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# Metformin treatment for diabetes prevention in Africa

**Submission date**
08/03/2019

**Recruitment status**
No longer recruiting

**Registration date**
22/03/2019

**Overall study status**
Completed

**Last Edited**
18/07/2023

**Condition category**
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
The numbers of people with type 2 diabetes in Africa are rising rapidly. We are looking for ways to prevent people who have already have raised blood sugar (called prediabetes), from going on to develop diabetes.
We will test a drug called metformin in HIV infected persons with pre-diabetes to see what effect, if any, it has on blood glucose. If the drug is able to lower their blood sugar levels, and appears to be safe, we hope to go on to test whether the drug can stop or delay a person developing diabetes in a subsequent large trial. Metformin has been tested for this purpose in high-income countries countries, but not in Africa among those who are on HIV treatment. The study will be conducted in Tanzania.

Who can participate?
Adults over the age of 18, who are HIV-infected and have been stable on treatment for HIV-infection for a minimum of 6 months.

What does the study involve?
We will screen people in HIV treatment programmes to identify those who are prediabetic. If they agree to take part in the study, we will allocate them at random to one of two groups. The first group will receive a slow-release preparation of metformin which only needs to be taken once a day; and the second group will receive a placebo that looks like the metformin and also is taken once a day. Neither the patient or the doctors will know who is receiving the drug and who is receiving the placebo (this is called a randomised double-blind placebo-controlled trial). Each participant will be followed up for 12 months, and at the end we will assess blood sugar levels in those who received metformin compared to those who received the placebo.

What are the possible benefits and risks of participating?
The benefits of participating are that the study will provide information on a possible prevention strategy for those that are at risk of developing diabetes. There are risks associated with taking metformin. A proportion of people who take this drug experience side effects, particularly of the gastro-intestinal system like nausea, abdominal pain, vomiting and diarrhoea, although these

symptoms should decrease with time. There are also more serious side effects like the development of a condition calls lactic acidosis, but is very rare and unlikely to occur. We will be monitoring the study closely.

Where is the study run from?
From 4 hospitals in Dar es Salaam, the Hindu Mandal Hospital, Amana Hospital, Temeke Regional Referral Hospital, and Mwanyanamala Hospital. All are in Tanzania

When is the study starting and how long is it expected to run for?
April 2019 to October 2021

Who is funding the study?
The National Institute for Health Research (NIHR).

Who is the main contact?
Prof Shabbar Jaffar at LSTM (Shabbar.jaffar@lstmed.ac.uk).

# Contact information

### Type(s)
Scientific

### Contact name
Prof Shabbar Jaffar

### ORCID ID
https://orcid.org/0000-0002-9615-1588

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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
Protocol version 14

# Study information

## Scientific Title
A randomised placebo-controlled double-blind phase II trial to determine the effects of metformin versus placebo on glycaemia in HIV-infected persons with pre-diabetes in Tanzania.

## Acronym
META

## Study objectives
Metformin significantly reduces progression to diabetes in prediabetic HIV infected persons on antiretroviral therapy compared to Placebo.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Liverpool School of Tropical Medicine (LSTM) Research Ethics Committee; reference (17-078)
National Institute of Medical Research and the Ministry of Health, Community Development, Gender, Elderly and Children.
Tanzania Food and Drug Authority

## Study design
Randomised placebo-controlled double-blind trial.

## Primary study design
Interventional

## Study type(s)
Prevention

## Health condition(s) or problem(s) studied
Prediabetes in person who are on HIV treatment

## Interventions
The intervention will be Metformin hydrochloride slow-release preparation, 2000 mg per day, compared with a matching placebo. The treatment will only be taken once a day. Participants who are HIV infected and on treatment, found to be prediabetic on screening, will be randomised using permuted block randomisation with varying block sizes chosen at random using the SAS software.

## Intervention Type
Drug

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
Metformin hydrochloride, slow release preparation

## Primary outcome(s)
Glycaemia at 12 months as ascertained by the oral glucose tolerance test.

### Key secondary outcome(s))
Current secondary outcome measures as of 20/05/2020:
1. Changes in glycaemia from baseline as ascertained by the oral glucose tolerance test at 6 and 12 months
2. Incidence of adverse events assessed using patient notes at 12 months
3. Rates of retention in care assessed using patient notes at 12 months
4. Estimated adherence to study drugs assessed using patient notes at 12 months

Previous secondary outcome measures:
1. Changes in glycaemia from baseline as ascertained by the oral glucose tolerance test
2. Incidence of adverse events assessed using patient notes at 12 months
3. Rates of retention in care assessed using patient notes at 12 months
4. Estimated adherence to study drugs assessed using patient notes at 12 months

### Completion date
26/10/2021

## Eligibility

### Key inclusion criteria
1. HIV-positive on antiretroviral therapy (ART) for at least 6 months and considered stable on treatment (i.e. in regular attendance for care).
2. BMI>30 combined with either impaired fasting glucose (6.1 to 6.9 mmol/L) and/or impaired glucose tolerance at 2 hours (7.0 to 11.10 mmol/L)
3. BMI<=30 combined with either impaired fasting glucose (6.3 to 6.9 mmol/L) and/or impaired glucose tolerance at 2 hours (9.0 to 11.10 mmol/L)
4. Planning to remain in the area for > 6-months
5. Written informed consent

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
All

### Total final enrolment
364

### Key exclusion criteria
1. Pregnant women
2. Renal disease or renal dysfunction (eGFR<45)
3. Signs and symptoms of any form of acute metabolic acidosis including lactic acidosis and diabetic ketoacidosis
4. Other acute conditions with:

4.1 the potential to alter renal function including: dehydration, severe infection or shock
4.2 the potential to cause tissue hypoxia including decompensated heart failure, respiratory failure, recent myocardial infarction, shock
5. Congestive heart failure requiring pharmacological treatment
6. Clinical evidence of liver disease
7. Evidence of alcoholism or acute alcohol intoxication
8. Known hypersensitivity to metformin or any excipients associated with the preparation (in this case: Magnesium stearate, sodium carboxymethylcellulose, hypromellose)
9. Other acute conditions requiring hospital admission.

### Date of first enrolment
05/11/2019

### Date of final enrolment
24/07/2020

## Locations

### Countries of recruitment
Tanzania

### Study participating centre
**Hindu Mandal Hospital**
Chusi Street
Dar es Salaam
Tanzania
-

### Study participating centre
**Amana Hospital**
Uhuru Street
Dar es Salaam
Tanzania
-

### Study participating centre
**Temeke Regional Referral Hospital**
Temeke Street
Dar es Salaam
Tanzania
-

### Study participating centre

**Mwanyanamala Hospital**
61665 Kinondoni
Dar es Salaam
Tanzania
-

# Sponsor information

**Organisation**
Liverpool School of Tropical Medicine

**ROR**
https://ror.org/03svjbs84

# Funder(s)

**Funder type**
Government

**Funder Name**
National Institute for Health Research

**Alternative Name(s)**
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

**Individual participant data (IPD) sharing plan**
The current data sharing plans for this study are unknown and will be available at a later date

**IPD sharing plan summary**
Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 18/07/2023 | 18/07/2023 | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |