



Hypertension in Africa
Research Team

INFORMED CONSENT FORM FOR THE African-PREDICT STUDY (RESEARCH PHASE):

TITLE OF THE RESEARCH PROJECT: African Prospective study on the Early Detection and Identification of Cardiovascular disease and HyperTension (African-PREDICT)

ETHICS REFERENCE NUMBER: NWU-00001-12-A1

PRINCIPAL INVESTIGATOR: Prof. Carina Mels (PhD)

Prof. Mels and the research team have the expertise and interest in Cardiovascular Physiology, namely to understand the biological processes in humans when high blood pressure and heart disease develop.

ADDRESS: NORTH-WEST UNIVERSITY (Potchefstroom Campus); Hypertension in Africa Research Team (HART); Hypertension Research and Training Clinic Building F12.

CONTACT NUMBERS: 018 299 1983 / 018 285 2466 / 018 299 2780

You are invited to take part in the follow-up phase of the African-PREDICT research study. Please take some time to read the information presented here, which will explain the details of this study. Please ask the researcher or person explaining the research to you any questions about any part of this study that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research is about and how you might be involved. Also, your participation is **entirely voluntary** and you are free to say no to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part now.

This study has been approved by the Health Research Ethics Committee of the Faculty of Health Sciences of the North-West University (NWU-00001-12-A1) and will be conducted according to the ethical guidelines and principles of Ethics in Health Research: Principles, Processes and Structures (DoH, 2015) and other international ethical guidelines applicable to this study. It might be necessary for the research ethics committee members or other relevant people to inspect the research records.



What is this research study all about?

You will know already from taking part in the screening phase of the study that heart disease and especially high blood pressure (or hypertension) is a big problem in South Africa. Also, many people are unaware of it, as it has no symptoms. High blood pressure is a very important risk factor which may result in heart disease, kidney disease and stroke. (*When blood stops flowing to the heart, this can cause a heart attack and part of the heart dies. A stroke is when there is a problem with the blood supply to the brain and a part of the brain is damaged.*) That is why many people in South Africa suffer from these diseases resulting in death.

Since heart disease is mostly seen in older people, the purpose of this study is to include and focus on young healthy people to understand how high blood pressure and heart disease develop. It is believed that our lifestyle (e.g. what we eat, drink, and do) may have an impact on whether we will develop high blood pressure and heart disease. Also, it is not well known whether there are perhaps certain measurements (e.g. in your blood or urine) that may predict whether you will develop heart disease when you are older.

The aim of this study is therefore to determine how high blood pressure and heart disease develop in a group of 1200 healthy young South Africans living in and around Potchefstroom, by tracking everyone over 5-20 years. It is therefore of great importance that we take detailed measurements of your lifestyle, and your current health (e.g. heart, blood vessels, eyes, blood and urine). These measurements will be made at the beginning of the study, but it will be most important to repeat these measurements in following visits every 5 years, to see how these health measurements have changed. We expect that some participants will remain healthy with normal blood pressures, and other will develop high blood pressure. Only by tracking the changes in blood pressures and other detailed measurements will be able to understand the influences of e.g. lifestyle on changes in blood pressure.

If your results show that a certain measurement predicts that high blood pressure will develop later in life, this information could help doctors and nurses to prevent more people in the local community having strokes and heart attacks in the future.



Why have you been invited to participate?

You were invited to participate in the baseline measurements of the African-PREDICT research study. Based on the inclusion of healthy participants aged between 20 to 30 years of age, you have now been contacted to have the same measurements conducted as with your previous appointment.

It is very important for us to be able to keep in touch with you. We kindly ask that you **tell us about any changes of your contact details** (address, telephone number, email address etc.).



What will be expected of you?

The research team will make an appointment with you, and if necessary, transport and accommodation will be provided to bring you to the Hypertension Clinic (Building F12) on the Potchefstroom Campus of the North-West University. Such an appointment will be made for early in the morning, as the measurements will start at approximately 08:00, and in total will take about 5 hours to complete.

To make sure that your results are valid and useful, it is important to take note of the following:

1. The **evening before** – **Do not eat or drink anything except water after 10pm** or before you come to the clinic in the morning.
2. **On the study day, please wear comfortable clothing** such as trousers and a top that can be easily removed for the tests (please avoid wearing skirts, dresses or tights as we will need to access your bare foot and put a blood pressure cuff around your thigh over your trousers).
3. **Please bring with you:**
 - All medication you currently are taking
 - Your ID document & clinic card/book
 - Some good quality sunglasses to protect your eyes after the measurements
4. Let us know if transport and accommodation should be arranged for you.

If you are happy to participate, we will ask you to sign this consent form stating that you are volunteering to participate in this follow-up measurements and that you understand all the procedures that will be performed. You are free to contact us with any questions should there be any uncertainty about any of the information

provided. Then we will take the measures listed in the table below. Tests will be done in the Hypertension Clinic and we will provide you with a meal during the day. You will not be able to bath or shower for 24 hours after your clinic appointment due to the equipment you will be wearing when you leave the clinic.

WHAT TESTS WILL BE DONE?

- **Body composition:** we will measure your height, weight, waist, hip and neck circumference in a private room, while you are wearing your underwear. In another room, while you are clothed and lying down on a bed, we will also measure your body fat percentage by using a device that connects with sensors on your hand and on your foot. This is a completely painless procedure. (the measurements should take about 20 minutes to complete).
- **Biological samples:** early in the morning while you are lying down on a bed, a research nurse will take a blood sample (100 ml) from a vein in your arm by using standard clinical procedures. (10-20 min) We will also ask you to provide a urine sample in the morning, in a private restroom. We will kindly request that you collect your urine over the next 24 hours (we will give you the containers and detailed instructions for this) starting on the day of participation. These urine and blood samples will be used to test for genetic and a detailed range of biochemical markers (biomarkers) related to high blood pressure, heart disease and diabetes, such as glucose, cholesterol and markers of inflammation. You are more likely to have high blood pressure if one of your parents or a close family member has high blood pressure. This is because high blood pressure can be caused by differences in our genes. Our genes are like a very complicated "manual" in each of our cells that tells the body how to work properly. When there are changes in the genes, it changes the "manual" and the body then does not work as well as it should for example causing high blood pressure. We share our genes with our family because half of the gene "manual" comes from your mother and half from your father. Therefore, if they have high blood pressure due to differences in their genes then it is likely that you will get the same changes in your genes and develop high blood pressure. We would like to find out what these differences are in order to better understand how they cause high blood pressure so that we can find ways to stop it happening.
If due to some reason we are unable to take a blood sample on the research day, we will make another appointment with you on a convenient day to take the blood sample.
Take note that some of your samples may be stored for many years in freezers before we will analyse the samples. We may also need to ship some of your to other local or international expert laboratories for analyses.
- **Blood pressure:** while you are sitting down in a private room, we will measure blood pressure twice on both arms, by placing a cuff around your upper arm. (20 min) Another blood pressure measurement will also be done by placing a small blood pressure cuff around your finger, and upper arm, while you are lying on a bed. We will then test your blood pressure responses when you do a colour word reading test and when you place your hand in cold water for 1 minute. (30 min) At the end of the measurement day, we will fit a portable blood pressure monitor to you which will assess your blood pressure over the next 24 hours, thus over a day and when you are sleeping at night. It is important that the device is not removed during this time to ensure a reliable measurement.
- **Blood vessel & heart health:** in a private room we will again ask you to lie down comfortably on a bed. We will first test your blood pressure at your upper arm, with a device that will also measure the blood pressure at your heart. We will then test how stiff your blood vessels are by using a small pen-like device rested on your neck to register the pulse in your neck on a computer. At the same time another blood pressure cuff will be placed around your thigh. (15 min) Afterwards, in a semi-dark room we will use a sonar device (usually used during pregnancy) to take some sonar pictures and video clips of the blood vessels in your neck and of your heart on the bare chest. We will provide a blanket for cover. (20 min)
- **ECG (Electrocardiography test) for heart health:** while you are lying down on a bed in a private

room, we will test the natural electrical activity of your heart by placing several stickers with sensors on your chest, shoulders and hips. We will take care to ensure your privacy. (10 min)

- **Eye Pressure:** a research nurse will put some eye drops in both eyes and then she will measure the pressure in your eyes with a device that touches lightly on your eye. (10 min) This test will inform us whether you have a condition called glaucoma, which means that the pressure within your eyes are quite high. If so, we will advise you and refer you for necessary treatment. If the pressure is normal, we will continue with the next eye test as described below.
- **Ear temperature:** The tip of a handheld thermometer will be placed in your ear to measure body temperature. This is to ensure that no fever is present indicating a condition e.g. flu. This may influence results obtained.
- **Testing the small vessels of the eye:** a research nurse will put an eye drop in one eye, and a researcher will ask you to look into a special camera, named a fundoscope. This is the same device used by ophthalmologists (eye doctors). This camera will shine a light into your eye and we will take some pictures of the small blood vessels at the back of your eye (there will be a camera-like flash). We will also check how well your small blood vessels respond to light flickering, by doing a light-flicker test with this special camera. (20-30 min) This test cannot be performed if you suffer from epilepsy/fits.
- **Physical activity:** a researcher will place a small monitor on your chest using stickers that will record your activity and movement levels for 4 days minimum. No pain or discomfort is associated with this device, and you are kindly requested not to remove the device before the 4 day measurements were completed.
- **HIV test:** As this test was done during the screening phase as well as baseline measurements, we will test again for HIV each follow-up visit.
- **Questionnaires:** during the course of the morning, you will be asked to complete several questionnaires with the help of a researcher. These include a general health questionnaires (with questions about your age, family history of disease, education, occupation, lifestyle habits, 15 min), Berlin sleep questionnaire (asking questions about how well you sleep, 5 min), physical activity questionnaire (to report on how active your lifestyle is, 5 min), dietary questionnaire (with the help of a dietician you will be asked what you ate during the past day (30 min). Within the next week the dietician will contact you again on two occasions to complete the questionnaire again. This should give us the best reflection on your eating habits). Finally, a trained psychology intern will help you to complete a number of questionnaires on your personal well-being (including questions on stress and how well you cope with stress, 30-45 min).



Will you gain anything from taking part in this research?

- You will receive direct feedback during each advanced measurement on your health status. All of these advanced clinic tests are provided to you at no cost (worth ±R5 000).
- Should any abnormalities be detected, we will refer you to doctors, clinics or hospitals for further tests or treatment and the test results may assist your doctor in making decisions about further treatment.
- Apart from this personal benefit, your research data will help biomedical health researchers to gain a better understanding on how high blood pressure and heart disease develops, and may help us to develop better programmes to prevent or treat these diseases in our community and elsewhere. The data may also be used to advise the Ministry of Health on changes to the health system that may benefit the broader South Africa.



Are there risks involved in you taking part in this research and what will be done to prevent them?

To help you with a better understanding of the potential risks, and what we are doing to prevent these, please refer to the table below:

Risks	Precautions
<ul style="list-style-type: none"> • Taking a blood sample at a vein in the upper arm, may cause some pain and discomfort; • Applying an eye drop may cause a slight burning sensation; • Performing the eye pressure test is slightly uncomfortable; • Performing a light flicker test may also be slightly uncomfortable. • After the eye measurement some discomfort may be experienced (similar to a visit to an eye doctor) while waiting for the pupil to constrict. • Placing the hand in an ice water bucket for 1 minute may cause some pain in your hand. • You may experience some discomfort when having to undress for the body measurements or heart sonar measurements. • When you complete the psychological questionnaires you may feel uncomfortable when giving personal information, such as feeling depressed or stressed. • All health measurements may cause some anxiety when you are worried about the results of the tests. • If a health abnormality is identified, others may become aware of this private information, e.g. diabetes. 	<ul style="list-style-type: none"> • A trained registered research nurse performs all blood sampling and regularly undergo training on clinical measurements. • She also performs the eye pressure test and applies the eye drop. To ensure correct procedures and minimum participant discomfort she has undergone training at an eye doctor to ensure that she use the safest techniques to make the measurement quickly and correctly. The light flicker test may cause discomfort but the researcher is highly experienced and ensures that the measurement is done quickly and accurately. It does not cause any long term harm and is comparable to standard eye doctor measures. Afterwards, when the pupil is dilated, the eye is sensitive to light. Therefore an eye patch is provided and all lights of the clinic turned off when these assessments start (at the end of the day's measurements). You are also encouraged to bring sunglasses for when you leave the clinic. We also provide transport to you after we are finished as you are not encouraged to drive if your eye has not yet returned to normal. • Placing the hand in ice water causes some pain due to the very cold water. The time is only for 1 minute to reduce discomfort to a minimum, and a small electric blanket or hot water bottle is provided afterwards to heat up the hand and ensure comfort. • All measurements are done in private temperature controlled rooms. All staff are also trained in these aspects to be highly professional and discreet and to ensure maximum comfort and to avoid any embarrassment. For heart sonars, an expert clinical technologist has vast experience in performing the sonars in a semi-dark room and also provides a blanket to ensure privacy. • For psychological questionnaires a psychology intern is well trained to complete the questionnaires in a private area. All necessary aspects are adhered to make sure it is done in a professional and comfortable manner. If any abnormality is detected, the psychologist informs the research nurse, who will then privately discuss the results with you. • For other health measurements, such blood pressure, the results may be stressful. We will therefor provide you with the information privately and if we note something abnormal, we will ensure that you are referred appropriately for further tests or treatment. • If any health abnormalities were identified, you will meet individually with the research nurse in a private room for a feedback session. She will explain your results to you and provide you with a letter of referral for further testing or treatment. This will also be placed in a sealed envelope.

<ul style="list-style-type: none"> As measurements take place during the working week you may suffer from a loss of income, or may get into trouble for not being at work due to time spent in the project. 	<ul style="list-style-type: none"> If you will lose wages due to your participation in the study, you need to inform the research nurse, who will make sure that communication is taken up with your employer. We will normally discuss your participation with your employer beforehand to make sure there won't be any loss in income. Once your employer agrees that you can attend the study during normal working hours without having to take leave or lose any wages, you can join the study.
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There are more gains for you in joining this study than there are risks.



How will we protect your confidentiality and who will see your findings?

Anonymity of your findings will be protected by all of the researchers involved. A number, and not your name, will be assigned to your research results, and all scientists using your data will only note this number, and not your name. Your privacy will be respected by making sure that all the measurements are taken in private rooms and performed by well-trained scientists. Your results will be kept confidential by storing hard copies of your documentation in a locked cupboard within the Hypertension Clinic, and only the Principal Investigator, Head of the Hypertension Clinic and Data Manager having direct access. Electronic files with data are stored and handled by the Data Manager in a password protected online database using the University web-network (with firewall and security features), as well as some backup files on external password protected harddrives. Only the researchers, their postgraduate students and local and international collaborators will be able to look at your findings – however, all findings will be anonymised using your unique participant number. As this is a long term project, your data will be stored for 20 years or longer.



What will happen with the findings or samples?

As indicated above, your research results are safely stored on electronic files, with some results on hard copies, and in the form of blood or urine samples in biofreezers. We will store your data and your blood and urine samples for at least 30 years. Over time the research team will make sure that all of this information is analysed in the utmost detail to create new knowledge on how high blood pressure, heart disease, and related diseases develop over time. It is important to store the data and samples for a long period, as new scientific discoveries on markers of high blood pressure will be made by other scientists or ourselves in the future. It will then allow us to test if these markers are also useful in your (the South African) samples, and whether these can be used throughout South Africa in the future.

Some of your biological samples (from urine and blood) will be analysed immediately, but others will be stored for many years before analyses are performed. Please note that we will perform the biochemical analyses in our laboratories on the Potchefstroom Campus. But we may need to ship some of your samples to other laboratories in South Africa or internationally, when we do not have the funds, skills or the equipment to perform the analyses locally. Samples will be shipped using courier services approved for handling biological samples, to ensure the safekeeping and protection of the samples during transit. We will also ensure that the appropriate approvals from the South African Department of Health (export permit) and the Health Research Ethics Committee are obtained prior to shipping the samples.

Apart from your samples, your anonymised data may also be shared with other national or international collaborators. It is therefore possible that your anonymised results will be reported as stand alone data as part of the African-PREDICT study, or your data may be pooled into other datasets from the province, country or

globally in further research studies on high blood pressure and related health status. Your data will therefore be used to analyse your original state of blood pressure and health – in South Africa and in comparison to other local and international populations – and to analyse how your health status changes over time.

If we were to share your anonymised data or samples with external groups, the external groups will sign confidentiality and data or material transfer agreements with us. This process is overseen by the Legal Services of the North-West University. This will ensure that your information is adequately handled and protected, and that your data is only used for the intended purpose as described in the agreement.

It is also possible that your data may be useful for other purposes apart from the aim of the present study. When the data is to be used for such purposes, new applications will be submitted to the Health Research Ethics Committee, where the Committee will stand in on your behalf.

Findings from the study will be published in scientific journals, and discussed locally and internationally with scientific experts and the Department of Health.



How will you know about the results of this research?

During the course of the day you will receive direct feedback from each research station on your health status and findings. As described earlier, if any abnormalities are detected, a detailed report within a referral letter will be compiled by the research nurse and you will be directed to the appropriate healthcare provider. If at any stage (also after you have visited the clinic) you wish to know any of your research results, you are welcome to contact the researchers at the Hypertension Clinic.

The research team also intends to publish the research findings of the larger study in scientific literature, but also in local media, and perhaps also national media. This will not include you as an individual, but the collective findings of all the research participants. Furthermore, as this is a longitudinal study, the research team may provide you with further results of the study when you return to the clinic during follow-up measurements. As the research team will contact you annually to ensure that your contact details are still correct, we will inform you if any important research findings became apparent that you need to take note of.



Will you be paid to take part in this study and are there any costs for you?

No, you will not be paid to take part in the study, but the research team will provide you with a R300 gift voucher as a token of appreciation for your participation. We hope that the results of the measurements will be useful to you to understand your own health status.

We will provide transport to all participants, and a meal will be served during the course of the morning after you have given a blood sample.

There will thus be no costs involved for you, if you do take part in this study.

To cover all of the research expenses, this study is funded by several local and international funding bodies, including the Department of Science and Technology (National Research Foundation), Medical Research Council of South Africa and the Medical Research Council of the United Kingdom, as well as scientific grants from industry (GlaxoSmithKline, Pfizer, Boehringer-Ingelheim, Medi-Clinic Hospital Group).



Note* What happens after the study day?

At the end of the study, you may have one eye covered so it is advisable not to drive until you see that your eye has recovered, due to a possible loss of depth perception. You will know that the eye is fully recovered when the black part of the treated eye (pupil) has been reduced to a similar size as the pupil of the untreated eye. In the week following the study day, we will make **three short appointments** with you to collect the blood

pressure monitor, your urine collection and the activity monitor and to do two more short interviews (20-30 minutes) about your diet. We will give you a diary sheet so you can keep track of these appointments and they will be arranged to suit your schedule.



Is there anything else that you should know or do?

- You can contact Sr. Adele Burger (or Prof. Carina Mels) at 018 285 2076/1983 if you have any further questions or have any problems. You are also welcome to contact the clinic reception 018 2263/2446.
- You can also contact the Health Research Ethics Committee via Mrs Carolien van Zyl at 018 299 1206 or carolien.vanzyl@nwu.ac.za if you have any concerns that were not answered about the research or if you have complaints about the research.
- You will receive a copy of this information and consent form for your own purposes.

Address: Building F11, Potchefstroom Campus, North-West University, Potchefstroom 2520
Tel: 018-285 2261 (Office hours Mon-Fri) Fax: 018-285 2260; Email: adele.burger@nwu.ac.za

Declaration by participant

By signing below, I agree to take part in the research study titled: The African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African-PREDICT).

I declare that:

- I have read this information/it was explained to me by a trusted person in a language with which I am fluent and comfortable.
- The research was clearly explained to me.
- I have had a chance to ask questions to both the person getting the consent from me, as well as the researcher and all my questions have been answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be handled in a negative way if I do so.
- I may be asked to leave the study before it has finished, if the researcher feels it is in the best interest, or if I do not follow the study plan, as agreed to.

I agree that my blood or urine samples may be sent to laboratories in South Africa or in other countries for analyses (with my personal details removed, and only identifiable by an anonymous number).

Yes

No

Signed at (place) on (date) 20....

Signature of participant

Signature of witness

Declaration by person obtaining consent

I (name) declare that:

- I clearly and in detail explained the information in this document to
- I did not use an interpreter.
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above.
- I gave him/her time to discuss it with others if he/she wished to do so.

Signed at (place) on (date) 20....

Signature of person obtaining consent

Signature of witness

Declaration by researcher

I, *Catharina MC Mels*, declare that:

- I explained the information in this document to the Clinic Manager, Project Coordinator, Subject Specialist, and research assistants.
- I did not use an interpreter.
- I encouraged them to ask questions and took adequate time to answer them.

And that I was available should they want to ask any further questions.

- The informed consent was obtained by an independent person.
- I am satisfied that she adequately understands all aspects of the research, as described above.
- I am satisfied that she had time to discuss it with others if she wished to do so.

Signed at Potchefstroom on (*date*) 20....

Signature of researcher

Signature of witness