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# Long-term follow-up of participants with electronic health records from the HPS2-THRIVE study

**Submission date**
04/08/2022

**Recruitment status**
Recruiting

**Registration date**
16/08/2022

**Overall study status**
Ongoing

**Last Edited**
30/01/2026

**Condition category**
Other

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

## Plain English summary of protocol

Background and study aims
HPS2-THRIVE (ISRCTN29503772) was a randomised, international multi-centre trial of 2g of extended-release niacin and 40 mg of laropiprant or a matching placebo daily. There were 25,673 participants (8,035 in the UK, 10,932 in China and 6,706 in Scandinavia (Denmark, Norway, Finland & Sweden)) with a history of vascular disease. Participants in HPS2-THRIVE were recruited to the trial between 2007 and 2010 and were followed up for a median of four years in the study clinics while they continued on their randomised treatment and background LDL-lowering treatment (with 40mg simvastatin daily plus 10mg ezetimibe daily, if required).

Results were presented at the American College of Cardiology meeting in 2013 and published in the New England Journal of Medicine in 2014.

THRIVE found that:
• Allocation to extended release (ER) niacin/laropiprant reduced LDL-cholesterol by 0.25 mmol/L and increased HDL-cholesterol by 0.16 mmol/L but this did not significantly reduce the risk of major vascular events (i.e. heart attacks, strokes or coronary or non-coronary revascularisation) compared to placebo.
• Allocation to ER niacin/laropiprant significantly increased the risk of disturbances in diabetes control and new onset diabetes and serious adverse events associated with the gastrointestinal and musculoskeletal systems, skin and, unexpectedly, both infection and bleeding.
• ER Niacin increased the risk of simvastatin-induced myopathy by about 4-fold.
• Participants from China were at higher risk of statin-induced myopathy than those from Europe.

The results of the THRIVE trial led to the withdrawal of ER niacin/laropiprant from the European market and Merck ceased development of the product.

Participants were recruited into the main trial using informed patient consent as a legal basis to process data. However, the researchers now have section 251 support (from the Confidentiality

Advisory Group (Ref: 19/CAG/0166)) in place to carry-out long-term research on this cohort. The data controller has approval from the West of Scotland Research Ethics Service (Ref: 19/WS /0116) to follow up the cohort, with continued data linkage to allow for future analyses.

The purpose of the HPS-THRIVE long-term follow-up study is to determine factors that contribute to the health of trial participants in the longer-term.

Who can participate?
The cohort is the original THRIVE participants recruited in UK hospitals between 2007 and 2010. No further participants will be added to this trial.

What does the study involve?
This is a long-term follow-up study. That means that we will be using data previously collected from participants during the main trial, and also collecting data about them from electronic health records (e.g. from NHS England, and equivalent bodies in Scotland and Wales). Participants will not be contacted directly.

What are the possible benefits and risks of participating?
No interventions are taking place for this long-term follow-up study so there are no direct risks or benefits to participants.

Where is the study run from?
University of Oxford, managed by researchers at the Nuffield Department of Population Health (UK)

When is the study starting and how long is it expected to run for?
The HPS-THRIVE long-term study will collect data from the start of the original trial for at least a 20-year period. Further analyses are planned to be run at approximately 5-yearly intervals after this based on ongoing linkage to NHS records.

Who is funding the study?
University of Oxford (UK)

Who is the main contact?
Professor Richard Haynes (Chief Investigator)
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# Contact information

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Scientific

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## Additional identifiers

### Integrated Research Application System (IRAS)
268340

## Study information

### Scientific Title
HPS2-THRIVE trial legacy study: long-term follow-up of participants with electronic health records

### Acronym
HPS2-THRIVE

### Study objectives
To determine the factors that contribute to the health of participants of the original HPS2-THRIVE trial (ISRCTN29503772) over many years, using electronic health records

### Ethics approval required
Old ethics approval format

### Ethics approval(s)

Approved 30/08/2019, West of Scotland REC 3 (Research Ethics, Clinical Research & Development, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44 141 314 0211; WoSERC3@ggc.scot.nhs.uk), ref: 19/WS/0116

### Primary study design
Observational

### Study design
Extended follow up of randomised controlled trial using electronic health records and other routinely collected data.

### Study type(s)
Other

### Health condition(s) or problem(s) studied
Cardiovascular disease, dementia, cancer

### Interventions
Record level electronic health data will be requested from NHS England and equivalent registries in Scotland & Wales. These records will be used to follow-up the original HPS2-THRIVE cohort for an extended period after the end of the main trial in 2012. No direct intervention will take place, and participants will not be contacted directly.

### Intervention Type
Drug

### Phase
Not Applicable

### Drug/device/biological/vaccine name(s)
ER niacin/laropiprant, simvastatin, ezetimibe

### Primary outcome(s)
The first planned analyses will be based on at least 15 years' follow-up from trial initiation with further analyses planned at approximately 5 yearly intervals based on on-going linkage to NHS records. Appropriate analysis methods will be used to compare the risk ratios for first occurrence post-randomisation of each outcome of interest (dementia, stroke, all major cardiovascular disorders, other vascular disease complications, myopathies, heart failure, renal impairment, other health and care outcomes and death) between both allocated treatment groups

### Key secondary outcome(s)
There are no secondary outcome measures

### Completion date
31/12/2035

## Eligibility

### Key inclusion criteria

Participants are all part of the original HPS2-THRIVE cohort (randomised between 2007 and 2010). They were between 50 and 80 years old when invited to participate. Participants had a history of one of the following:

1. History of myocardial infarction
2. Cerebrovascular atherosclerotic disease (history of presumed ischaemic stroke, transient ischaemic attack or carotid revascularisation)
3. Peripheral arterial disease (i.e. intermittent claudication or history of revascularisation)
4. Diabetes mellitus with any of the above or with other evidence of symptomatic coronary heart disease (i.e. stable or unstable angina, or a history of coronary revascularisation or acute coronary syndrome)

For inclusion into the legacy cohort, participants had to be resident in the UK

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
1. Participants who have opted out from having their data provided by NHS England
2. Participants who have read the privacy notice and have decided that they do not want their data used in this study.

### Date of first enrolment
21/06/2022

### Date of final enrolment
31/12/2035

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre

**Nuffield Department of Population Health**
Oxford Population Health
University of Oxford
Richard Doll Building
Old Road Campus
Oxford
England
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# Sponsor information

**Organisation**
University of Oxford

**ROR**
https://ror.org/052gg0110

# Funder(s)

**Funder type**
University/education

**Funder Name**
Nuffield Department of Population Health, University of Oxford

**Alternative Name(s)**
Oxford Population Health, University of Oxford, Nuffield Department of Population Health, Oxford_NDPH, Nuffield Department of Population Health of Oxford University, Nuffield Department of Population Health, NDPH

**Funding Body Type**
Government organisation

**Funding Body Subtype**
Universities (academic only)

**Location**
United Kingdom

# Results and Publications

**Individual participant data (IPD) sharing plan**

Procedures for accessing the data for this study are available on: https://www.ndph.ox.ac.uk/data-access

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |
| Protocol file | version 1.0 | 15/05/2019 | 05/08/2022 | No | No |
| Protocol file | version 1.1 | 01/08/2025 | 30/01/2026 | No | No |
| Study website | | 11/11/2025 | 11/11/2025 | No | Yes |