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Hybrid closed loop insulin pumps and early worsening of diabetic retinopathy in Type 1 diabetes

Submission date
10/11/2025

Recruitment status
Recruiting

Registration date
22/12/2025

Overall study status
Ongoing

Last Edited
22/12/2025

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
People with type 1 diabetes need insulin to control their blood sugar levels. New technologies called hybrid closed loop (HCL) insulin pumps, sometimes called “artificial pancreas” systems, automatically adjust insulin delivery using continuous glucose monitoring. These systems help people achieve much tighter glucose control.
However, when blood sugar levels improve very quickly, there can sometimes be a temporary worsening of eye disease known as early worsening of diabetic retinopathy (EWDR). This effect has been seen in the past when diabetes treatment was intensified, but it is not known how often it happens with new HCL systems.
The INSIGHT 1 study will follow people with type 1 diabetes who are starting on HCL insulin systems and compare them with people who continue using multiple daily insulin injections (MDI) or stand alone (open loop) pumps.

Who can participate?
Anyone with type 1 diabetes who is within 28 days of starting a HCL system or anyone who chooses to remain on MDI or open loop insulin pumps

What does the study involve?
Participants will have detailed eye examinations including:
1. Retinal photographs and optical coherence tomography (OCT) scans to achieved detailed 2D and 3D pictures of the back of the eye
2. Electroretinography (ERG) to measure how the nerves around the retina function
3. Blood samples to look for biological markers (such as growth factors and inflammation) which may be implicated in EWDR

What are the possible benefits and risks of participating?
The only direct benefit from this study would be the identification of a previously unknown health problem whose prompt treatment may improve your health. We don’t envisage there to

be any significant risks of taking part. The knowledge gained from this study may affect the tests and structure of clinic appointments employed in the future that aim to assess the eye-health needs of people with type 1 diabetes who are started on hybrid closed loop technologies.

Where is the study run from?
The study will take place at St Paul's Eye Unit, Royal Liverpool Hospital, University Hospitals of Liverpool Group, Liverpool, UK

When is the study starting and how long is it expected to run for?
The study started recruiting in May 2025 and we envisage recruitment to end in July 2027. We envisage the end of study visits to be July 2028 and the data collection to be July 2029.

Who is funding the study?
This study is jointly funded by Breakthrough T1D and the Novo Nordisk UK Research Foundation, with support for reading of the images provided by a University Hospitals of Liverpool Charity Grant.

Who is the main contact?
Please contact Dr Matthew Anson (manson1@liverpool.ac.uk) for any queries

Contact information

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
349443

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 65120

Study information

Scientific Title
Evaluating the association between hybrid closed-loop insulin pump therapy and early worsening of diabetic retinopathy in adults with Type 1 diabetes over a 24-month period: a prospective cohort comparison with multiple daily injections or stand-alone CSII

Acronym
INSIGHT-1

Study objectives
The aim of INSIGHT-1 is to evaluate whether HCL insulin delivery is associated with development of EWDR, and to gain mechanistic insights into the condition.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/12/2024, London - Harrow Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048 154; harrow.rec@hra.nhs.uk), ref: 24/PR /1353

Study design
Prospective non-interventional cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied

Type 1 diabetes

Interventions
All participants will undergo digital colour fundoscopy, optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), electroretinography (ERG), routine blood tests, additional blood tests for inflammatory cytokines, height and weight measurement, measurement of visual acuity and undertake an eye health questionnaire. These assessments will be done at baseline, and repeat and 3, 6 and 12 months. A virtual review of health records will be conducted at 24 months.

Intervention Type
Other

Primary outcome(s)
The rate of early worsening of diabetic retinopathy (EWDR) in individuals who are newly initiated on a hybrid closed loop insulin pump (HCL). EWDR will be defined as either:
1.Two-step change in the Early Treatment of Diabetic Retinopathy Study scale (ETDRS) or
2. Progression to clinically significant macular oedema (CSMO) or
3. Progression to treatment of diabetic retinopathy
(baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)

Key secondary outcome(s))
1. The rate of one-step change in ETDRS (baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)
2. The difference in rate of EWDR between individuals on HCL and individuals on multiple daily injections (MDI) measured using either: i) two-step change in ETDRS or ii) progression to clinically significant macular oedema (CSMO) or iii) progression to treatment of diabetic retinopathy] (baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)
3. Quantification of the changes in the retinal microvasculature in individuals who are started on a HCL (retinal thickness, ganglion cell layer, retinal nerve fibre layer, capillary plexus, retinal neurophysiology, foveal avascular zone, acicularity index measured using in-built automated software and image segmentation techniques) (baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)
4. Evaluation of continuous glucose monitoring (CGM) metrics (% time in range, % time above and below range, glycaemic variability, glucose management index, average glucose) in relation to two-step and one-step change in ETDRS (baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)
5. Alterations in serum growth factors in individuals who develop EWDR compared to individuals who do not, measured using multiplex assays (baseline vs 3 months; baseline vs 6 months; baseline vs 12 months)

Completion date
04/08/2029

Eligibility

Key inclusion criteria
HCL group:
1. Able to attend screening visit within 28 days of initiation on a HCL
2. Baseline HbA1c ≥58 mmol/mol

Control group:
1. Does not meet the national criteria for HCL initiation (MDI or stand alone/open loop insulin pump)

Participant type(s)
Population

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Pregnancy. This is because pregnancy is an established risk factor for EWDR and would be a significant confounding variable
2. Unable to give informed consent
3. Type 2 diabetes, MODY, cystic fibrosis related diabetes, other secondary causes of diabetes

Date of first enrolment
07/05/2025

Date of final enrolment
31/07/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Clinical Eye Research Centre (CERC) at St Paul's Eye Unit
Royal Liverpool University Hospital
St Paul's Eye Unit
Lower Ground Floor

Liverpool
England
L7 8YE

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
Breakthrough T1D UK

Alternative Name(s)
Juvenile Diabetes Research Foundation Limited, JDRF

Funding Body Type
Government organisation

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

Location
United Kingdom

Funder Name
Novo Nordisk UK Research Foundation

Alternative Name(s)
Novo Nordisk UK Research Foundation (NNUKRF), The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Funder Name
University Hospitals of Liverpool Charity

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available in an anonymised format upon request (contact Dr Matthew Anson, manson1@liverpool.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes