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ASPirin in Reducing Events in the Elderly

Submission date 03/05/2005	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 14/07/2005	**Overall study status** Completed	[X] Statistical analysis plan [X] Results
Last Edited 28/04/2025	**Condition category** Circulatory System	[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Study website
https://www.aspree.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number
Nil known

ClinicalTrials.gov number
NCT01038583

Secondary identifying numbers
Nil known

Study information

Scientific Title
ASPirin in Reducing Events in the Elderly: a randomised controlled trial

Acronym
ASPREE

Study objectives
Added 13/01/2017: Null hypothesis as of 2010:
Daily 100 mg enteric-coated aspirin will have no benefit over placebo in prolonging life, or life free of dementia or life free of significant physical disability in healthy participants aged 70 years and over.

Hypothesis amended as of 14/03/2008:
Null hypothesis: Low-dose aspirin does not prolong life free of mental or physical disability in those aged 70 years and over who has not manifested cardiovascular disease or dementia.

Provided at time of registration:
Null hypothesis: Low-dose aspirin has no overall benefit in those aged 70 years and over who do not have manifest cardiovascular disease or dementia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. The Royal Australasian College of General Practitioners Ethics Committee, approved 2002, ref: NREEC 02/22b
2. Monash University Human Research Ethics Committee, approved 2006, ref: 2006/745MC
3. The Tasmanian Human Research Ethics Committee, approved 2006, ref: H0008933
4. The Goulburn Valley Health Ethics & Research Committee, Shepparton, approved 2007, ref: GVH-21/07
5. The ACT Health Human Research Ethics Committee, Canberra, approved 2007, ref: 11/07.997
6. The University of Adelaide Human Research Ethics Committee, approved 2011, ref: H-250-2011
7. Numerous IRBs in the USA

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Prevention

Participant information sheet

Health condition(s) or problem(s) studied
Mental and physical disability in the elderly

Interventions
Acetylsalicylic acid 100 mg: enteric coated unscored white tablet
Placebo of acetylsalicylic acid: enteric coated unscored white tablet with identical appearance

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Acetylsalicylic acid

Primary outcome measure
Amended 02/03/2009:
1. Death from any cause
2. Incident dementia, defined according to the Diagnostic and Statistical Manual for Mental Disorders 4th edition (DSM-IV) criteria
3. Persistent physical disability, defined as the onset of a lot of difficulty to inability to perform any one of 6 Katz Activities of Daily Living

Updated as of 14/03/2008:
1. Death from any cause
2. Death from incident dementia, defined according to the Diagnostic and Statistical Manual for Mental Disorders 4th edition (DSM-IV) criteria
3. Death from persistent physical disability, defined as progression by at least 2 intervals on a 5-point scale of any one of the 6 Katz Activities of Daily Living

Provided at time of registration:
1. Coronary artery disease death
2. Cardiac failure death (with coronary cause), and other coronary death
3. Cardiac failure death - due to heart failure (prior grade III-IV dyspnea New York Heart Association [NYHA]), with any defined non-coronary cause
4. Other vascular death
5. Non-coronary cardiac death
6. Cerebrovascular disease death
7. Non-fatal cardiovascular events
8. Non-fatal cerebrovascular events

Secondary outcome measures
Added 13/01/2017: Secondary outcome measures since 2009:
1. All-cause mortality

2. Fatal and non-fatal cardiovascular events including a) coronary heart disease death, b) non-fatal MI, c) fatal and non-fatal stroke, and d) any hospitalization for heart failure
3. Fatal and non-fatal cancer, excluding non-melanoma skin cancer
4. Dementia (added in 2013)
5. Mild cognitive impairment
6. Physical disability
7. Depression
8. Major hemorrhagic events

Secondary outcome measures updated as of 14/03/2008:
1. All-cause mortality
2. Fatal and non-fatal cardiovascular events including:
2.1. Coronary heart disease death
2.3. Non-fatal myocardial infarction
2.3. Fatal and non-fatal stroke
2.4. Hospitalisation for heart failure
3. Fatal and non-fatal cancer, excluding non-melanomatous skin cancer
4. Dementia
5. Cognitive decline
6. Physical disability
7. Major haemorrhagic events

Secondary outcome measures provided at time of registration:
1. All-cause dementia Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria
2. Cognitive decline - defined as 2 point decline on 3MSE supplemented by a Color Trail test
3. Clinically significant bleeding including gastrointestinal hemorrhages or hemorrhages at other sites that required transfusion, hospitalization and or surgery

Current tertiary outcome measures as of 29/08/2018:
1. Cognitive function
2. Physical performance
3. Quality of life
4. Haemoglobin levels
5. Hospitalisations - total and for reasons other than endpoints
6. Urinary albumin:creatinine ratio

Original tertiary outcome measures:
1. Haemorrhagic stroke
2. Transient ischaemic attack
3. Hospitalisation for unstable angina
4. Total mortality
5. Cognitive decline
6. Depression score
7. Quality of life
8. Disability
9. A fall in haemoglobin
10. Fatal and non-fatal cancer
11. Total hospitalisations
12. Hospitalisation for reasons other than primary endpoints
13. Institutionalisation
14. Cost-effectiveness of aspirin

15. Public health outcomes
16. Development of a multivariate model which predicts in different age strata (70-79 and 80+ years) the likelihood of death, dementia, disability, and self-assessed quality of life
17. Risk-benefit trade-off associated with the use of aspirin in different categories

Overall study start date
01/03/2003

Completion date
31/12/2017

Eligibility

Key inclusion criteria
Current inclusion criteria as of 13/01/2017:
1. African American and Hispanic men and women 65 years of age and over (in the USA), all other men and women 70 years of age and over
2. Willing and able to provide informed consent, and willing to accept the study requirements

Previous inclusion criteria:
All subjects will be aged 70 years or more and capable of attending their usual family physician's clinic and providing informed consent

Participant type(s)
Healthy volunteer

Age group
Senior

Lower age limit
65 Years

Sex
Both

Target number of participants
19,000

Total final enrolment
19114

Key exclusion criteria
Current exclusion criteria as of 13/01/2017:
1. A history of a diagnosed cardiovascular event defined as MI, congestive heart failure, angina pectoris (± nitrate use), stroke, transient ischemic attack, >50% carotid stenosis or previous carotid endarterectomy or stenting, coronary artery angioplasty or stenting, coronary artery bypass grafting, or abdominal aortic aneurysm
2. A clinical diagnosis of atrial fibrillation
3. A serious intercurrent illness likely to cause death within the next 5 years, such as terminal cancer or obstructive airways disease

4. A current or recurrent condition with a high risk of major bleeding, e.g. cerebral aneurysm or cerebral AV malformation, any bleeding diathesis, gastrointestinal malignancy, recent peptic ulcer, liver disease, esophageal varicosities, uremia, aortic aneurysm or any other condition known to be associated with a high risk of serious bleeding
5. Anemia, i.e. hemoglobin level below the normal value for the gender of the participant (males: <12 g/dL, females: <11 g/dL) (Note: Hemoglobin levels within the normal range in a participant taking therapy for anemia will not be an exclusion criterion).
6. Absolute contraindication or allergy to aspirin
7. Current participation in a clinical trial
8. Current continuous use of aspirin for secondary prevention
9. Current continuous use of other anti-platelet drug or anticoagulant
10. A systolic blood pressure ≥180 mmHg and / or a diastolic blood pressure ≥105 mmHg
11. A history of dementia or a Modified Mini-Mental State Examination (3MS) score 77 as measured at Visit 1: Lifestyle Profile and Screening
12. Severe difficulty or an inability to perform any one of the 6 Katz ADLs, as determined at Visit 1: Lifestyle Profile and Screening
13. Pill-taking compliance below 80% during the placebo run-in phase.

Previous exclusion criteria:
1. A history of cardiovascular morbidity defined as myocardial infarction, stroke, peripheral vascular disease, angina, transient ischaemic attack, greater than 50% carotid stenosis or previous carotid endarterectomy or stenting, coronary artery angioplasty or stenting, or coronary artery bypass grafting
2. A serious intercurrent illness likely to cause death within the next 5 years
3. A current or recurrent condition with a high risk of major bleeding e.g. cerebral aneurysm or cerebral arteriovenous (AV) malformation, any bleeding diathesis, gastrointestinal malignancy, peptic ulcer, liver disease, uraemia, aortic aneurysm or any other condition known to be associated with a high risk of serious bleeding
4. Absolute contraindication or allergy to aspirin
5. Current participation in a clinical trial
6. Current continuous use of aspirin or other anti-platelet drug or anticoagulant
7. A history of diabetes or dementia
8. In addition those who lie outside of tolerance levels of 8-104% during placebo run-in phase will not be randomised

The following criteria were added as of 14/03/2008:
9. An inability to perform independently one of the 6 Katz Activities of Daily Living (walking, bathing, dressing, transferring from chair or bed, toileting, eating)
10. Pill taking compliance below 80% on tablet count during a placebo run-in phase

The following criterion was amended to the below text as of 20/02/2009:
7. A history of dementia

Date of first enrolment
31/03/2010

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
Australia

United States of America

Study participating centre
Monash University
Melbourne
Australia
3004

Study participating centre
Berman Center for Clinical Outcomes Research
Minneapolis Medical Research Foundation
Hennepin County Medical Center
Minneapolis
United States of America
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Sponsor information

Organisation
Monash University (Australia)

Sponsor details
Research and Graduate Programs Office
Faculty of Medicine, Nursing and Health Sciences
PO Box 64
Victoria
Australia
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+61 (0)3 9905 1206
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Sponsor type
University/education

Website
http://www.monash.edu.au/

ROR
https://ror.org/02bfwt286

Funder(s)

Funder type
Research council

Funder Name
National Health and Medical Research Council (ref: 334047)

Alternative Name(s)
NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Funder Name
National Institute on Aging

Alternative Name(s)
U.S. National Institute on Aging, The National Institute on Aging, NIH NATIONAL INSTITUTE ON AGING, NIA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Funder Name
National Cancer Institute

Alternative Name(s)
Instituto Nacional del Cáncer, National Cancer Institute at the National Institutes of Health, Instituto Nacional del Cáncer de los Institutos Nacionales de la Salud, NCI

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United States of America

Funder Name
Monash University

Alternative Name(s)
Monash Uni | Melbourne, Monash Uni, University of Monash, Universitas Monash, MU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Australia

Funder Name
Victorian Cancer Agency

Alternative Name(s)
Victorian Cancer Agency, Department of Health and Human Services, VCA

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Australia

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	rationale	01/07/2003		Yes	No
Other publications	design	01/11/2013		Yes	No
Other publications	rationale for ASPREE-D substudy	01/10/2016		Yes	No
Other publications	baseline characteristics	12/10/2017		Yes	No
Other publications	rationale for SNORE-ASA sub-study	01/01/2018		Yes	No
Statistical Analysis Plan	statistical analysis plan	01/04/2018		No	No
Other publications	development of a standardized definition for clinically significant bleeding	22/05/2018	03/07/2019	Yes	No
Results article	results	18/10/2018	03/07/2019	Yes	No
Results article	results	18/10/2018	03/07/2019	Yes	No
Results article	results	18/10/2018	03/07/2019	Yes	No
Results article	results	09/12/2019	10/12/2019	Yes	No
Results article	results	01/05/2019	01/04/2020	Yes	No
Results article	results	27/12/2019	02/04/2020	Yes	No
Results article	results	01/09/2020	04/08/2020	Yes	No
Results article	results	01/12/2020	03/11/2020	Yes	No
Results article		01/08/2020	26/05/2021	Yes	No
Results article		01/01/2021	29/06/2021	Yes	No
Results article		01/06/2021	29/06/2021	Yes	No
Results article		06/07/2021	29/06/2021	Yes	No
Results article		01/03/2021	30/07/2021	Yes	No
Results article		01/10/2020	01/09/2021	Yes	No
Results article		26/02/2020	26/11/2021	Yes	No
Results		30/01	31/01		

article		/2023	/2023	Yes	No
Other publications	Secondary analysis	03/07 /2023	27/07 /2023	Yes	No
Other publications	Secondary analysis	21/11 /2023	27/11 /2023	Yes	No
Other publications	Associations between low sex steroid concentrations and incidence of knee and hip replacement for osteoarthritis in community-dwelling older women	14/12 /2024	19/12 /2024	Yes	No
Other publications	Frailty incidence by diabetes treatment regimens	17/03 /2025	18/03 /2025	Yes	No
Other publications	Performance of the American Heart Association PREVENT cardiovascular risk equations in older adults	28/04 /2025	28/04 /2025	Yes	No