Official Title:

Improving Neonatal Health Through Rapid Malaria Testing in Early Pregnancy With High-Sensitivity

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Consent to Participate in a Research Study - ADULT
Improving Neonatal health Through Rapid malaria testing in Early Pregnancy with high-sensitivity Diagnostics (INTREPiD) study
Version 2.0; Protocol version date: 26Jan2024

CONCISE SUMMARY

The purpose of this research study is to test if screening and treating women for malaria in the first trimester of pregnancy improves their pregnancy outcomes. We are seeking your consent to participate, and participation is completely voluntary. The alternative to participation is to receive your routine antenatal care from your usual providers.

Participants in this study will either receive normal antenatal care or undergo a single test for malaria in the first trimester, followed by normal antenatal care. If the test is positive, you will be treated with an antimalarial medication, called Artemether-Lumefantrine. This medicine is approved to treat malaria. After this, all participants will return to normal antenatal care, although we will continue to collect at each visit information and a blood sample by fingerprick from everyone. We will follow-up with you until 1 month after your baby is born.

There are some risks to the study, including discomfort from fingerprick blood sampling as well as those from antimalarial treatment, including headache, loss of appetite, dizziness, and low energy. There may be benefit to you or your baby by detecting and treating malaria in pregnancy.

If you are interested to possibly participate in this research study, please continue reading below.

You are being asked to take part in this research study because you are pregnant and at risk of malaria infection. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

A grant from the National Institutes of Health (NIH) of the United States will sponsor this study. Portions of ***Dr Tshefu/Laktabai*** and his/her research team's salaries will be paid by this grant.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, ***Dr Tshefu/Laktabai*** will be your doctor for the study and if needed will be in contact with your regular health care provider throughout the time that you are in the study.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to test if we can improve pregnancy outcomes by testing women in the first 3 months (1st trimester) for malaria parasites and treating the women who are infected.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 2500 people will take part in this study at several different hospitals and clinics.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign and date or mark this consent form. You will also need to remain in the local area for the duration of your pregnancy and be willing to deliver your baby at a study-associated health facility. You will have the following tests and procedures to make sure that you are eligible:

- Physical exam, including height and weight
- Medical history, including medications
- Vital signs
- Fetal ultrasound, an imaging test that uses sound waves to see an image of your baby

If this information confirms that you are eligible, you will be enrolled in the study and then randomly assigned (like the flip of a coin) to receive either usual antenatal care (standard of care) or testing with a rapid diagnostic test for malaria parasites. You have a 1 in 2 chance of receiving the malaria test.

If you are randomized to testing, we will immediately perform in the clinic a test of blood (approximately 0.5mL) collected by fingerprick for malaria parasites. If after a few minutes the result is positive, then you will be immediately treated by mouth with the combination antimalarial Artemether-Lumefantrine, a medicine that is approved to treat malaria. You will then be returned to usual antenatal care. If you are not randomized to testing, we will collect a blood sample by fingerprick and you will simply return to antenatal care.

After return to antenatal care, we will collect the following at each routine antenatal care and sick visit:

- Interval history and brief physical exam, including height and weight
- Medications, including any new allergies
- Vital signs
- Fingerprick blood, approximately 0.5 mL

At the conclusion of your pregnancy, and at 1 week and approximately 1 month after birth, we will collect information about you and the baby, and perform a brief physical exam of the baby. No other procedures will be performed on your baby.

HOW LONG WILL I BE IN THIS STUDY?
You will remain in the study until 4 weeks after delivery. You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE RISKS OF THE STUDY?
As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

Risks associated with drawing blood from your finger include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Artemether-Lumefantrine may cause some, all or none of the side-effects listed below.

More likely

- Headache
- Loss of appetite

Less likely

- Vomiting
- Irregular heartbeat

- Dizziness
- Low energy
- Muscle of joint pains
- Nausea
- Fever or chills
- Abdominal pain
- Fatigue
- Enlarged spleen or liver
- Diarrhea
- Cough
- Low blood counts
- Difficulty sleeping
- Itching
- Rash

There is no evidence among women who receive Artemether-Lumefantrine in the 1st, 2nd, or 3rd trimester of an increased risk of major birth defects, miscarriage, or adverse fetal outcomes. There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be direct medical benefit to you or your baby, by detecting and treating malaria early in pregnancy. We hope that in the future the information learned from this study will benefit other pregnant women and their babies who live in places with malaria.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
If you do not want to participate in this study, you can still access usual antenatal care from your regular providers.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, ultrasound, and procedures may be reported to the US NIH and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives and affiliates of the Duke Clinical Research Institute, Duke University, the Kinshasa School of Public Health/Moi University, and their ethical review boards, and the US NIH. If any of these groups review your research record, they may also need to review your entire medical record.

The US Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or

3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the Food and Drug Administration (FDA).

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

All of the blood and ultrasound studies are being done only because you are in this study. The study results will not be provided to you OR sent to your physician.

The study results will be retained in your research record forever. Any research information in your medical record may also be kept indefinitely.

This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations.

If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed. 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.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of the study, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS TO YOU?
There will be no additional costs to you for participation in this study.

WHAT ABOUT COMPENSATION?
There will be no money or compensation for your participation in this study.

WHAT ABOUT RESEARCH RELATED INJURIES?

Immediate necessary medical care is available at your district hospital in the event that you experience an injury related to research participation. However, there is no commitment by the Kinshasa School of Public Health/Moi University, Duke University through its Duke Clinical Research Institute, or the NIH to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact the study team at the telephone number below during any time.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at your antenatal clinic. If you do decide to withdraw, we ask that you contact the study team at the telephone number below to inform them of your decision. You will be asked to continue to attend usual antenatal care clinic visits.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. If this occurs, you will be notified and your study doctor will discuss other options with you.

WHAT WILL BLOOD SAMPLES BE USED FOR?

During the course of this study, we will collect blood by fingerprick at each antenatal visit and at delivery from you and from your placenta at delivery. These samples will be used for malaria parasite testing at a later date.

After testing, the samples can be stored for other research purposes that are not yet known. We would not use these samples for other purposes without approval by an institutional review or ethics board, and the samples will remain under the authority of ***Dr Tshefu/Laktabai***, which means that she/he will have to give approval for any future use of the samples. The use of your data and samples may result in commercial profit. You will not be compensated for the use of your data and samples other than what is described in this consent form. We hope that future uses would help us better protect pregnancies and babies.

If you agree to allow your blood samples to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. We

ask that you contact the study team at the number below. At that time we will ask you to indicate if you want the unused identifiable blood samples destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

Do you agree to allow storage of your samples for future unspecified research?

□ Yes, I agree □ No, I do not agree _____
Initial or Mark

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, or if you choose to withdraw from the study, contact the study team of ***Dr Tshefu/Laktabai*** at XXX-XXX-XXXX.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the

- Moi University Institutional Research Ethics Committee (IREC) at +254 078 772 3677
  OR
- Kinshasa School of Public Health Institutional Review Board at XXXXX

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study or to allow my dependent to be in this trial, with the understanding that I/she may withdraw at any time. I have been told that I will be given a signed or marked and dated copy of this consent form."

_____ _____ _____
Signature or Mark of Subject or Legal Guardian Date Time

_____
Printed Name of Subject or Legal Guardian

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent

_____	_____	_____
Signature of Witness (if applicable)	Date	Time

_____
Printed Name of Witness (if applicable)