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A study to assess whether a system of automated image software can be developed to read retinal images taken without dilating the pupils in patients attending diabetic eye screening

Submission date	Recruitment status	[ ] Prospectively registered
04/08/2021	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
09/02/2022	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
11/01/2024	Eye Diseases	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Diabetes affects 4.7 million people in the UK. A common complication is diabetic retinopathy (DR), which is damage to the blood vessels in the eye. Screening for the early detection of DR has contributed to a reduction in blindness due to diabetes in the UK. This is carried out each year by using photography of the back of the eye (the retina). In England and Wales, the pupils are dilated with eye drops and then two 45-degree photographs of each eye are taken which gives a combined photographic width of 60 degrees of retina.

Scanning confocal ophthalmoscopes (SCO) are cameras that use low-powered laser or LED light to scan across the retina without the need for a bright flash and the width of one photograph varies from 60 - 200 degrees. This means only one photo of each eye is needed and pupil dilation may not be required. This would be an advantage as pupil dilation takes time, can be uncomfortable, and blurs the vision for several hours, meaning most people need to be accompanied to screening appointments and can't drive afterwards. Better accuracy, shorter appointment times, and the elimination of eye drops could increase the number of people who attend eye screening and DR could be caught earlier which may reduce the risk of vision loss.

At present, it is unknown whether white light LED or laser light is better for detection of DR, or if a wider photo might pick up more disease in the wider retina but may pick up less in the centre. Both might have an effect on referral to hospital eye clinics. This study will assess the accuracy of two new cameras when screening for any eye disease caused by diabetes and show whether the new cameras are as good as the current system or offer improved detection.

A company called RetinaScan Ltd have developed automated analysis software to detect diabetic retinopathy in the standard (two-field digital) images and they wish to extend this work to include images from wide-field scanning confocal ophthalmoscopes. To do this they need to have images of the back of the eye to develop and test their computer programmes.

Finding out whether these cameras can capture images of adequate quality without using drops to dilate the pupils is an important secondary objective of this study. The screening programme

in Scotland takes images without dilating the pupils and only does so if the images are of poor quality. This is around one third still needing to have drops. Fewer patients could require dilation with these new wide-field cameras, they provide a much wider field of image, and using computers to read the images could improve the service.

Who can participate?
People with diabetes who meet the inclusion criteria for the National Diabetes Eye Screening Programme in the UK. These will be people with diabetes over the age of 12 years (except for those under 16 years attending their first screening appointment) who give their consent to take part.

What does the study involve?
People attending their routine screening appointment have two extra photographs taken of each eye by each of the cameras before pupil dilation, followed by the normal screening procedure. If the image quality is poor they will be asked to have a further photograph taken of each eye with the new cameras after their pupils are dilated. The images and the results of the screening for diabetic eye disease will shared with the company developing the computer programme. The researchers will also combine the results with another study called CONCORDIA 1 to see which camera provides the best photographs for screening. Participants will be asked for their opinion on having their eyes examined on the existing and new cameras. This is a single appointment visit and no study follow up is required.

What are the risks?
The extra images will add an extra 30 minutes to a participant's appointment time but this was felt to be acceptable providing clear information is given and the extra parking costs reimbursed. There are no anticipated risks of taking part in the study or any direct benefits to the study population. The benefits may be in the future if these devices are considered an improvement and are adopted into the National Screening Programme.

Where is the study run from?
Gloucestershire Hospitals NHS Foundation Trust (UK)

When will the study take place?
November 2019 to December 2022

Who is funding the study?
1. Innovate UK
2. RetinaScan Ltd (UK)

Who is the main contact?
Prof. Peter Scanlon
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
275896

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Version 2.1, 24 March 2021, IRAS 275896, CPMS 44499

Study information

Scientific Title
Artificial image detection of diabetic retinopathy in wide-field images and assessment of non-mydriatic image quality of wide-field scanning confocal ophthalmoscopes

Acronym
AIDED

Study objectives
To assess whether retinal images taken on the Optos California and Zeiss Clarus Scanning ophthalmoscopes can be read using artificial imaging software

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/02/2020, South West - Cornwall & Plymouth Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)207 104 8019; cornwallandplymouth.rec@hra.nhs.uk), ref: 20/SW/0009

Study design
Non-randomized controlled trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Diabetic eye disease

Interventions
The interventions are two different scanning confocal ophthalmoscopes (SCO) devices (the Optos California and Zeiss Clarus Scanning ophthalmoscopes) and the images are compared with the standard digital images taken in the English National Screening Programme. The device order is randomised but not concealed for the operator as this isn't possible. The random order of the camera use is generated by the software used. The study software randomises the camera order to ensure there is an equal split on which camera is used first for imaging. If a subject is withdrawn from the study either during or post imaging the study software will recalculate required numbers for an even spilt and set the randomisation process accordingly.

The duration of participation in the trial is short, around 30 min per participant, as they will have additional images taken with the new devices before their pupils are dilated and then have their normal screening images taken for comparison. They will be asked to complete a short satisfaction questionnaire and the EuroQoL EQ5D-5L which is part of the data collection for the health economics element in work package 3 of a linked study (CONCORDIA 1 study). If the images on the new device are not readable, they will be re-taken after the pupils are dilated. After this their participation is finished as there is no follow-up for the study.

The retinal images and grading information are compared to support the development of an algorithm for the detection of diabetic retinopathy (DR) on wide-field SCO images that can be tested in a larger-scale study. Images from the devices will be uploaded to a secure NHS server, checked and prepared into 'reading lists' for assessors. Image grading will be performed in a masked fashion by expert graders from the Gloucester Reading Centre and the National Screening College (NSC). A dedicated state-of-the-art image grading platform will be used on a secure server. All grading is carried out in line with the English Diabetic Eye Screening programme using trained retinal image graders. Double grading with adjudication will be

performed and detection of individual lesions by the different cameras within the standard screening 45-degree fields will be recorded.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Optos California ophthalmoscope, Zeiss Clarus Scanning ophthalmoscope

Primary outcome(s)
The presence or absence of diabetic eye disease in the retinal images taken by the Optos California and Zeiss Clarus Scanning ophthalmoscope as assessed by the grading system used in the England Diabetic Eye screening service at a single timepoint

Key secondary outcome(s))
1. The proportion of those with non-mydriatic images that the screener considers are ungradable and decides that a mydriatic image is required with that SCO device, measured using the grading system used in the England Diabetic Eye screening service at a single timepoint
2. The proportion of those in whom a second mydriatic image is taken that then become gradable, measured using the grading system used in the England Diabetic Eye screening service at a single timepoint
3. Screener and participant's perspectives on the devices:
3.1. Participant feedback: immediately after imaging on the SCO device, participants will be asked to complete a graphical feedback question. Participants will be asked to score the experience of the SCO devices from one of four options: No problem, Okay, Not nice, unpleasant.
3.2. Research imager feedback: as soon as each participant has completed imaging on each SCO device and has left the room, the imager will score the experience of screening the patient on each SCO from one of the following four options: No problem, Okay, Difficult, Very difficult.
4. Time taken to capture and grade images by device type. The time taken to capture the images is recorded automatically via the software used in the screening department. The graders will record the time spent grading each image.
5. Quality of life measured using the EuroQuol EQ-5D 5L at the screening appointment. The researchers will convert the responses to the EQ-5D-5L instrument into health utilities as per national guidelines (https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l)
6. Seek consent from participants to link images with their clinical information relating to diabetic care for a future cost-benefit analysis.
Data from outcomes 3-6 will contribute to the CONCORDIA 1 study

Completion date
31/12/2022

Eligibility

Key inclusion criteria

1. People with diabetes giving informed consent
2. Those meeting the inclusion criteria for the English National Diabetic eye screening programme (DESPs) who are people with diabetes over the age of 12 years except for those under 16 years attending their first screening appointment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
1013

Key exclusion criteria
1. People in whom it is not possible to take retinal images
2. People or parents unable or unwilling to give informed consent
3. Those with eye disease that might affect the interpretation of DR levels
4. Children under 16 years attending for their first retinal screening appointment, which will automatically exclude 12 year old children as this is when they are first invited

Date of first enrolment
11/08/2020

Date of final enrolment
06/07/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Gloucestershire Royal Hospital
The Orchard Centre
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Sponsor information

Organisation
Gloucestershire Hospitals NHS Foundation Trust

ROR
https://ror.org/04mw34986

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
UK Research and Innovation Innovate UK, innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Retinascan

Results and Publications

Individual participant data (IPD) sharing plan
Sharing data will be considered on a case by case basis. All data including retinal images will be anonymised. The contact for this would be the Chief investigator Prof. Peter Scanlon (p.scanlon@nhs.net).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes