# ASPirin in Reducing Events in the Elderly

Submission date	Recruitment status	[X] Prospectively registered
03/05/2005	No longer recruiting	<pre>Protocol</pre>
Registration date	Overall study status	[X] Statistical analysis plan
14/07/2005	Completed	[X] Results
Last Edited	Condition category	Individual participant data
18/09/2025	Circulatory System	

### Plain English summary of protocol

Not provided at time of registration

### Contact information

### Type(s)

Scientific

### Contact name

Prof John McNeil

#### Contact details

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## Additional identifiers

### Integrated Research Application System (IRAS)

Nil known

### ClinicalTrials.gov (NCT)

NCT01038583

#### Protocol serial number

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

### Study type(s)

Prevention

### 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(s)

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

### Key secondary outcome(s))

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

#### 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

### Healthy volunteers allowed

No

### Age group

Senior

### Lower age limit

65 years

#### Sex

All

### 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)

#### **ROR**

https://ror.org/02bfwt286

# Funder(s)

### Funder type

Research council

#### **Funder Name**

National Health and Medical Research Council (ref: 334047)

### Alternative Name(s)

National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, 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)

National Cancer Institute at the National Institutes of Health, Instituto Nacional del Cáncer, 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

### 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**

### Individual participant data (IPD) sharing plan

Not provided at time of registration

### IPD sharing plan summary

### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient- facing?
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 Yes /2021	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 article	30/01 /2023	31/01 /2023 Yes	No
Other rationale publications	01/07 /2003	Yes	No
Other design	01/11	Yes	No
<u>Other</u> rationale for ASPREE-D substudy	/2013 01/10	Yes	No
<u>publications</u> <u>Other</u> baseline characteristics	/2016 12/10	Yes	No
<u>publications</u> <u>Other</u> rationale for SNORE-ASA sub-study	/2017 01/01	Yes	No
<u>publications</u> development of a standardized definition for clinically significant	/2018		INO
Other publications bleeding	22/05 /2018	03/07 /2019 Yes	No
Other Secondary analysis publications	03/07 /2023	27/07 /2023 Yes	No
Other Secondary analysis publications	21/11 /2023	27/11 /2023 Yes	No
Associations between low sex steroid concentrations and incidence other knee and hip replacement for osteoarthritis in community-dwelling publications older women		19/12 /2024 Yes	No
Other Frailty incidence by diabetes treatment regimens publications	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
Other publications Associations between declining testosterone concentrations and cognitive performance	14/08 /2025	15/08 /2025 Yes	No
Other publications Long-Term Blood Pressure Variability and Physical Performance in Older Adults	17/09 /2025	18/09 /2025 Yes	No
Statistical Analysis Plan Statistical analysis plan	01/04 /2018	No	No
Study Study website website	11/11 /2025	11/11 /2025 No	Yes