ISRCTN22295060 https://doi.org/10.1186/ISRCTN22295060

Performance evaluation of type 1 diabetes genetic risk test

Submission date
29/05/2025

Recruitment status
No longer recruiting

Registration date
12/06/2025

Overall study status
Completed

Last Edited
29/05/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
There are several forms of diabetes including Type 1 Diabetes and Type 2 Diabetes. It is not always easy for a doctor to be certain what type of diabetes a person has. It is important that the correct type is confirmed as the patient treatment and care pathways are very different. This study aims to evaluate the performance of a test which provides a genetic risk profile for Type 1 Diabetes. The genetic component of Type 1 Diabetes is well known and remains unchanged throughout life offering a means to identify individuals who are at a higher genetic risk for this condition helping with disease identification before symptoms arise and improving patient care, treatment and potential outcomes.

Who can participate?
Study is confined to leftover samples (whole blood or DNA) and as such no additional individuals can participate. Leftover samples originate from University of Exeter through the NIHR Exeter Clinical Research Facility, Exeter 10,000 & Peninsula Research Bank (EXTEND/PRB) Exeter Clinical Research Facility // Exeter 10,000 & Peninsula Research Bank (EXTEND/PRB) from several research studies including EXTEND (ethical approval number: 19/SW/1059), EXE-T1D (Understanding beta-cell destruction through the study of Extremely Early Onset Type 1 Diabetes) (ethical approval number: 17/EM/0255) and StartRight (getting the right classification and treatment from diagnosis of diabetes) (ethical approval number: 16/SW/0130) with fully informed consent for research use.

What does the study involve?
The study involves testing pre-characterised leftover samples from individuals who are non-diabetic (n=100), have early onset Type 1 Diabetes (n=100), adult-onset Type 1 Diabetes (n=100) or Type 2 Diabetes (n=200) using the test (Type 1 Diabetes (T1D) SNP Array EV4489A/B). A Type 1 Diabetes genetic risk of low, medium or high will be provided for each sample tested.

What are the possible benefits and risks of participating?
As the study involves testing of pre-characterised leftover clinical samples there are no risks to participating. The test itself has the potential benefit of identifying individuals at higher genetic risk which could result in disease prediction prior to symptom onset leading to improved overall patient care, treatment plans and outcomes.

Where is the study run from?
Randox Clinical Laboratory Services (RCLS), Northern Ireland (UK).

When is the study starting and how long is it expected to run for?
The study started on 7th April 2025. Testing commenced on 28th May 2025 and should be complete within 10 working days.

Who is funding the study?
Randox Laboratories Limited, Northern Ireland (UK)

Who is the main contact?
Dr Helena Murray, Molecular R&D Manager, Randox Laboratories Limited
helena.murray@randox.com

Contact information

Type(s)
Principal Investigator

Contact name
Mr Kristopher Pentland

Contact details
Randox Science Park
30 Randalstown Road
Antrim
United Kingdom
BT41 4FL
+44 2894422413
Kristopher.Pentland@randox.com

Type(s)
Public, Scientific

Contact name
Dr Helena Murray

Contact details
55 Diamond Road
Crumlin
United Kingdom
BT29 4QY
+44 2894422413
helena.murray@randox.com

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
357706

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Clinical performance evaluation of type 1 diabetes (T1D) SNP Array (EV4489A/B)

Study objectives
This study will be conducted to demonstrate that, under the anticipated conditions of use, the Type 1 Diabetes (T1D) SNP Array will meet the intended use and labelling claims.
The T1D SNP Array is intended for in vitro diagnostic use enabling the rapid qualitative genotyping of ten SNPs associated with T1D risk, direct from nucleic acid. The array can be used to calculate a Genetic Risk Score (GRS), that in combination with other clinical factors (e.g. age, BMI, T1D autoantibody status) can aid the clinician in discriminating T1D from other non-autoimmune diabetes such as T2D, monogenic diabetes or secondary diabetes.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/05/2025, West Midlands - South Birmingham Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 2071048384; southbirmingham.rec@hra.nhs.uk), ref: 25/WM/0091

Study design
Single centre observational study using left over samples

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Laboratory

Study type(s)
Diagnostic

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied

Discrimination of Type 1 Diabetes from other non-autoimmune diabetes such as type 2 diabetes, monogenic diabetes or secondary diabetes.

Interventions

An observational clinical performance study will be conducted to demonstrate that, under the anticipated conditions of use, the Type 1 Diabetes (T1D) SNP Array will meet the intended use and labelling claims. The main objective of the study is to ensure discrimination of T1D from other non-autoimmune diabetes through the assessment of leftover pre-characterised clinical samples (genotypes and GRSs) covering individuals without diabetes and those with either Type 1 Diabetes (T1D) or Type 2 Diabetes (T2D). Samples originate from the University of Exeter through the NIHR Exeter Clinical Research Facility, Exeter 10,000 & Peninsula Research Bank (EXTEND/PRB). Genotypes were generated using Illumina GSA Beadchip GSA MD (Illumina GSA Arrays "Infinium iSelect 24x1 HTS Custom Beadchip Kit") and will cover all possible genotypes present on the Type 1 Diabetes (T1D) SNP Array. GRSs were generated at University of Exeter utilising their in-house pipeline. Inclusion criteria for the study were based on the clinical diagnosis of Type 1 Diabetes or Type 2 Diabetes or absence of the disease (non-diabetic). Age criteria were utilised to define early onset (< 18years) or adult onset (> 18 years) for Type 1 Diabetes. A total of 500 samples will be assessed covering 100 non-diabetics, 100 early onset (< 18years) T1D cases, 100 adult-onset (>18 years) T1D cases and 200 T2D cases. All samples will be processed as per device Instructions for Use (IFU) with final data input via an Excel Workbook. The workbook generates the correct genotype for all the 10 SNPs detected by the device and calculates the respective T1D-GRS. A final T1D-GRS report is generated by the workbook providing a genetic risk score and risk level for T1D (high, medium or low) based on the percentile of UK European Ancestry T1D population (refer to below table).Two types of report can be generated, one for a diabetic individual and another for non-diabetics. Reports including genotypes and GRSs will be available for all samples tested. Each sample will have a unique identification number with no personal information available.

Parameters of clinical performance to be evaluated include Diagnostic Sensitivity, Diagnostic Specificity, Positive Predictive Value, Negative Predicted Value, Likelihood Ratios and Receiver Operating Characteristic (ROC) Curve analysis. Refer to Section 7 for further details. An additional method comparison analysis (as presented by a percentage difference) will also be performed against reference method genotyping and GRSs generation.

Intervention Type

Genetic

Primary outcome measure

1. DNA concentration is measured using spectrophotometry at baseline (sufficient quantity 7.5ng /µl)
2. DNA purity (260/280 ratio) is measured using spectrophotometry at baseline (sufficient quality 260/280 ratio ≤ 3.0)
3. Genotype concordance is measured using comparison between the T1D SNP Array and the Illumina GSA Beadchip GSA MD at baseline
4. Genetic Risk Score (GRS) concordance is measured using comparison between the T1D SNP Array and the Illumina GSA Beadchip GSA MD at baseline
5. Risk level classification (low, medium, high) is measured using the T1D SNP Array and compared to the Illumina GSA Beadchip GSA MD at baseline
6. Agreement with established reference method (Illumina GSA Beadchip GSA MD) of clinical samples' genotypes, GRSs and risk level (low, medium or high). Clinical Performance Study acceptance criteria will be as follows:

• Diagnostic Sensitivity ≥ 90%
• Diagnostic Specificity ≥ 90%
• Likelihood Ratios >10 or <0.1
• ROC (Receiver Operating Characteristic) Area Under the Curve ≥ 0.75

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
07/04/2025

Completion date
09/06/2025

Eligibility

Key inclusion criteria
Inclusion criteria for the study were based on the clinical diagnosis of Type 1 Diabetes or Type 2 Diabetes or absence of the disease (non-diabetic). Age criteria were utilised to define early onset (< 18years) or adult onset (> 18 years) for Type 1 Diabetes. A total of 500 samples will be assessed covering 100 non-diabetics, 100 early onset (< 18years) T1D cases, 100 adult-onset (>18 years) T1D cases and 200 T2D cases.

Participant type(s)
Patient

Age group
Mixed

Lower age limit
1 Days

Upper age limit
54 Years

Sex
Both

Target number of participants
500

Total final enrolment
500

Key exclusion criteria
Not applicable. Refer to inclusion criteria.

Date of first enrolment
07/04/2025

Date of final enrolment
09/06/2025

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Study participating centre
Randox Clinical Laboratory Services
Randox Science Park
30 Randalstown Road
Antrim
United Kingdom
BT41 4FL

Study participating centre
NIHR Exeter Clinical Research Facility
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Exeter 10,000 & Peninsula Research Bank (EXTEND/PRB)
Barrack Road
Exeter
United Kingdom
EX2 5DW

Sponsor information

Organisation
Randox Laboratories Limited

Sponsor details

55 Diamond Road
Crumlin
Northern Ireland
United Kingdom
BT29 4QY
+44 2894422413
helena.murray@randox.com

Sponsor type
Industry

Website
https://www.randox.com

Funder(s)

Funder type
Industry

Funder Name
Randox Laboratories Limited

Results and Publications

Publication and dissemination plan
Study results will be submitted to regulatory authorities for market authorisation of the Type 1 Diabetes SNP Array device.
Study results may also be published in a peer-reviewed journal.

Intention to publish date
09/06/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to genetic risk scores and genotypes having already been established for these patients; the current clinical study aims to show that the Type 1 Diabetes SNP Array will generate equivalent results to the standard research assay used.

IPD sharing plan summary
Not expected to be made available