

Long-term follow-up of participants in the electronic health records from the SEARCH Study

Submission date 16/08/2022	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 25/08/2022	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 13/12/2024	Condition category Other	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

The SEARCH study (<https://doi.org/10.1186/ISRCTN74348595>) was a randomised, multi-centre, factorial trial of LDL (low-density lipoprotein) cholesterol lowering, comparing higher versus standard dose simvastatin (a drug used to lower cholesterol for people diagnosed with high blood cholesterol), and homocysteine (an amino acid) lowering comparing folic acid and vitamin B12 supplementation versus placebo in 12,064 patients with an average age of 64 and with a history of heart attacks (myocardial infarction (MI)). It was run in 88 UK clinical centres for ten years. Participants in SEARCH were recruited to the trial between September 1998 and October 2001, with all final follow-up assessments completed by June 2008. Results were presented at the American Heart Association meeting in 2008 and published in the Lancet & JAMA in 2010.

SEARCH found that:

1. The allocation of simvastatin 80 mg daily versus 20 mg daily reduced LDL-cholesterol by 0.35 mmol/L and reduced major vascular events (i.e. heart attacks, strokes or coronary or non-coronary revascularisation) by 6% (95% CI 12% to +1%). This reduction was in line with expectations and contributed to the Cholesterol Trialists' Collaboration (CTT) meta-analysis that showed that more intensive LDL-cholesterol lowering produces additional benefits.
2. Supplementation with folic acid plus vitamin B12 significantly reduced homocysteine levels and is safe, but did not reduce the risk of major vascular events or cancer
3. Simvastatin 80 mg daily was associated with an increased risk of myopathy (muscle symptoms with raised blood creatine kinase) with 53 versus 2 cases respectively among those allocated 80 mg versus 20 mg simvastatin daily

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/0167)) 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/0115) to follow up on the cohort, with continued data linkage to allow for future analyses.

The purpose of this SEARCH 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 SEARCH participants recruited in UK hospitals between 1998 and 2001. 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 and is managed by researchers at the Nuffield Department of Population Health (United Kingdom)

When is the study starting and how long is it expected to run for?

July 2019 to December 2035

Who is funding the study?

University of Oxford (UK)

Who is the main contact?

Prof. Jane Armitage (Chief Investigator), search@ndph.ox.ac.uk

Study website

<https://www.ctsu.ox.ac.uk/research/search>

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

266042

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

IRAS 266042, PID14408-SP001-AC001

Study information

Scientific Title

SEARCH trial legacy study: Long-term follow-up of participants using electronic health records

Study objectives

To determine the factors that contribute to the health of UK participants of the original SEARCH trial (ISRCTN74348595) 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, United Kingdom; +44 (0) 141 314 0211; WoSERC3@ggc.scot.nhs.uk), ref: 19/WS/0115

Study design

Extended follow-up study

Primary study design

Observational

Secondary study design

Cohort study

Study setting(s)

Medical and other records

Study type(s)

Other, Treatment

Participant information sheet

No participant information sheet available

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 on the original SEARCH cohort for an extended period after the end of the main trial in 2008. No direct intervention will take place, and participants will not be contacted directly.

Intervention Type

Other

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 ongoing 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 were part of the original SEARCH cohort (randomised between 1998 and 2001). They were between 18 and 75 years old when invited to participate. Participants had to fulfil all of the following criteria:

1. History of prior myocardial infarction
2. Current use of a statin or clear indication for statin therapy
3. No clear indication for folic acid
4. No clear contraindications to the study treatments
5. No other medical problem

For inclusion into the legacy cohort, participants had to be residents of the UK

Participant type(s)

Patient

Age group

Mixed

Lower age limit

18 Years

Upper age limit

75 Years

Sex

Both

Target number of participants

12064

Key exclusion criteria

1. Participants who have opted out of 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

15/06/2022

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

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OX3 7LF

Sponsor information

Organisation

University of Oxford

Sponsor details

Research Governance, Ethics & Assurance

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rgea.sponsor@admin.ox.ac.uk

Sponsor type

University/education

Website

<https://www.ox.ac.uk/>

ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

University/education

Funder Name

University of Oxford

Alternative Name(s)

University in Oxford, Oxford University, , Universitas Oxoniensis

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 at <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	15/05/2019	17/08/2022	No	No
HRA research summary			28/06/2023	No	No