ISRCTN39960384 https://doi.org/10.1186/ISRCTN39960384

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

Submission date 04/08/2022	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 16/08/2022	**Overall study status** Ongoing	
Last Edited 13/12/2024	**Condition category** Other	

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 Jane Armitage (Chief Investigator)
thrive@ndph.ox.ac.uk

Study website
https://www.ctsu.ox.ac.uk/research/hps2-thrive

Contact information

Type(s)
Scientific

Contact name
Prof William Whiteley

ORCID ID
https://orcid.org/0000-0002-4816-8991

Contact details
Oxford Population Health
Nuffield Department of Population Health
University of Oxford
Old Road Campus
Oxford
United Kingdom
OX3 7LF
+44 1865 743743
william.whiteley@ed.ac.uk

Type(s)
Public

Contact name
Ms Michelle Nunn

ORCID ID
https://orcid.org/0000-0003-3195-2613

Contact details
Oxford Population Health
Nuffield Department of Population Health
University of Oxford
Old Road Campus
Oxford
United Kingdom
OX3 7LF
+44 1865 743743
michelle.nunn@ndph.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
268340

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

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

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Medical and other records

Study type(s)
Other

Participant information sheet
Not applicable (retrospective study)

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 measure
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

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
16/07/2019

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

Age group
Mixed

Sex
Both

Target number of participants
8035

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
England

United Kingdom

Study participating centre
Nuffield Department of Population Health
Oxford Population Health
University of Oxford
Richard Doll Building
Old Road Campus
Oxford
United Kingdom
OX3 7LF

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Governance, Ethics & Assurance
1st floor, Boundary Brook House
Churchill Drive
Oxford
England
United Kingdom
OX3 7GB
+44 1865 289885
rgea.sponsor@admin.ox.ac.uk

Sponsor type
University/education

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

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

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
30/06/2026

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?

Protocol file	version 1.0	15/05/2019	05/08/2022	No	No
HRA research summary			28/06/2023	No	No