those. You may choose to stop participating in either group if you choose.

There may not be any direct benefits to you for being in this study.

There may be other studies going on here or in the community that you may be eligible for or other places where you can go for HIV testing and counseling. If you wish, we will tell you about those things.

This study is sponsored by the University of Washington and the National Institutes of Health, which are located in the United States of America.

Before you learn more about the study, it is important that you know the following:

- You may decide not to take part in this study and you may also stop taking part in the study at any time without losing your usual medical care;
- You will still be eligible for future studies even if you decide not to join this study;
- You cannot join this study if you are taking part in another study of drugs or medical devices.
- You are asked to tell the study staff about any other studies you are taking part in or thinking of taking part in. This is very important for your safety. We will use the **Biometric Co- enrolment Prevention System (BCEPS)** at each visit to ensure that you are not enrolled on other studies throughout the duration of our study for your safety. BCEPS is an electronic finger print system that uses a finger print reader. By agreeing to be part of this study, you give us permission to use this system to read your fingerprints to check whether you are participating in other studies listed on the system. This database is only accessed by a few members of the study team using a secure password.

Why is this study being done?

This study is for young women aged 18-25 who may be at risk of getting HIV. Taking a medication to prevent becoming HIV-infected is called "pre-exposure prophylaxis" or "PrEP". PrEP has been recommended by the World Health Organisation (WHO) and the South African National Department of Health as part of a package of HIV prevention to be offered to people who may be vulnerable to infection. Women who take oral PrEP daily have a much lower chance of getting infected with the HIV virus, but it can be difficult to take PrEP every day. The purpose of this study is to understand what kind of support makes it easier for young women to take oral PrEP daily.

If you want to know more about PrEP and how it works, you can find out information here: www.myprep.co.za. This website is endorsed by the South African Department of Health.

Who can join this study?

You can join this study if you are between the ages of 18-25 years, sexually active and interested in taking oral PrEP to protect yourself against HIV. You will need to have access to a cell phone that can receive both WhatsApp and text messages. Approximately 500 young women will be enrolled in this study at this clinic in Johannesburg, South Africa.

What will happen if I take part in this research study?

If you decide to join the study, your first visit will be today after you read, discuss, understand, and sign this form.

- You will be in the study for **up to 9 months**.
- After today's visit, we will ask you to **return every month for 3 months** and then, at least once every 3 months after that for a total of 7-10 visits depending on your group.
    - All participants will be asked to attend visits at months 1, 2, 3, 6, and 9.
    - Some women will also be asked to come more frequently for additional counselling.
- Each study visit will take about **1-3 hours**. This visit will be the longest.
- At each visit, we will confirm **where you live and how to contact you**, and verify your cell phone number.
- We will also ask you **questions about yourself** - including about your health, your sexual practices, and your sexual partners, and whether you use alcohol or drugs. The questions related to your sexual practices and partners may include questions about your partner's HIV status, if you think your partner has other partners, and the type of sex you have with your partner. The

questions related to your alcohol and drug use may include the frequency with which you use alcohol and drugs and the frequency with which you use those substances.

- We will ask you if we can collect a **blood sample** [up to 34 ml / about 2½ tablespoons]. This blood sample will be used for testing.
    - We will test for HIV, kidney function, and to see if you have hepatitis B. We will test for syphilis, a sexually transmitted infection (STI). If your HIV test is positive today you will not be eligible for the study even if additional tests show that you do not have HIV.
    - At every visit, we will do an HIV test and if it is negative, talk with you about ways to protect yourself from getting it and offer you condoms.
    - If you have a positive test at a later visit, we will ask you to stop taking PrEP and you will be referred for further HIV testing. If needed, you will be referred for further appropriate medical care here or at a clinic that is convenient to you.
    - Two months after you start taking PrEP, and at subsequent follow up visits, we will test your blood and/or urine to see how much PrEP medication is in your body.
- We will collect a **urine sample** and conduct pregnancy testing to see if you are pregnant. If you are pregnant today, you cannot join the study.
- Today and during some of the other visits we will collect a **genital swab** to test you for common infections you can get when you have sex (gonorrhoea, chlamydia and trichomonas).
- You will be provided with the **results of all of your tests** at your next study visit. If your test results are not normal, we will call you to ask you to return to the clinic for your test results. If you have gonorrhoea, chlamydia, trichomonas or syphilis, you will be provided treatment.
- We will provide you **PrEP** and talk with you about possible side effects. We will discuss your plans for remembering to take it. At some of your visits, we may ask you if it is ok to record our conversations with you about PrEP to see how our staff counsel you. The recordings will not be used to collect information about what you say specifically.

How will I be supported to take PrEP daily?

At today's visit, you will be assigned to participate in one of two study groups. You will not be able to choose which group you will be in. The study staff will also not choose your group. Instead, a computer program will choose your group by chance (like flipping a coin or rolling a dice):

- WhatsApp group
    - If you are chosen to take part in a Whatsapp group, you will be in the group with between 25-50 women who are all enrolled in the study and taking PrEP. A study staff member and a young woman with experience using PrEP will also be in the group to provide answers to questions that group members may have and to make sure the members are all following the group rules.

OR

- SMS group
    - If you are chosen to receive the weekly text messages, we will ask you to sign up with a special confidential system that will send you a text (SMS) message every week. The text message will ask you about your health but we will not specifically refer to your health status or your use of PrEP. You may also receive text messages with general health information.

Regardless of the group you are assigned, you will also receive one-way SMS messages reminding you of your study visits. If you have any problems, you can contact the 24-hour number listed on the front of this form.

If, at your month 3 visit, your blood test from your month 2 visit shows that there is sufficient PrEP in your body, your study procedures will remain the same and your study visits will move to every three months.

Additional PrEP support

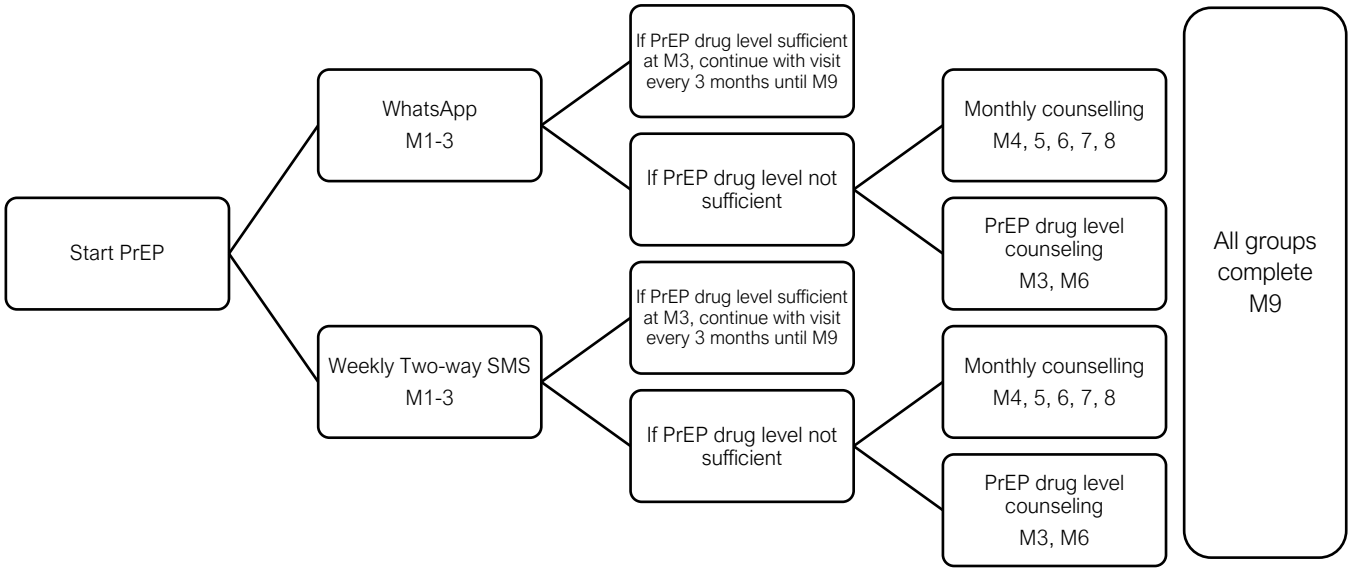
If, at your **month 3 visit** your blood test from your month 2 visit shows that that **there is not sufficient PrEP in your body or if you have missed a PrEP refill**, you will continue with your group (WhatsApp group or SMS group) and we will use the same computer system to assign you by chance to another one of two groups:

- **Monthly counselling visits**
  - During these visits you will only talk to a counsellor. The counsellor will talk to you about your experiences taking PrEP and what makes it easier or harder to take your PrEP pills. These visits will continue up until your month 9 study visit.

OR

- **Drug level feedback counselling**
  - You will have study visits every three months and you will receive additional counselling based on how much PrEP is in your body. We will conduct testing to see how much PrEP is in your body at two time points after you are enrolled in the study. We will use a blood test from blood samples collected at the Month 2 and Month 6 visits. We will talk to you about your results at your study visits. We will talk to you about the amount of PrEP drug in your body, and what makes it easier and harder to take your PrEP pills.

Figure. Diagram showing PrEP support interventions and study groups.



We will also offer ALL participants the option to have additional drug level feedback counselling at their Month 9 visit, using an experimental urine test kit from urine samples collected at that visit. We will ask questions about this experience.

Will any of my visits be conducted remotely?

In order to maximise physical distancing, we may offer you the opportunity to complete some visits remotely, i.e. over the phone,

- We will ask you to confirm that you are able to complete your visit safely and privately.
- We will ask you some questions about your health over the phone. We will also do the drug-level feedback or monthly counselling by phone.

We may also conduct some visit procedures remotely, where you do testing yourself and share with us the results,

- We will provide you with an HIV self-test and a urine pregnancy test to take at home on the day of your remote visit. One of our study staff members will explain to you how to do these tests at home and read the results. We can also share an instruction video. We will ask you to send us a picture of your results by phone.
    - If you have a positive test, we will ask you to stop taking PrEP and invite you to come to the study clinic for further HIV testing to confirm the result. If needed, you will be referred for further appropriate medical care at a clinic that is convenient to you.
- If during the course of the remote visit we identify any health concerns, we will ask you to come to the clinic or refer you to your nearest health care provider.
- Once these remote procedures have been successfully completed, we will deliver PrEP to your home.

Are there any potential risks or discomforts that I can expect from this study?

- You may become nervous, anxious, or worried when talking about your sexual behaviour, drug and alcohol use, and while you are waiting for your HIV test results. However, you do not have to answer any question that you do not want to and you can stop answering the questions at any time. If the questions in the interview make you anxious, you can also ask to speak to a counsellor or other health care provider about your concerns. You will also receive counselling from trained study counsellors about challenges you might be experiencing with your partners or violence you might be experiencing in your relationship, and referred for further help if necessary. We will provide you with information on where to seek help.
- Taking blood samples may cause some pain, bruise your arm, or make you feel lightheaded. In rare cases you may faint. There is also a slight chance of infection when blood is drawn.
- If the tests show that you have HIV or another infection you can get through sex, you may worry about your health and future. You will receive counselling before and after the HIV test by trained study staff who will help you deal with any feelings or questions you have.
- It is possible that the timing or volume of SMS or WhatsApp messages may be inconvenient or that you may receive unwanted comments from group members. We will tell you when you can expect text messages if you are in the text message group. If you no longer want to be in the WhatsApp group, you can remove yourself at any time. If you decide you would no longer like to receive the weekly text messages, you may reply 'STOP" to discontinue them.
- If you are in the WhatsApp group and have a photo linked to your account, it is also possible that other group members will know who you are. We will inform everyone in the WhatsApp group of the rules of being in the group, including the importance of keeping group member identities confidential. This includes not sharing phones, and immediately reporting any replaced, lost or stolen phone so that the associated number can be removed from the WhatsApp group. We strongly recommend that you have a password on your phone so people cannot easily access your WhatsApp account and that you delete any messages you do not want other people to see. We strongly recommend that you also use an app locker to secure access to WhatsApp using a personal identification number (PIN). The study staff can assist you with setting this up. There will be a study staff person monitoring WhatsApp group messages and who will delete participants who violate the rules from the WhatsApp group. Information that you send us from your mobile phone programs will be kept confidential. If you are in the WhatsApp group, you can contact the group facilitator to discuss any issues privately.
- Despite these measures, it is possible that others outside the WhatsApp group might view your information, such as your personal phone number, group discussions, and messages. We

strongly recommend that you not associate a photo of yourself or your full name with your WhatsApp profile to limit the information anyone might have about you.We will not be able to **access any private information on your mobile phone** and any text you send us will not be shared with anyone outside the research team. However, it may be possible for your information to be viewed by others who have access to your phone. You can lock your phone with a pin to prevent others from accessing your phone. We can help you understand how to delete the messages from your phone if you are concerned about others seeing them.

- If your partner finds out that you are on PrEP, this may lead to disagreements or physical/verbal abuse. It may also lead to economic risks such as loss of income or financial support. We anticipate that these risks will be rare. If threats of violence arise, avoid confrontation and consider seeking help from family, friends, your other social networks or study staff.
- We will make every effort to protect your confidentiality during the study. However, it is possible that **others may learn that you are part of this study** and they may think that you are infected with HIV or at high risk for infection with HIV. Because of this you could have trouble finding or keeping a job. You could also have problems with your family, friends and community.
- If we use the investigational urine test, there is a very small chance that it will indicate false results. The adherence counselling you would normally receive will not be affected in such situations.

What should I do if I become pregnant or am breastfeeding during the study?

Current information shows that those women who were taking PrEP at the time that they became pregnant did not experience any harmful effects on their pregnancy or on their infants, and there is no safety-related reason for stopping PrEP during pregnancy. If you become pregnant while taking PrEP you will be counselled on the benefits of continuing PrEP to reduce the risk of HIV infection to both yourself and your baby, and any potential concerns you have about exposing your growing baby to the PrEP medications. You will be allowed choose if you want to continue taking PrEP or not during your pregnancy.

If you are breastfeeding, current information shows that little if any PrEP drug is detected in breastmilk; women who are breastfeeding may also continue to breastfeed while taking oral PrEP if they choose.

Are there any potential benefits if I participate?

We will provide you PrEP to avoid HIV. We will provide you with condoms and contraception, and test you for pregnancy, HIV and other sexually transmitted infections (STIs) throughout this study. If you become HIV infected or have another sexually transmitted infection, we will either treat you here or refer you for care and treatment. We will link you to other health and social services should you require them during the study. You or others in your community may also benefit in the future from the information learned in this study.

What other choices do I have if I choose not to participate?

There also may be other places where you can go for HIV counselling and testing, condoms, contraception and management for STI symptoms. We will tell you about those places if you wish. We can also tell you about other clinics that are offering PrEP. There may be other studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about.

Will I be told about new information?

You will be told any new information including about the new urine test learned during this study that might affect your willingness to stay in the study. You will also be told when the results of the study may be available, and how to learn about them.

What are my rights if I take part in this study?

Your participant is entirely voluntary. You may also stop taking part in the study at any time without losing your usual medical care. However, you may be withdrawn from the study without your consent if the study is stopped or cancelled or if staying in the study would be harmful to you. If you withdraw early from the study, we will ask you to come in for a final visit with all the exams and tests listed above.

Will there be any costs to me?

There will be no cost to you for study related visits, study products, physical examinations, laboratory tests, SMS or other procedures. If you are in the WhatsApp group, you will be given reimbursement for WhatsApp in the form of vouchers up to the value of R100 to cover data costs for participation.

You will receive R 150-00 for expenses related to your effort, and travel to and from the clinic at each scheduled visit.

How will my information be kept confidential?

To keep your information private, your samples and information about you will be labelled only with a code. The link between your name and code will be kept in a secure location at this clinic only. Any publication of this study will not use your name or identify you personally. A description of this clinical trial will be available on www.sanctr.gov.za and www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Your records may be reviewed by study staff and representatives of the Wits Human Research Ethics Committee (HREC), South African Health Products Regulatory Authority, the University of Washington, and the United States National Institutes of Health who watch over this study to see that we are protecting participants' rights, keeping participants safe, and following the study plan. Your study data may also be reviewed by the US Federal Drug Administration, including your identifying information to make sure we are conducting the urine testing appropriately. Every effort will be made to keep your personal information confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. In this case, we will let you know of our plan to disclose such information to the relevant government authority.

Use of information and specimens for future studies

This research will not use any specimens we collect from you for genetic sequencing. We may use your information and/or samples that we obtain from this study for future studies. We will provide further information on this and ask your permission to store your samples for future studies in a separate consent form. Future studies using your information or samples will not be done without approval from Wits HREC at least. They will advise us on whether or not we need to get additional approval from you.

What can I expect if I am injured or need emergency care?

If you feel you have been injured because of being in this study, it is important that you tell us. We will offer you treatment for your injuries at the study clinic free of charge. You will be told where you can get additional treatment for your injuries. Truvada ® is licensed for use as PrEP in South Africa and as such there is no program to pay money or give other forms of compensation for such injuries either through Wits RHI, University of Washington or the US NIH. You do not give up any legal rights by signing this consent form.

If you seek emergency care and hospitalisation at any time during the study, please tell the treating doctor that you are in this study and that we will request a copy of your medical records.

Who can I contact about problems or questions?

This clinical study protocol has been submitted to the University of the Witwatersrand, Human Research Ethics Committee (HREC) and written approval has been granted by that committee. The study has been structured in accordance with the Declaration of Helsinki (last updated: October 2013), which deals with the recommendations guiding doctors in biomedical research involving human participants. A copy may be obtained from me should you wish to review it. This study is funded by the US NIH. We do not have any financial or personal interests with this organisation that may bias our actions.

If you ever have **any questions about the study, or if you have a research-related injury**, you should contact: Study Coordinator Nontokozo Ndlovu, tel: 011 358 5447, cell: 072 635 9437 (after hours); email: nondlovu@wrhi.ac.za OR Prof. Sinead Delany-Moretlwe, tel:011 358 5300; cell: 082 377 6275; email: sdelany@wrhi.ac.za

If you have **questions about your rights as a research participant**, you should contact: Prof. Clement Penny, Chairperson for the Committee for Human Research Ethics Committee (HREC), University of the Witwatersrand, which is an independent committee established to help protect the rights of research participants on 011 717 2301 OR the South African Health Products Regulatory Authority: Dr Boitumelo Semete-Makokotlela, The Chief Executive Officer, South African Health Products Regulatory Authority, Department of Health, Private Bag X828, Pretoria 0001; Tel: (012) 842 7629/26; E-mail: Boitumelo.Semete@sahpra.org.za.

SIGNATURE PAGE FOR CONSENT FOR ENROLLMENT

Evaluation of stepped PrEP adherence support for young South African Women using a SMART Design (PrEP SMART) (Version 2.0, 26 August 2020)

I hereby confirm that I have read the information provided above. I have asked all the questions I have at this time. I understand my rights and responsibilities as a research participant. I voluntarily agree to participate in this research study.

_____	_____
Participant name	Participant signature and date (DD/MMM/YYYY)

_____	_____
Study staff member conducting consent discussion	Study Staff Signature and date (DD/MMM/YYYY)

CONSENT FOR PERSONAL DOCTOR/SPECIALIST NOTIFICATION

☐ I do not have a personal doctor

_____
Participant signature and date

☐ Yes, I want you to inform my personal doctor

_____
Participant signature and date

☐ No, I do not want you to inform my personal doctor

_____
Participant signature and date

CONSENT TO BE CONTACTED ABOUT FUTURE RESEARCH

Wits RHI may have other studies in the future that you might be eligible to participate in. We would like your permission to contact you by telephone, SMS or voice message to inform you about these studies.

Your agreement to have us contact you in the future is optional. Should you choose not to agree for us to contact you about other studies, this choice will NOT affect your participation in the PrEP SMART study or the quality of health care you will receive.

☐ YES, I would like to be contacted _____

Participant Signature and date

☐ NO, I would not like to be contacted _____

Participant Signature and date