ISRCTN60635500 https://doi.org/10.1186/ISRCTN60635500

ASCEND: A study of cardiovascular events in diabetes

Submission date	Recruitment status	[_] Prospectively registered
14/07/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/09/2005	Ongoing	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
15/11/2024	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
ASCEND is a clinical trial which aimed to find out whether aspirin and/or omega-3 fatty acids (fish oils) reduced the risk of heart attacks and strokes in people with diabetes who did not already have any existing problems with their heart or blood circulation, when they started the study.
The main trial has now ended. Participants stopped taking study treatment in 2017, and results were reported in 2018. These main trial results showed that aspirin prevented serious vascular events (such as heart attacks and strokes) in these individuals, but the benefits were largely counterbalanced by an increase in major bleeds and there was no effect on the development of cancers.
ASCEND researchers continue to collect information on health outcomes by obtaining routinely collected data via central data registries and NHS sources. This Long-term Follow-up (LTFU) research will continue until 2037. The ASCEND researchers are especially interested in finding out whether taking aspirin protects against cancer, dementia/cognitive decline, or development of heart failure.
Additional information about this LTFU work is given on the study website: https://ascend.medsci.ox.ac.uk/about/long-term-study

Who can participate?
The original study participants were people who had diabetes, but did not already have cardiovascular disease. This is now a static cohort. Recruitment stopped in July 2011.

What does the study involve?
The ongoing Long-term Follow-up research is collecting Healthcare Systems Data (HSD) directly from NHS Custodians e.g. NHS England, NHS Wales (the Secure Anonymised Information Linkage Databank (SAIL), Digital Health and Care Wales (DHCW)), and NHS Scotland (Public Health Scotland (PHS) and the NHS Central Register (NHSCR)). Other Central Registries holding Healthcare Systems Data may also provide data. There is no further direct involvement for the participants.

What are the possible benefits and risks of participating?
Participants stopped study treatment in 2017 so there are no direct risks to them of the Long-

term Follow-up research. All participants were informed of the main trial results in 2018. We are no longer in contact with the participants, but disseminate data about new results via the ASCEND website.

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

When is the study starting and how long is it expected to run for?
Participants were first recruited between June 2005 and July 2011. The main trial (when participants were on active treatment) ended in 2017. The Long-term Follow-up (via Healthcare Systems Data) will continue until 2037.

Who is funding the study?
Current funding is being provided by the British Heart Foundation (BHF).
In the past the study has received funding from: the BHF, Bayer Healthcare, Abbott Laboratories, Alzheimer's Research UK, and the Macular Society.

Who is the main contact?
Professor Jane Armitage
ascend@ndph.ox.ac.uk

Study website
https://ascend.medsci.ox.ac.uk/

Contact information

Type(s)
Scientific

Contact name
Prof Jane Armitage

ORCID ID
http://orcid.org/0000-0001-8691-9226

Contact details
ASCEND Office
CTSU, Nuffield Department of Population Health
Richard Doll Building
University of Oxford
Old Road Campus
Oxford
United Kingdom
OX3 7LF
+44 (0)1865 743743
ascend@ndph.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
341798

ClinicalTrials.gov number
NCT00135226

Secondary identifying numbers
CTSU ASCEND 1

Study information

Scientific Title
A randomised 2 x 2 factorial study of aspirin versus placebo, and of omega-3 fatty acid supplementation versus placebo, for primary prevention of cardiovascular events in people with diabetes

Acronym
ASCEND

Study objectives
To determine whether 100 mg daily aspirin versus placebo and/or supplementation with 1 g daily omega-3 fatty acids or placebo prevents 'serious vascular events' (i.e. non-fatal heart attack, non-fatal stroke or death from vascular causes) in patients with diabetes who are not known to have occlusive arterial disease and to assess the effects on serious bleeding or other adverse events.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/12/2003, North West - Haydock REC (previously North West Multi-centre Research Ethics Committee) (Barlow House, 4 Minshull St, Manchester, M1 3DZ, UK; +44 2071048138; haydock.rec@hra.nhs.uk), ref: 03/8/087

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)

Prevention

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Diabetes (type 1 & 2)

Interventions
100 mg daily aspirin versus placebo and/or supplementation with 1 g daily omega-3 fatty acids or placebo.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Aspirin, omega-3 fatty acids

Primary outcome measure
Current primary outcome measure as of 15/11/2024:

Long-term Follow-up Primary Outcome:
The primary long-term efficacy assessment of aspirin will involve intention-to-treat comparisons among all randomized participants of the original allocation to aspirin versus placebo on the first occurrence of any incident gastrointestinal tract cancer.

_____

Previous primary outcome measure as of 07/05/2019:
1. The primary efficacy assessments involve intention-to-treat comparisons among all randomized participants of allocation to aspirin versus placebo and, separately, of omega-3 fatty acids versus placebo on the first occurrence of any "Serious Vascular Event" (SVE), defined as:
1.1. Non-fatal myocardial infarction; or
1.2. Non-fatal stroke (excluding confirmed intracranial hemorrhage) or TIA; or
1.3. Vascular death excluding confirmed intracranial hemorrhage (defined as International Classification of Diseases 10th revision [ICD-10] I00-52 or I63-99, i.e. excluding subarachnoid hemorrhage [I60], intracerebral hemorrhage [I61], and other non-traumatic intracranial hemorrhage [I62]).
Time frame: Randomised treatment phase during a mean of 7.4 years.
2. The primary safety assessments involve intention-to-treat comparisons among all randomized patients of allocation to aspirin versus placebo on the first occurrence of "any major bleed", defined as:
2.1. Any confirmed intracranial hemorrhage (including intracerebral, subarachnoid, subdural or any other intracranial hemorrhage); or
2.2. Sight-threatening eye bleeding; or
2.3. Any other serious bleeding episode
Time frame: Randomised treatment phase during a mean of 7.4 years.

_____

From 26/05/2016 to 07/05/2019:

Effect of aspirin versus placebo and separately omega-3 fatty acids versus placebo on serious vascular events or TIA (defined as the combination of non-fatal myocardial infarction, non-fatal stroke or vascular death, excluding confirmed cerebral haemorrhage, or TIA) at the end of the scheduled treatment period (average of 7.5 years).

_____

Original:

The combination of non-fatal myocardial infarction, non-fatal stroke or vascular death, excluding confirmed cerebral haemorrhage

Secondary outcome measures
Current secondary outcome measures as of 15/11/2024:

Long-term Follow-up Secondary Outcomes:
Secondary long-term efficacy assessments of aspirin will involve intention-to-treat comparisons among all randomized participants of the original allocation to aspirin versus placebo on the first occurrence of:
i. Any cancer (excluding non-fatal non-melanoma skin cancer);
ii. Colorectal cancer;
iii. Death from cancer;
iv. Incident GI tract cancer by time since randomization: <3; ≥3 <5; ≥5 <10; ≥10 <20; ≥20 years

_____

Previous secondary outcome measures as of 07/05/2019:

1. Secondary efficacy assessments involve intention-to-treat comparisons among all randomized participants of allocation to aspirin versus placebo and, separately, of omega-3 versus placebo on the first occurrence of the expanded vascular endpoint of "SVE or revascularization" (including coronary and non-coronary revascularizations).
Time frame: Randomised treatment phase during a mean of 7.4 years
2. Secondary efficacy assessments of aspirin involve intention-to-treat comparisons during the scheduled treatment period among all randomized participants on the first occurrence of any incident gastrointestinal (GI) tract cancer (i.e. any GI cancer excluding pancreas and hepatobiliary), overall and after exclusion of the first three years of follow-up.
Time frame: Randomised treatment phase during a mean of 7.4 years

_____

From 26/05/2016 to 07/05/2019:

1. Effect of aspirin versus placebo and separately omega-3 fatty acids versus placebo on serious vascular events in various prognostic groups at the end of the scheduled treatment period (average of 7.5 years)
2. Effect of aspirin versus placebo and separately omega-3 fatty acids versus placebo on cerebral haemorrhage at the end of the scheduled treatment period (average of 7.5 years)

Original:

1. Serious vascular event in various prognostic subgroups
2. Cerebral haemorrhage

Overall study start date
14/03/2005

Completion date
31/07/2037

Eligibility

Key inclusion criteria
1. Male or female with diabetes (Type 1 or 2)
2. Aged greater than or equal to 40 years
3. No previous history of vascular disease
4. No clear contra-indication to aspirin
5. No other predominant life-threatening medical problem

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
15,000

Total final enrolment
15480

Key exclusion criteria
The following point has been amended as of 11/02/2009:
2. Currently prescribed warfarin

Initial information at time of registration:
1. Definite history of myocardial infarction, stroke or arterial revascularisation procedure
2. Currently prescribed aspirin, warfarin or any other blood thinning medication

Date of first enrolment
14/03/2005

Date of final enrolment
31/07/2011

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
ASCEND Office
CTSU, Nuffield Department of Population Health
Richard Doll Building
University of Oxford
Old Road Campus
Roosevelt Drive
Oxford
United Kingdom
OX3 7LF

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Research Governance Ethics & Assurance (RGEA)
University of Oxford
Boundary Brook House
Churchill Drive
Oxford
England
United Kingdom
OX3 7GB
+44 (0)1865 289855
RGEA.Sponsor@admin.ox.ac.uk

Sponsor type
University/education

Website
https://researchsupport.admin.ox.ac.uk/contacts/rgea

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 15/11/2024:

The initial ASCEND results were published in 2018.
Long-term Follow-up work is ongoing and
publications for this are next planned in 2025/2026. Other ongoing work is being published regularly (see Study Outputs section).
Results are also available on the study website https://ascend.medsci.ox.ac.uk/

———

Previous publication and dissemination plan:

Planned publication in a high-impact peer reviewed journal in 2038.
Results will also be available on the study website https://ascend.medsci.ox.ac.uk/

Intention to publish date
01/12/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request. Procedures for accessing the data for this study are available at: https://www.ndph.ox.ac.uk/about/data-access-policy.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results				No	Yes
Other publications	recruitment methods	13/06/2016		Yes	No
Results article	Baseline paper	01/04/2018	01/02/2019	Yes	No
Participant information sheet	version V1	16/11/2016	07/05/2019	No	Yes
Participant information sheet	version V8	12/10/2010	07/05/2019	No	Yes
Results article	Aspirin	18/10/2018	07/05/2019	Yes	No
Results article	n-3 fatty acids	18/10/2018	07/05/2019	Yes	No
Results article	Effect of low-dose aspirin on urinary 11-dehydro-thromboxane B2 in the ASCEND (A Study of Cardiovascular Events iN Diabetes) randomized controlled trial	04/03/2023	06/03/2023	Yes	No
Results article	Reliability of major bleeding events in UK routine data versus clinical trial adjudicated follow-up data	03/06/2023	05/06/2023	Yes	No
Results article	ASCEND-Eye: Rationale, design and baseline characteristics for a sub-study of the ASCEND randomised trial	05/07/2023	25/09/2023	Yes	No
Results article	Effects of aspirin and omega-3 fatty acids on composite and subdomain scores from the NEI-VFQ-25 questionnaire: the ASCEND-Eye randomized controlled trial	05/11/2024	06/11/2024	Yes	No
Results article	ASCEND-Eye: Effects of Aspirin on Diabetic Retinopathy	01/07/2024	15/11/2024	Yes	No
Results article	ASCEND-Eye: Effects of Omega-3 Fatty Acids on Diabetic Retinopathy	01/05/2024	15/11/2024	Yes	No
Results article	Comparison of the Accuracy and Completeness of Records of Serious Vascular Events in Routinely Collected Data vs Clinical Trial-Adjudicated Direct Follow-up Data in the UK: Secondary Analysis of the ASCEND Randomized Clinical Trial	01/12/2021	15/11/2024	Yes	No
Results article	Decrements in healthrelated quality of life associated with adverse events in people with diabetes	20/12/2021	15/11/2024	Yes	No
Results article	Effects of aspirin on dementia and cognitive function in diabetic patients: the ASCEND trial	01/06/2022	15/11/2024	Yes	No
Results article	Hospital costs associated with adverse events in people with diabetes in the UK	29/06/2022	15/11/2024	Yes	No
Results article	Thromboxane biosynthesis and future events in diabetes: the ASCEND trial	14/04/2024	15/11/2024	Yes	No