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The use of different diagnostic tests for the detection of poor circulation in people with diabetes

Submission date 15/10/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 18/10/2021	**Overall study status** Completed	
Last Edited 11/11/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Diabetes is a lifelong condition that causes a person's blood sugar level to become too high. In people with diabetes, if high blood glucose levels are experienced over a period of years, blood vessels can become damaged which can lead to plaque forming in the blood vessels, rendering them unable to deliver enough blood to neighbouring cells. Poor blood circulation can lead to a higher chance of developing serious foot problems. In the UK there are over 7,000 leg amputations each year because of diabetes. The most important cause of this is poor circulation. The detection of poor circulation in patients with diabetes is difficult. A number of tests exist to detect poor circulation. However, there is confusion as to which is the best test. The aim of this study is to determine which test is best.

Who can participate?
Adult patients with diabetes

What does the study involve?
Patients will be asked to attend two study visits. At the first visit, which will take 40 minutes and coincide with a routine appointment, patients will undergo five tests:
1. Blood pressure at the ankle (called ankle-brachial pressure index or ABPI)
2. Blood pressure at the ankle after doing heal raises (called exercise ABPI)
3. Blood pressure at the big toe (called toe-brachial pressure index or TBPI)
4. Visible blood flow waveform (called Doppler)
5. Audible blood flow waveforms (called Doppler)
In some centres the researchers will also test the performance of an additional sixth test. They have developed this test and studied its performance in a study of 305 patients. It consists of an ultrasound test at the ankle, using a sensor and gel on the skin.
The second visit will take place within 2 weeks of the first visit. In the second visit, which will take 30 minutes, patients will have a more detailed scan of the blood vessels in their leg using a computed tomography angiography (CTA) or magnetic resonance angiography (MRA) scan. The results from the bedside tests will be compared to the results of the CTA or MRA to identify the most accurate test.

What are the possible benefits and risks of participating?
Participants will undergo comprehensive testing and imaging for peripheral arterial disease (poor circulation) as part of this study. If previously undiagnosed, the diagnosis of peripheral arterial disease may prompt their doctor to initiate medicines that will help reduce their chance of having a stroke, heart attack and worsening of their peripheral arterial disease.
Additionally, if participants are diagnosed as having peripheral arterial disease, they may be eligible for additional measures to reduce the risk of developing a foot ulcer. These additional measures may include more frequent foot checks or new footwear.
If participants have an active ulcer, a diagnosis of peripheral arterial disease will trigger a specialist review by a vascular surgeon for consideration of timely revascularisation to improve the chance of ulcer healing and reduce the risk of amputation.
Participants may have a Computed Tomography Angiography (CTA) procedure, which, for the majority of participants (about 80%), will be added to the procedures they would have if they did not take part. This procedure uses ionising radiation to form images of the body and provide the doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study may increase the chances of this happening to you to about 0.12% or 1 in 800.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
September 2021 to February 2024

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

Who is the main contact?
Laura Burgess, l.burgess@imperial.ac.uk

Study website
https://www.imperial.ac.uk/department-surgery-cancer/research/surgery/clinical-trials/dm-pad-trial/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
301408

ClinicalTrials.gov number
NCT05009602

Secondary identifying numbers
CPMS 50623, NIHR131855, IRAS 301408

Study information

Scientific Title
Diagnostic tools to establish the presence and severity of peripheral arterial disease in people with diabetes

Acronym
DM PAD 1.1

Study objectives
To determine the diagnostic performance of index tests (audible handheld Doppler, visual handheld Doppler, ankle-brachial pressure index [ABPI], exercise ABPI and toe brachial pressure index [TBPI]) for the diagnosis of peripheral arterial disease (PAD) in patients with diabetes as determined by a reference test (CTA or MRA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/10/2021, London Central REC (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8225; londoncentral.rec@hra.nhs.uk), REC ref: 21/PR/1221

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Peripheral arterial disease in people with diabetes

Interventions
VISIT 0 (REMOTE SCREENING)
To minimise patient burden, the researchers have adopted a remote screening process and incorporated the index tests into a routine visit episode to reduce the number of additional visits to one. Patients will be remotely screened at least 72 hours prior to their routine visit by their clinical team. If eligible for recruitment, they will be contacted by phone regarding the study. The study will be explained and if the patient gives verbal consent to receiving study information material, then these will be emailed or posted to the patient for consideration. They will be told that formal consent will be taken at visit 1 if they agree to partake in the study and that if they choose not to then this wouldn't affect their usual clinical care.

VISIT 1 (INDEX TESTS)
Visit 1 will occur at a planned/ routine visit i.e., this would have occurred regardless of whether the patient was recruited onto the study or not. Patients will undergo routine assessment and care by the local clinical team. There is some overlap regarding tasks that would be performed as part of routine/usual care and as part of the study. Such tasks will be highlighted as 'ROUTINE' when describing the order of events below. A routine visit usually lasts 30 minutes. The researchers expect that the study will add 40 minutes to the usual episode.

The researchers are primarily evaluating five index tests across all research centres; ABPI, expertise ABPI, TBPI, visual handheld Doppler and audible handheld Doppler. However, in four centres, they will evaluate the PAD scan as a sixth test. They have chosen not to evaluate this test at all centres as DUS machines are moderately costly and not currently available at every site. Index tests will be performed by a member of the local clinical team. Tests will be performed on one limb only; the most problematic side in symptomatic patients or randomly selected side in asymptomatic patients. Index tests will be performed in a predetermined order to minimise influence carrying over from one test to the other. Audible and visual handheld Doppler involve semi-objective interpretation of arterial waveforms and therefore could be influenced by knowledge of the tests with an objective output (TBPI, ABPI and exercise ABPI. Therefore, semi-objective tests will be performed first followed by objective tests

Order of events at visit 1:
- Eligibility check; 5 min
- Recording of demographic details and medical history; 5 min
- Assessment for neuropathy (ROUTINE); 5 min
- Assessment of diabetic foot ulcer severity, if relevant (ROUTINE); 5 min
- Index tests for the diagnosis of peripheral arterial disease:

1. Audible handheld Doppler (ROUTINE); 5 min
2a. Visual handheld Doppler; 5 min
2b. PAD-scan (in 4 selected centres); 5 min
N.B the order of 2a. and 2b. will be randomised
3. ABPI (ROUTINE); 5 min
4. TBPI; 5 min
5. Exercise ABPI i.e., ABPI performed following repetitive heal raising; 5 min
- Patient acceptability; patients will be asked to rate their experience of each test on a Likert scale
- Blood test to assess renal function (ROUTINE in a proportion of patients); 5 min
- Repeating of index tests (only performed in the first 100 volunteering patients); 40 min

The first 100 volunteering patients will have all index tests repeated (in the same leg) on the same day, by the same operator and also by an alternative operator to assess the inter- and intra-rater reliability.

VISIT 2 (REFERENCE TEST)
- MRI or CTA; 30 min
The reference test will be performed within 2 weeks of the index tests. The final decision regarding whether the patient undergoes CTA or MRA will depend on local protocol and patient choice. A proportion of patients would undergo a CTA or MRA regardless of whether they were taking part in the trial or not.

FOLLOW UP
Patients will be followed up 12 months from the time of the index tests. Follow up will be performed by review of the clinical notes. The purpose of follow up will be to ascertain whether the index tests can be used to predict ulcer healing, ulcer recurrence, revascularisation, amputation, cardiovascular events and mortality.

RECRUITMENT OF INPATIENTS
The above description is relevant to the recruitment of patients from clinics. The researchers will also be recruiting patients admitted for hospital care.
Patients admitted for inpatient hospital care will be first identified by the inpatient podiatry, vascular or diabetes teams.
Patients will have at least 24 hours to consider the patient information material. Participating patients will have index tests performed at their bedside. Where possible, the reference test will be performed during their inpatient stay to avoid additional hospital visits.

Intervention Type
Other

Primary outcome measure
Diagnostic accuracy of the PAD scan and the other bedside tests for the diagnosis of peripheral arterial disease will be compared to the results of magnetic resonance angiography (MRA) or computed tomography angiography (CTA) (reference test) at 2 weeks

Secondary outcome measures
1. Health economic outcome - the cost of the test, including direct costs and amortisation of capital equipment and use of other healthcare resources for prevention and treatment of the disease over a time horizon of 5 years
2. Health economic outcome - incremental cost-effectiveness ratio at 5 years

3. Health economic outcome - Quality Adjusted Life Years at 5 years
4. Specificity of index tests, comparing index tests to reference tests at 2 weeks
5. Likelihood ratios of index tests, comparing index tests to reference tests at 2 weeks
6. Predictive values of index tests, comparing index tests to reference tests at 2 weeks
7. Diagnostic odds ratio of index tests, comparing index tests to reference tests at 2 weeks
8. Patient acceptability of each index test, measured on a Likert scale following the completion of the tests at visit 1
9. Technical success including inability to perform, refusal and discontinuation of tests at 2 weeks
10. Inter- and intra-rater reliability by repeating of index tests by the same and by an alternative operator for the assessment at 2 weeks

Overall study start date
01/09/2021

Completion date
14/02/2024

Eligibility

Key inclusion criteria
Known history of diabetes

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 600; UK Sample Size: 600

Total final enrolment
604

Key exclusion criteria
1. Peripheral arterial disease (PAD) status known on imaging
2. Known history of PAD intervention
3. CTA and MRA contraindications; renal impairment, pregnancy, contrast medium hypersensitivity/allergy, non-compatible implants (MRA only)
4. Interim surgical interventions (occurring in the time interval between the index and reference tests) will be considered a protocol violation and patients will be excluded
5. Unable to provide appropriate informed consent

Date of first enrolment
01/03/2022

Date of final enrolment

28/02/2023

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
St Mary's Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Chelsea & Westminster Hospital
369 Fulham Road
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Study participating centre
Leicester Royal Infirmary
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Study participating centre
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Study participating centre
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Sponsor type
University/education

Website
http://www.imperial.ac.uk/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Funder Name

National Institute for Health Research (NIHR) (UK)

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

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. Additional documents will be available once REC approval is in place.

Intention to publish date
28/02/2025

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No