PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY

WHO-recommended Periodic Presumptive Treatment versus Doxycycline Post-Exposure Prophylaxis for STI Control among Cisgender Men Who Have Sex with Men in Kenya

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INTRODUCTION

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called "informed consent."

Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a research study:

1. Your decision to participate is entirely voluntary.
2. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.
3. Refusal to participate in the research will not affect the services you are entitled to in this health facility or other health facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

KEY STUDY INFORMATION

We are conducting this study to test two different interventions to improve sexually transmitted infection (STI) control among young gay, bisexual, and other men who have sex with men (GBMSM) in Kenya. You are being asked to participate in this study because you are a young GBMSM who is at risk for STI including gonorrhea, chlamydia, and syphilis.

If you decide to participate, we will ask you to attend quarterly study visits over 18 months to help determine which of the two interventions we are testing does a better job of controlling STI among GBMSM, compared to standard of care. This box presents key information to help you decide whether to participate. Ask the research team questions if you have them now. If you have questions later, the contact information for the research investigators in charge of the study is below.

WHY ARE WE DOING THIS STUDY?

One intervention that may reduce STIs among GBMSM is periodic presumptive treatment (PPT), in which you are treated every 3 months for STI regardless of your symptoms. STI PPT has been recommended by the World Health Organization for GBMSM but never tested in a randomized trial. The other intervention is called doxyPEP, which consists of taking a medication called doxycycline 24-72 hours after you have condomless sex, as post-exposure prophylaxis (PEP) to prevent STI. DoxyPEP has been found to reduce STI among GBMSM in the United States and France but has not been tested among GBMSM in sub-Saharan Africa. No one knows if STI PPT or DoxyPEP is better at reducing STI among GBMSM in Kenya and similar settings.

WHAT WILL YOU BE ASKED TO DO IF YOU PARTICIPATE?

By doing this study, we hope to learn which intervention is most effective, acceptable, feasible, and safe for GBMSM in Kenya. If you agree to participate:

- We will ask for a telephone number and other information so our study staff can contact you if necessary.
- You will receive either STI PPT or doxyPEP or standard of care. The study doctor will not pick which intervention you will take. We will use a computer to place you in one of the three study groups. The group the computer picks for you is by chance, like a flip of a coin. We will tell you which group you are assigned to. You or your study doctor cannot change your group once you are assigned to it.
- All participants in all three groups will be treated for STI whenever they have STI symptoms or are diagnosed with syphilis. Those in the STI PPT will receive PPT at each quarterly visit. Those in the doxyPEP group will be given a supply of doxycycline at each study visit and instructed how to use this for PEP.
- You will have seven quarterly research visits during the study, for 18 months from enrollment.
- At each study visit, you will take a computer-assisted survey on a tablet and then see the study doctor for a review of any STI symptoms you have had. If you have symptoms of an STI, you will be treated. Otherwise, you will receive care according to your assigned group.
- The study doctor will collect two throat swabs, two rectal swabs, urine, blood, and a small hair sample at each visit.
- Your blood will be tested for syphilis and, if you have this infection, you will be treated according to standard of care as soon as results are available.
- The swab and urine samples will be tested for gonorrhea and chlamydia at the end of the study, to determine which intervention worked best to reduce STI.
- At the end of the study, we will share our results with study participants, community organizations serving cisgender MSM, the Kenyan Ministry of Health and the World Health Organization.

WHY MIGHT YOU <u>NOT</u> WANT TO BE IN THIS STUDY?

If you are in this study, you will be assigned to one of the three groups, but you will not get to choose which one. If you decide not to be in the study, you will still have access to standard of care STI treatment. STI PPT and doxyPEP are not routinely provided to Kenyan GBMSM outside of this trial.

WHY MIGHT YOU WANT TO BE IN THIS STUDY?

Both interventions tested in this study have been shown to reduce STI in some settings and populations, and include medications that are commonly used to treat STI in Kenya. No matter

which group you are assigned to, you will receive standard of care STI treatment if you have symptoms. The study provides the STI medicines and research visits to you at no cost. The research team will also give you guidance on how to prevent STI and HIV. You will know which group you are assigned to, in case there is a reason for your regular doctor to know. If you are in this study, you will contribute to our understanding of how to reduce STI among GBMSM in Kenya and similar settings in the future.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you want to volunteer. If you decide not to take part, you will not lose any services, benefits, or rights you would normally have. You will still receive treatment for your STI. You can choose to withdraw from the study at any time.

WHAT IF YOU WANT MORE INFORMATION?

The rest of this document gives you more information about the study, like:

- Details of what will be done at the research visits
- The risks (side effects) of the medicines used in the interventions
- What will happen if you are injured from the study procedures
- How we will protect your privacy
- Who to talk to if you have problems, suggestions or concerns

STUDY SUMMARY / WHAT IS THIS STUDY ABOUT?

The researchers listed above are recruiting individuals who identify as gay or bisexual men or men who have sex with men (GBMSM) in Nairobi, Kisumu, and Mombasa to participate in a study that aims to reduce the burden of gonorrhea, chlamydia and syphilis infections among GBMSM in Kenya. The purpose of the interview is to find out if you are eligible and willing to participate.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to decide about participating. You can discuss your decision with your family, friends and health providers, if you would like.

Gonorrhea, chlamydia, and syphilis are serious health problems impacting GBMSM and their sexual partners. While some infections cause symptoms, these infections can be asymptomatic. Participants in this research study will be assigned to one of three different groups to test the effectiveness of two interventions to reduce chlamydia, gonorrhea, and syphilis, compared to the current standard of care. The first intervention is called “periodic presumptive treatment” (PPT) and consists of two oral antibiotic medications called cefixime and azithromycin, directly observed every three months at the research clinic. The second intervention is called “doxycycline post-exposure prophylaxis” (doxyPEP) and consists of an antibiotic medication called doxycycline that GBMSM can take after sexual contact without a condom. Both interventions aim to reduce the burden of STI to a greater extent than standard of care, which consists of treating STI only when individuals have symptoms. If you enroll into this study, you will be randomly assigned to one of the three groups: PPT, doxyPEP, or standard of care.

DETAILED STUDY INFORMATION

You are being asked to take part in this study because you are a man (assigned male gender at birth) who has sex with men (MSM) who has had anal sex with another man without using a condom and either multiple sex partners or a sex partner with an STI in the past 6 months.

Why is this study being done?
The purpose of this study is to understand how well two different interventions reduce chlamydia, gonorrhea and syphilis among GBMSM in Kenya, compared to standard of care treatment, in which men with symptoms are treated but those without symptoms are not. The study also aims to understand how these interventions impact the resistance of gonorrhea against the treatment given, and whether the study interventions are safe and acceptable to patients and feasible for their providers.

While all three antibiotics used in these interventions are approved by the United States Food and Drug Administration (FDA) and the Kenyan Pharmacy & Poisons Board (KPPB), taking cefixime and azithromycin every three months to prevent STI (the PPT intervention) and taking doxycycline after condomless sex to prevent STI (the doxyPEP intervention) are investigational and are not currently approved by the FDA or KPPB for these purposes.

The Division of Microbiology and Infectious Diseases (DMID), which is a part of the National Institutes of Health (NIH) is paying for the conduct of this study.

How many people will take part in this study?
About 2,900 people will take part in this study. About 985 will be enrolled in Kisumu, 985 in Nairobi, and 985 in Mombasa.

Randomization
After enrolling in the study, you will be "randomized" into one of the 3 study groups described below: the STI PPT group, the doxyPEP group, or the standard of care group. Randomization means that you are put into one of the groups by a computer program that does this by chance and without knowing in advance which group will be selected. Regardless of which group you are assigned to, you will receive treatment if you present to the clinic with STI symptoms at any time.

- **If you are in the STI PPT group**, you will receive directly observed treatment with the antibiotic cefixime (400 mg, 1 oral tablet) and the antibiotic azithromycin (1 gram, 1 oral tablet) every 3 months until study completion.
- **If you are in the doxyPEP group**, you will be provided with a supply of the antibiotic doxycycline. You will be asked to take two doxycycline pills within 24 hours, and no later than 72 hours, after sex without a condom. You can take up to two pills a day but no more than that. Refills will be provided to you throughout the study.
- **If you are in the standard of care group**, you will receive the standard of care in Kenya, which is treatment provided if you present to the clinic with STI symptoms at any time.

Other enrollment visit procedures
If you choose to take part, we will do the following at the enrollment visit:

- We will collect information including your name, phone number, and other contact information so that we can locate you if we need to.
- Additionally, we will ask to take your digital fingerprint scan to allow us to confirm your identity at study visits without using your name or other identifiers. This scan will also help prevent mistakes

whereby our staff enroll you twice and help in the event that you need to move to a different study site.

- You will be asked to complete a brief survey lasting 50-60 minutes on a tablet computer.
  - This survey will include questions about your age, gender identity, sexual behavior, STI symptoms, antibiotic use, substance use, and mental health.
- You will see a study doctor, who will do the following:
  - Ask if you have any symptoms of an STI, such as pain or discharge with urination, throat pain, rectal pain or discharge, genital lesions, or a rash.
  - Ask if you have any symptoms that can be associated with taking cefixime, azithromycin, or doxycycline.
  - Perform a focused physical examination depending on your symptoms.
  - Collect two swabs of your throat and two swabs of your rectum.
  - Ask you to provide a urine sample.
  - Draw 10 milliliters (2 teaspoons) of blood for syphilis testing.
  - Provide treatment according to Kenyan guidelines for any STI symptoms you have (standard of care).
  - Link you to programmatic HIV testing and prevention services if you are HIV negative and HIV care if you are HIV positive, according to Kenyan guidelines (standard of care). The program can also offer you condoms, lubricants and counseling about how to reduce your STI risk.
- If you participate in our programmatic HIV prevention and care services, we will ask your permission to link your program clinic record to this study.
- If you have symptoms between scheduled visits, such as a sore throat, discharge from your penis, burning when you urinate, or rectal pain or discharge, you will be asked to come to the research site for sample collection to test for possible STI.
- If your blood test is positive for syphilis, you will be contacted so you can come to the clinic and receive treatment.

Contact during the study

During the study, research staff may contact you by SMS to remind you of study visits. If you miss a study visit or have a positive syphilis test needing treatment, we will contact you by phone or SMS. If we cannot reach you, we will send a study staff to find you at the address provided to us. We may also contact you to follow up on any adverse event you report. After the study, research staff may contact you to provide information on future studies that may interest you.

During each study follow-up visit

You will undergo the following procedures:

- You will be asked to complete a brief survey lasting 30-45 minutes on a tablet computer with questions about your sexual behavior, STI symptoms, antibiotic use, substance use, and mental health since the last visit.
- You will be asked your opinion about the STI control intervention you are assigned to.
- You will see a study doctor, who will do the following:
  - Ask if you have any symptoms of an STI, such as pain or discharge with urination, throat pain, rectal pain or discharge, genital lesions, or a rash.
  - Ask if you have any symptoms that can be associated with taking cefixime, azithromycin, or doxycycline.

  - Perform a focused physical examination depending on your symptoms.
  - Collect two swabs of your throat, two swabs of your rectum, and a small sample of hair (approximately 20 hairs from the back of the head).
  - Ask you to provide a urine sample.
  - Draw 10 milliliters (2 teaspoons) of blood for syphilis testing.
  - Provide treatment according to Kenyan guidelines for any STI symptoms you have (standard of care).
  - Link you to programmatic HIV testing and prevention services if you are HIV negative and HIV care if you are HIV positive, according to Kenyan guidelines (standard of care). The program can also offer you condoms, lubricants and counseling about how to reduce your STI risk.
- If you have symptoms between scheduled visits, such as a sore throat, discharge from your penis, burning when you urinate, or rectal pain or discharge, you will be asked to come to the research site for sample collection to test for possible STI.
- If your blood test is positive for syphilis, you will be contacted so you can come to the clinic and receive treatment.

Timing of study visits and procedures:
- The initial enrollment visit will take approximately 90-120 minutes.
- Scheduled follow-up visits every 3 months will take approximately 60-90 minutes.
- Interim visits for symptom evaluation or for treatment of syphilis, when needed, will take approximately 15-30 minutes.

Study location
All study procedures will be carried out at research clinics in Kisumu (the Anza Mapema clinic), Nairobi (the SWOP City clinic), or Mombasa (the University of Washington/ University of Nairobi clinic at Ganjoni Municipal Clinic). We will ask that you continue at the site where you enrolled. However, if you need to move during the study, we can transfer you to a different study clinic if you request this.

Can I stop being in the study?
Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. It is important to tell the study doctor if you are thinking about stopping, in order to discuss what follow-up care and testing could be most helpful for you. The study doctor may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

ARE THERE ANY RISKS, HARMS, OR DISCOMFORTS ASSOCIATED WITH THIS STUDY?
Medical research has the potential to introduce psychological, social, emotional, and physical risks. Efforts are always put in place to minimize the risks. One potential risk of being in this study is loss of privacy. For example, because you will receive SMS messages to remind you of clinic visits, it is possible that someone else who has access to your phone may see these messages, revealing your participation in the study. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records for this study in a locked file cabinet in a locked room. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in the study and could find out information about you.

Answering questions in the computer-assisted survey may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the survey or any questions asked during the survey. It may be embarrassing for you to have a physical examination to evaluate possible STI symptoms or to have rectal swabs or urine specimens collected. You may feel some discomfort when blood is drawn or when throat or rectal swabs are collected. We will do everything we can to ensure your privacy and minimize discomfort. After a blood draw, you may have a small bruise or swelling where the blood was drawn. In case of an injury, illness or complications related to this study, contact the study team right away at the numbers provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

If you are assigned to one of the two interventions, the risks include side effects of the medications provided, such as:

- Doxycycline, cefixime, and azithromycin can all cause nausea, vomiting, diarrhea, headache, flatulence, rash, and yeast infections.
- Doxycycline may cause irritation of the esophagus, increased skin sensitivity to the sun, and rash.
- Azithromycin may cause increased sun-sensitivity, palpitations, dizziness, and hepatitis.
- Cefixime may cause jaundice, hepatitis, and dizziness.
- All antibiotics may cause rare but serious reactions, including serious allergic reactions and breathing problems (called “anaphylaxis”), severe skin rash, headache caused by elevated pressure in the brain, inflammation of the heart or pancreas, and decreases in blood cells (white cells, red cells or platelets). If you have a history of such reactions to doxycycline, cefixime, or azithromycin, you should not participate in this study.

Unknown risks: You will be assigned to one of the study groups by chance, and the intervention to which you are assigned may prove to be less effective at reducing STI burden than the other groups or may lead to more side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

ARE THERE ANY BENEFITS OF BEING IN THIS STUDY?

You may benefit from participating in the study by receiving regular physical exams, free syphilis testing, and counselling about STI prevention. If you are assigned to the PPT group, there is evidence that this intervention reduced the burden of STI in a study of female sex workers in Kenya. If you are assigned to the doxyPEP group, there is evidence that these interventions reduced the chances of getting an STI in studies of GBMSM in the United States and France.

Regardless of which group you are assigned to, the information you provide will help us better understand how to reduce the burden of STI among GBMSM in Kenya. This is a contribution to science and will help inform health policy for GBMSM in Kenya and similar resource-limited settings.

WILL BEING IN THE STUDY COST ANYTHING?

There is no cost for you to be in this study. We will provide a reimbursement of 1,000 Kenya shillings to help offset your cost of attending each study visit in terms of time and transportation.

WHO WILL HAVE ACCESS TO THE INFORMATION I GIVE?

In all cases, the knowledge gained from this research will be shared in summary form, without revealing individuals’ identities. We will not publish or discuss in public anything that could identify you. Study monitoring and regulatory staff may review this to make sure that study procedures are

being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm. In future, information collected or generated during this study may be used to support new research related to STI control.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you tell the study team if you feel that you have been injured because of taking part in this study. Please report any injuries or problems to the study staff or contact the study doctor in charge of your site: Dr. Eduard Sanders (+254-723-593762, Mombasa), or Dr. Fredrick Otieno (+254-721-759867, Kisumu), or Dr. Joshua Kimani (+254-733-719711, Nairobi). Our clinic teams will provide immediate care at the clinic and refer you for additional medical or psychosocial care as needed.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you, and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your regular medical care from the clinics at our research site or from other local clinics outside of this study. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study as soon as possible.

WHAT IF YOU HAVE QUESTIONS IN THE FUTURE?
If you have further questions or concerns about participating in this study, you can talk to the study doctor in charge of your site: Dr. Eduard Sanders (+254-723-593762, Mombasa), or Dr. Fredrick Otieno (+254-721-759867, Kisumu), or Dr. Joshua Kimani +254 715 684509, Nairobi).

For more information about your rights as a research participant you may contact: The Committee Chairperson, KEMRI Scientific and Ethics Review Unit, P. O. Box 54840-00200, Nairobi; Telephone numbers: 020-2722541, 0717719477; Email address: seru@kemri.org. The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

A description of this clinical trial will be available on https://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. In addition, a description of this clinical trial will be available on https://pactr.samrc.ac.za/, as required by Kenyan law.

WHAT ARE MY OTHER CHOICES?
Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits. If you decline participation or withdraw, you will still receive standard of care for HIV and other STI as you usually would.

HOW WILL MY SPECIMENS AND INFORMATION BE USED?
Researchers will use your specimens and information to conduct this study. Once the study is done using your specimens and information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this “de-identified” information, which cannot be used to harm you.

SHARING YOUR INFORMATION.

The National Institutes of Health (NIH) has developed data (information) banks that collect study data. The NIH will store your de-identified information in these data banks for other researchers to use in future studies on any topic. The researchers could be from government, academic, or commercial institutions. You will not receive any results from allowing your data to be placed in the NIH data banks. You will not be able to withdraw your information after it has been submitted to the NIH data banks.

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STATEMENT OF CONSENT

Participant's statement
I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study staff. I have had all my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study:	**Yes**	**No**	
I agree to provide contact information for follow-up:	Yes	No	
I agree to have my fingerprint scanned to help identify me for the research:		Yes	No
I agree to have my samples and data preserved for later study:	Yes	No	
I agree to link my program clinical records to this study:	Yes	No	
I agree to have my samples shipped to Seattle, USA for analysis:	Yes	No	

Participant printed name: _____

Participant signature / Thumb stamp _____ Date _____

Researcher's statement
I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his consent.

Researcher's Name: _____ Date: _____

Signature _____

Role in the study: _____ ***[i.e. study staff who explained informed consent form.]***

Witness (If necessary, a witness is a person mutually acceptable to both the researcher and participant)

Witness's Name _____

Contact information _____

Signature /Thumb stamp: _____ Date: _____