

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

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 22/12/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 22/12/2025	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> 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](mailto:manson1@liverpool.ac.uk)) for any queries

## Contact information

### Type(s)

Public, Scientific

### Contact name

Dr Matthew Anson

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

349443

### 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  $\geq 58$  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](mailto:manson1@liverpool.ac.uk))

**IPD sharing plan summary**

Available on request