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Individual risk-based Screening for Diabetic Retinopathy

Submission date
08/05/2014

Recruitment status
No longer recruiting

Registration date
08/05/2014

Overall study status
Completed

Last Edited
05/11/2020

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
All people with diabetes are at risk of developing diabetic retinopathy which could lead to a loss of vision. The risk is different for each person based on factors such as type of diabetes, blood pressure and diabetes control. Currently in England all people with diabetes are invited for photographic eye screening once a year as part of the National Diabetic Eye Screening Programme. Screening aims to detect eye changes which may soon affect the vision so that the person can be referred to the hospital eye service for close monitoring and treatment. In this way the risk of losing vision can be reduced. However, there is evidence that not everyone needs to be screened every year because the chances of them developing eye changes are low. Also, there are some people who are at high risk and would benefit from screening more frequently. As part of a 5-year programme of research, we have developed an electronic tool (risk engine) to predict an individual's likelihood of developing sight-threatening diabetic retinopathy by using information from their previous screening results and their medical records. This means some people may benefit by attending screening more often than once a year while others may not need to attend so often. We have called this approach to screening 'personalised risk-based screening'. Nobody has assessed the effect of personalised risk-based screening intervals compared to annual screening on patients. We have designed this study to compare the safety and acceptability of changing from annual screening to personalised risk-based screening intervals.

Who can participate?
Patients aged 12 or above who attend the community clinic for retinal screening.

What does the study involve?
Participants will be contacted because they have diabetes and will shortly be attending for screening. When the participant arrives for their screening appointment they will be met by a research nurse who will answer any questions they may have after reading a Participant Information Leaflet. If they agree to take part they will be asked to sign a consent form and also may be asked to complete two short questionnaires on their general state of health and any personal costs associated with the screening visit, such as travel costs. The participant will be taken out of the study if their eye examination photographs show eye changes that need referral to the hospital eye service. These may be diabetic changes, or it may be that the

research nurses have not obtained clear enough photographs of the participant's eyes to grade them for diabetic retinopathy (this is usually due to early cataract or small pupils). We will randomly divide the participants into two groups. Half of the participants will continue to receive annual photographic screening. For the other half, their personalised screening interval will be determined using risk factors from their past screening data and medical information, including type of diabetes, blood pressure, and diabetes control. According to their individual risk patients in this group will be screened every 6 months, every 12 months or every 2 years. Participants will receive a letter within 6 weeks of their screening visit to inform them of their results from their recent screening appointment, which group they have been assigned to (annual or personalised screening interval) and when their next screening appointment will be. If the participant is in the personalised screening interval their risk will be assessed each time they attend for screening. If their risk has reduced (because diabetes is under better control) they may be screened at a longer interval. If their risk has worsened (due to poorer control) the participant may be screened more frequently. Towards the end of the study they will be asked about their experience and opinion on the study.

What are the possible benefits and risks of participating?
It is not possible to tell whether the participant is likely to benefit from entering the study or not. Results produced from the study will be used to improve eye care for people with diabetes in the future. Expected benefits associated with personalised risk-based screening are that people with diabetes will feel reassured that their own personal risk is being determined. This may reduce the anxiety associated with screening. For patients who are at low risk of developing sight-threatening diabetic retinopathy there will be fewer screening appointments. For patients who are at high risk of developing sight-threatening diabetic retinopathy there maybe earlier detection of their eye disease, and therefore better outcomes in terms of vision and a need for less treatment. If the patient is in the 2 yearly screening group (i.e. in the low-risk group) it is possible that their diabetic retinopathy may be detected later than would have been the case with fixed annual screen intervals. The consequence of this is that treatment might be needed immediately (normally there is a reasonable period of time between needing referral to the hospital eye service and needing treatment). More treatment might be needed than would have been the case if their diabetic retinopathy had been detected earlier or treatment might be less successful. We believe the risk of this happening to be very low as the risk will be determined using the patient's personal data.

Where is the study run from?
Screening takes place in seven fixed sites across Liverpool, UK:
1. Breeze Hill Neighbourhood Medical Centre
2. Everton Road Health Centre
3. Fiveways Family Health Centre
4. Picton Neighbourhood Health and Children's Centre
5. South Liverpool Treatment Centre
6. Yew Tree Centre
7. Clinical Eye Research Centre, Royal Liverpool University Hospital

When is the study starting and how long is it expected to run for?
May 2014 and is expected to run until March 2019

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

Who is the main contact?
Prof Simon Harding
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
16429

Study information

Scientific Title
Introducing personalised risk-based intervals in screening for diabetic retinopathy: development, implementation and assessment of safety, cost-effectiveness and patient experience

Acronym
ISDR

Study objectives
The purpose of this research programme is to introduce screening intervals that are based on individual risk of developing changes in the retina which may lead to visual impairment or blindness rather than screening all people with diabetes every year. The risk is related to factors such as how long the person has had diabetes, what their sugar levels are and how well their diabetes is controlled (blood pressure, sugar levels and cholesterol). The primary purpose of the randomised controlled trial is to assess whether it is safe and acceptable to patients to change the screening interval by measuring rates of attendance in both arms of the trial. The secondary objectives are to compare personalised risk-based intervals to annual screening in terms of: rates of development and severity of diabetic eye changes; visual outcomes; impact on general

diabetes care; acceptability; and cost-effectiveness in terms of actual cost and impact on quality of life.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/NW/0034; First MREC approval date 07/03/2014

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Screening

Study type(s)
Screening

Health condition(s) or problem(s) studied
Topic: Diabetes; Subtopic: Both; Disease: Retinopathy, Diabetic Control

Interventions
Patients will be randomised to two arms: either personalised risk-based screening intervals or annual screening (usual care) intervals. The grading result will be sent to the ISDR data warehouse as this completes the risk factor data collection for each individual patient. Failsafe methods in the LDESP will be used to ensure that all patients are informed about their appointments and non-attenders are followed up. This is an established part of the LDESP. Participants who fail to attend their screening appointment will be sent a further appointment, usually within 3-4 weeks. If they fail to keep this appointment a letter will be sent to them and the GP informing them that they will be recalled again in the next round of screening. This will be in 12 months' time for patients in the annual screening arm, and at 6, 12 or 24 months for patients in the personalised risk-based screening arm. Patients can be given a further appointment if they ring the department requesting screening.

Participants will be randomised using a secure (24-hour) web-based randomisation programme controlled centrally by the CTRC. Participants who have been screened will be identified by E-number and this will be used to generate the randomisation number. Block randomisation with stratification will be used to ensure adequate representation in each arm of the trial for groups where there are small numbers of participants (such as children aged 12-15 and minority ethnic groups). It will also be necessary to ensure that equivalent numbers of patients in each arm of the trial complete quality of life and visit questionnaires.

Randomisation can only be completed once the patient's images have been graded as it is only possible at this point to complete the inclusion and exclusion criteria. The ISDR data warehouse will be used to populate the fields in the baseline and follow-up electronic CRFs. This data will include inclusion and exclusion criteria information , age, ethnicity and other values of risk variables used to assess risk in the risk engine but not strictly needed for the randomisation, as well as whether the patient has completed the quality of life and cost questionnaires. Randomisation will be performed by a health service professional and participant screening

allocation will be displayed on a secure web page. An automated email confirmation sent to the authorised randomiser and the PI or Co-investigator (where applicable). Confirmation of the randomisation arm will be sent via email to the trial administrative team.

A health service professional will interrogate the risk engine for those patients in the trial using the related NHS number and date of birth. The risk engine will generate percentage risk and the appropriate screen interval and inform the administrative team and this information will be fed into the screening software (OptoMize) and recorded in the CRF. OptoMize will generate a letter to the patient informing them of the screening result, randomisation arm and their next planned review date. It is a national requirement that patients, and the GP, are informed of the screening result within 3 weeks of their screening appointment see appendix 1.

In the event of an internet connection failure between the centre and the randomisation system, the centre should contact the CTRC immediately to try to resolve the problem. If the problem can't be resolved the CTRC will open randomisation back-up envelopes. These envelopes will be sequentially numbered, opaque, envelopes similar to those used for pay slips, which cannot be viewed without fully opening and their construction is resistant to accidental damage or tampering.

Once the patient has been randomised follow up data will be collected based on the Randomisation Arm and variable screening interval. Follow up data will include collection of Health Economics surveys (if the patient was selected previously at the Baseline Screening Assessment).

The trial will continue for 48 months to ensure that all patients in the extended screen interval group (24 months) have attended for follow up screening at least once. The trial will close 6 months before the end of the grant. An allowable window is not appropriate for this trial due to the nature of population screening and the multiple variable factors affecting attendance. If patients do not attend their first appointment for screening they are offered a second appointment (usually within 6 weeks of the first appointment). If patients fail to attend for their second appointment a letter is sent to the patient advising them of the importance of screening and inviting them to contact the screening programme for a new appointment.

After the Follow Up Assessment patients will continue to have their grading results assessed up to 6 weeks which will be recorded on the Follow up Grading Log and will detail outcome of the screening assessment including continuation in the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Comparison of attendance rates for follow-up screening in the two arms of the study. [Non-attendance is defined as failure to attend two appointments for screening (usually within 6 weeks of each other)].

Key secondary outcome(s)
1. Number of cases of STDR detected
2. Retinopathy level at screening (Liverpool and NDESP grading)

3. Maculopathy level at screening (Liverpool and NDESP grading)
4. Number of false positive screening episodes
5. Number of screening appointments
6. Number of dedicated diabetes assessment clinic appointments
7. Number of other eye appointments for diabetic eye disease
8. Visual acuity (logMAR)
9. New visual impairment (≥ +0.50 logMAR)
10. New visual impairment due to diabetic retinopathy (≥ +0.50 logMAR)
11. Number of missed appointments to screening
12. Patient acceptability measures (using a questionnaire designed for the trial)
13. Quality-adjusted life years (QALYs) estimated using EQ-5D-5L and Health Utilities Index Mark 3 (HUI3)
14. Cost per QALY gained

Completion date
01/03/2019

Eligibility

Key inclusion criteria
Patients who:
1. Are aged 12 years and over
2. Attend for retinal screening in a community clinic or a screening assessment clinic during the recruitment period
3. Are registered with a participating GP practice
4. Are included in the study data warehouse (have not opted out)
5. Have no retinopathy or have retinopathy and maculopathy less than the definition of screen positive DR
6. Have gradeable digital retinal images
7. Give their informed consent for participation
8. Are not involved in any trial investigating a treatment aiming at preventing or modifying the development of STDR

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
4538

Key exclusion criteria

Patients who:
1. Are under 12 years
2. Are not registered with a participating GP practice
3. Have opted out from the study data warehouse
4. Have screen positive DR
5. Have significant other eye disease requiring referral to the HES
6. Are ineligible for screening for whatever reason, including having ungradeable digital retinal images
7. Do not give consent for participation in the RCT
8. Are involved in any trial investigating a treatment aiming at preventing or modifying the development of STDR

Date of first enrolment
12/11/2014

Date of final enrolment
31/05/2016

Locations

Countries of recruitment
United Kingdom

Study participating centre
Breeze Hill Neighbourhood Medical Centre
United Kingdom
-

Study participating centre
Everton Road Health Centre
United Kingdom
-

Study participating centre
Fiveways Family Health Centre
United Kingdom
-

Study participating centre
Picton Neighbourhood Health and Children's Centre
United Kingdom
-

Study participating centre
South Liverpool Treatment Centre
United Kingdom
-

Study participating centre
Yew Tree Centre
-
United Kingdom
-

Study participating centre
Clinical Eye Research Centre, Royal Liverpool University Hospital
United Kingdom
-

Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospital NHS Trust

ROR
https://ror.org/009sa0g06

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

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

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2021	05/11/2020	Yes	No
Protocol article	protocol	17/06/2019	02/07/2020	Yes	No
HRA research summary			28/06/2023	No	No