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Artificial intelligence-supported diabetic retinopathy (a complication of diabetes, caused by high blood sugar levels damaging the back of the eye) screening in Tanzania

Submission date
01/03/2023

Recruitment status
No longer recruiting

Registration date
02/03/2023

Overall study status
Completed

Last Edited
04/04/2024

Condition category
Eye Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Diabetes is an increasingly important public health problem. The latest estimates are that Tanzania has the highest age-adjusted prevalence of diabetes in Africa. Diabetic retinopathy is a common eye complication of diabetes and can lead to blindness if it is not detected and treated. As diabetic retinopathy typically has no symptoms until it is at an advanced stage screening is recommended to detect and refer people with the disease for assessment and treatment. Screening is done by taking photographs of the retina (back of the eye) which can then be reviewed by appropriately trained staff to determine whether the patient needs to be reviewed by an ophthalmologist (eye doctor).

Screening for diabetic retinopathy, using retinal photography, has been undertaken in the Kilimanjaro region of Tanzania since 2010. However, the screening programme has faced a number of challenges including not enough skilled eye care staff to effectively run the programme and also poor rates of follow-up for those referred from screening to the specialist eye clinic with only 42% of people referred attending.

There is increasing evidence to support the use of artificial intelligence for diabetic eye screening. AI systems work by automating the interpretation of retinal photographs. This means that specialist staff are not needed to interpret the images and, as the results can be made available immediately after screening, patients can be given their results at the point of screening.

We plan to implement and evaluate the use of an AI system in an active diabetic retinopathy screening programme in the Kilimanjaro region of Tanzania. We are interested in assessing whether using an AI system for diabetic retinopathy screening in Tanzania can improve the service by increasing the rates of follow-up for persons referred after screening and also assessing the diagnostic accuracy of AI screening in an active Tanzanian screening programme.

Who can participate?
Adults aged over 18 years with diabetes in the Kilimanjaro or Arusha regions of Tanzania who attend a DR screening event.

What does the study involve?
Consented eligible participants attending screening for diabetic retinopathy will be randomised to either the current practice diabetic retinopathy screening pathway or the AI-supported DR screening pathway. The AI-supported screening arm will include automated retinal image analysis with an immediate referral decision and point-of-screening counselling. The current practice diabetic retinopathy screening involves retinal image grading 2-4 weeks after screening with a delayed referral decision. We will assess the proportion of people with true referable diabetic retinopathy who attend a follow-up appointment at the central ophthalmology clinic within 8 weeks of screening.

What are the possible benefits and risks of participating?
Benefits:
All participants will receive free eye screening for diabetic retinopathy
Participants will contribute towards improving diabetic eye care in Tanzania
Risks:
Retinal photography is non-invasive and safe and there are negligible risks to participants. Participants will have their pupils dilated which causes blurry vision that lasts a few hours and can cause mild stinging for a few seconds when the drops are instilled.

Where is the study run from?
Kilimanjaro Christian Medical Centre, Moshi, Tanzania

When is the study starting and how long is it expected to run for?
January 2021 to March 2025

Who is funding the study?
1. British Council for the Prevention of Blindness
2. Christian Blind Mission
3. Sir Halley Stewart Trust

Who is the main contact?
Dr Charles Cleland (charles.cleland@lshtm.ac.uk)

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
LSHTM 25839

Study information

Scientific Title
Artificial intelligence-supported diabetic retinopathy screening in Tanzania: A randomised controlled trial

Study objectives
Artificial intelligence-supported diabetic retinopathy screening with an immediate referral decision and point-of-screening counselling increases the proportion of people with true referable diabetic retinopathy that attend the central ophthalmology clinic following referral after screening for assessment and treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 28/01/2022, London School of Hygiene & Tropical Medicine Ethics Committee (Keppel Street, London, WC1E 7HT, UK; +44 2076368636; ethics@lshtm.ac.uk), ref: 25839
2. Approved 02/06/2022, Kilimanjaro Christian Medical University College Ethics Committee (P. O. Box 2240, Moshi, Tanzania; +255 272754377; no email provided), ref: 2571
3. Approved 03/08/2022, National Institute for Medical Research (3 Barack Obama Drive, P.O. Box 9653, 11101 Dar es Salaam, Tanzania; +255222121400; ethics@nimr.org.tz), ref: NIMR/HQ/R. 8a/Vol.IX/4074

Study design
Single-masked parallel group individually randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Diabetic retinopathy

Interventions
Participants will be randomised to either the artificial intelligence-supported diabetic retinopathy screening pathway with an immediate referral decision and point-of-screening counselling or the standard of care diabetic retinopathy screening pathway with a delayed referral decision. A computer-generated randomisation list will be prepared by a statistician at the London School of Hygiene & Tropical Medicine. The sequence will be in a 1:1 allocation ratio of standard DR screening to AI-supported DR screening, blocked with a random block size of 4 to 8.

The randomisation sequence will be concealed in sequentially numbered, opaque envelopes. The envelopes will be prepared by an administrator with experience of trial randomisation who is independent of all other aspects of the trial. A trained research team member will be responsible for opening the next envelope in numbered sequence and allocating the patient to either the AI-supported or current practice DR screening pathway. As immediate feedback is provided in the intervention arm versus no point-of-screening feedback in the standard of care arm, it will not be possible to mask participants or screening staff to the allocation. However, the participants arm allocation will only be apparent after randomisation has occurred.

The intervention in this trial is a complex intervention including AI-supported retinal image analysis for diabetic retinopathy grading and point-of-screening patient counselling.

The use of AI to grade retinal images for diabetic retinopathy enables point-of-screening, face-to-face counselling as the automated analysis provides immediate feedback, with a referral decision. The screening team member will inform the participant whether they need referral to the eye hospital and proceed with the counselling component of the intervention. The point-of-screening counselling will include an explanation of what diabetic retinopathy is, the potential to cause vision loss, the referral process and will emphasise that there are effective and safe treatments for diabetic retinopathy.

The standard of care screening pathway is the process by which patients have been screened for diabetic retinopathy in the Kilimanjaro diabetic retinopathy screening programme for >10 years. After retinal image capture, the photographs will be stored on a laptop and taken back to the referral eye hospital. The images will be graded by an ophthalmology resident for the level of diabetic retinopathy. Persons with referable diabetic retinopathy will be contacted by text message or phone call some weeks after screening and advised to attend KCMC eye department for assessment +/- treatment. The counselling participants in the standard of care arm receive

will follow the same format as the counselling given in the intervention arm of the trial, except that it will be delivered by telephone.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
SELENA+

Primary outcome measure
The proportion of true referable diabetic retinopathy cases attending the central ophthalmology clinic within 8 weeks of screening out of all those with true referable diabetic retinopathy, by trial arm. All retinal images will be graded by UK certified graders to provide the reference standard. It will be these gradings that will determine which participants have true referable diabetic retinopathy in each trial arm and this figure will be the denominator in our primary outcome analysis.

Follow-up data will be collected from hospital administrative records at the referral eye hospital (Kilimanjaro Christian Medical Centre). The hospital has an electronic patient record system.

Secondary outcome measures
1. The proportion of persons that attend the central ophthalmology clinic within 8 weeks of screening out of all those referred, by trial arm (eye hospital administrative records and reference standard gradings)
2. Sensitivity and specificity for grading any diabetic retinopathy and referable diabetic retinopathy (comparison of AI retinal image gradings against the reference standard retinal image gradings after recruitment completed)
3. Number of false positive cases attending the central ophthalmology clinic, by trial arm (eye hospital administrative records and reference standard retinal image gradings within 8 weeks of screening)
4. Number of patients receiving their first treatment for diabetic retinopathy treatment after referral, by trial arm (reviewing patient notes)
5. Number of gradable versus ungradable retinal images (reference standard retinal image gradings)
6. Time to presentation at hospital (eye hospital administrative records)
7. Incremental cost per quality-adjusted life year (QALY) gained (using a Markov model)
8. Acceptability, appropriateness and fidelity of AI screening (semi-structured interviews with relevant stakeholders and spot checks of intervention delivery throughout the trial)

Overall study start date
01/10/2021

Completion date
31/03/2025

Eligibility

Key inclusion criteria

Current inclusion criteria as of 11/01/2024:

1. Adult (18 years and older) diabetic patients attending diabetes clinics in Kilimanjaro or Arusha regions.
2. Willing and able to give consent.
3. Agree to be randomised to either AI-supported or standard of care diabetic retinopathy screening

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Previous inclusion criteria:

1. Adult (18 years and older) diabetic patients attending diabetes clinics in Kilimanjaro region.
2. Willing and able to give consent.
3. Agree to be randomised to either AI-supported or standard of care diabetic retinopathy screening

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
2,364

Key exclusion criteria
Current exclusion criteria as of 11/01/2024:

1. Unable or unwilling to give consent
2. Less than 18 years old
3. Already attending the central ophthalmology clinic or had a diabetic eye exam in the previous 12 months

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Previous exclusion criteria:

1. Unable or unwilling to give consent
2. Less than 18 years old

Date of first enrolment
08/03/2023

Date of final enrolment

31/08/2024

Locations

Countries of recruitment
Tanzania

Study participating centre
Kilimanjaro Christian Medical Centre
Eye Department
Moshi
Tanzania
PO Box 3010

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

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Sponsor type
University/education

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ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research council

Funder Name
British Council for Prevention of Blindness

Alternative Name(s)
BCPB

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Christian Blind Mission

Funder Name
Sir Halley Stewart Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The data collected in this study will be reported to the Tanzanian Ministry of Health and to meetings of clinicians in the regions through the College of Ophthalmology for Eastern, Central and Southern Africa. Results will also be presented at international conferences. The results will be submitted for open access publication.

Intention to publish date
31/03/2025

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Dr Charles Cleland (charles.cleland@lshtm.ac.uk). The full data set will be available with all patient identifiable details removed. Data will be available after formal reporting of the study findings in a peer-reviewed scientific publication. Datasets will only be available to bona fide scientific investigators. Requests should be made to the Chief Investigator in writing detailing the scientific investigator's background and intended use for the data. Consideration will be given to all proposed analyses.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	14/12/2021	02/03/2023	No	Yes
Protocol article		25/01/2024	30/01/2024	Yes	No