



ASPREE Clinical Trial

“Does low-dose aspirin increase the healthy, active lifespan of older people?”

ASPREE Cohort Study

An infrastructure resource for Victorian research

ASPREE: scope



- Randomised, double-blind, placebo-controlled trial in healthy elderly 70yrs and above.
- 20,500 subjects randomised to daily 100 mg enteric-coated aspirin or placebo and followed annually for 5 years.
- Will reduction of vascular disease, stroke & cognitive decline outweigh adverse effects (mainly bleeding).
- Powered to detect 15% reduction in CV events
- Based on ANBP2 trial infrastructure (*New Eng J Med* 2003;348:583-91).

ASPREE STEERING COMMITTEE



- **Professor David Ames MBBS PhD FRACP**
Department of Psychiatry
University of Melbourne
- **Professor Lawrence J Beilin MD FRACP FRCP**
Department of Internal Medicine
Royal Perth Hospital, WA
- **Professor Geoffrey A Donnan MBBS MD FRACP**
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- **Professor Colin I Johnston MBBS FRACP**
Professor of Medicine
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Monash University
- **Professor John J McNeil MBBS MSc PhD FRACP**
Head, Dep of Epidemiology and Preventive Medicine
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- **Professor Mark R Nelson MBBS(Hons) MFPM
FAFPHM FRACGP PhD**
Chair of Discipline of General Practice
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- **Assoc Prof Chris M Reid BA MSc PhD**
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- **Professor Elsdon Storey MBBS D.Phil FRACP**
Head, Department of Neurosciences and Van Cleeef
Roet Center for Nervous Disease,
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- **Professor Andrew Tonkin MD FRACP**
Dep of Epidemiology and Preventive Medicine
Monash University

CANCER SUB-COMMITTEE

- **Professor Tony Burgess**
- **Dr Peter Gibbs**

COGNITION SUB-COMMITTEE

- **Professor Elsdon Storey**
- **Professor David Ames**
- **A/Professor Marc Budge**

Supporting editorials & reviews



Baigent C British Medical Journal 2005; 330:1442-1443.

“We therefore need further randomised trials comparing low dose aspirin with placebo, such as the aspirin in reducing events in the elderly (ASPREE) study 11 which aims to randomise 15 000 people aged 70 or over to aspirin 100 mg daily versus placebo. A recommendation that aspirin be used for primary prevention of vascular disease in unselected people over a certain age could result in net harm, and we must have very good evidence to the contrary before instituting such a policy.”

Patrono C et al New England Journal of Medicine, Dec 2005; 353:2373-2383.

Page 2380: “The lack of randomized trials involving older people makes it difficult to assess whether any possible benefits of aspirin would exceed the known risks of upper gastrointestinal bleeding in this age group. 84”

Page 2381: “...and the **Aspirin in Reducing Events in the Elderly study** should provide such information about patients older than 70 years of age.” (ie, the need for placebo-controlled trials in this group)

Hennekins CH et al Nature clinical Practice: cardiovascular medicine , Jan 2006; 3: 4-5.

“In order to resolve the current uncertainty, data are needed from large-scale, randomized trials of aspirin in the elderly. This is planned, for example, in the **Aspirin in Reducing Events in the Elderly (ASPREE)** trial 9, which aims to randomize 15,000 people aged 70 years or over to 100 mg aspirin daily or placebo.”

ASPREE PROTOCOL



At baseline and then annually for 5 years.

- **Demographic & social**
- **Lifestyle (smoking, alcohol, exercise, mobility)**
- **Clinical (CV parameters, glucose, CRP, lipids, Cr)**
- **Cognition, depression, disability, quality of life (SF36).**
- **Evidence of significant bleeding (haemorrhagic stroke or GI)**
- **Cardiovascular (CVD events – fatal & non-fatal MI, stroke)**
- **Dementia (clinical and 3MS / Color Trails)**
- **Cancer (incidence and tissue type)**

ASPREE Funding Partners

- funding consortium



- **Cost for ASPREE RCT is \$30 million over seven years (~\$4.5 million per annum).
ASPREE Cohort baseline study cost is additional \$3 million.**

- **Current funding in-hand (million dollars)**
 - **NHMRC project grant 3.5**
 - **Bayer provision of drug 2.5**
 - **Bayer Healthcare USA 0.33**
 - **NHF project grant 0.10**

- **Funds applied for**
 - **NIH 20.0**

- **Smaller amounts of support have been provided by the National Heart Foundation of Australia, Monash University and the Bayside Healthcare Network.**

FDA Cardiovascular and Renal Drugs Committee



“a trial that would target..people..at moderate levels of risk and...had sufficient ..follow-up..and..an even distribution of males and females...would require 1,500 events, and approximately..15,000” subjects is “...very much the study that actually needs to be done”. “With regard to a study, I think it would be profoundly difficult in the United States in 2004 to do any study except revisit low risk in those patients who sit right on the border of low and moderate risk”.

United States of America, Food and Drug Administration Centre for Drug Evaluation and Research, Cardiovascular and Renal Drugs Advisory Committee Meeting. Cardiovascular and Renal Drugs Advisory Committee. Gaithersburg: SAG Corp. Washington D.C., 2003.



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What it requires,

- Additional blood collection at baseline.
- Additional information gathering during follow-up
 - Social, behavioral, financial

What it costs,

- \$3 mill.

Advantages,

- Bio-bank
- Socioeconomic / financial information / resource
- Training / graduate opportunities
- Health service provision information
- Research base for rural clinical schools
- Capacity development in major studies

Summary: The Ducks



Experience with ANBP2



Potential of aspirin re dementia, cancer



Problems with aspirin competitors



International endorsement



Problems with aspirin studies in USA



Focus on 'public interest' studies

Plus major NHMRC funding and international support

Summary: The Opportunities:



 ***Ongoing cohort at marginal cost***

 ***Bio-bank***

 ***Research training***

 ***Capacity development for major studies***

 ***Support rural research***

 ***Attraction of research funding***

ASPREE & dementia

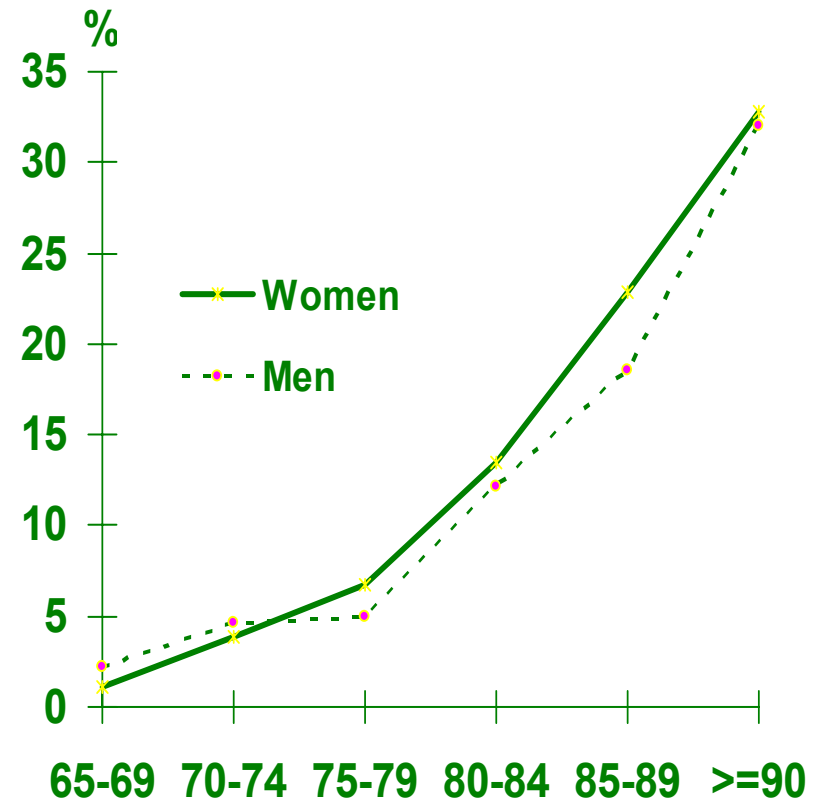


- **High prevalence :**

- 5% > 65 yrs
- 25% > 85 yrs
- 50% > 95 yrs

- **No known curative or preventive treatment**

- **Delaying onset by 1yr would reduce US cases by 800thousand***



- **Overlap of vascular dementia & Alzheimer's disease.**

**Brookmeyer et al Am J Public Health 1998*

ANBP2 infrastructure



- Family practice based
 - (2600 - 11% of all Australian family physicians).

- 6083 women and men from 54,288 screened in metropolitan and rural Australia (24,702 subject years of follow-up).

- Quality
 - Vital status ascertained in all but 2 subjects.

Purpose



- Should all healthy individuals aged 70 and above take regular low-dose aspirin

- Will the benefits outweigh the risks
 - Vascular disease (heart , stroke)
 - Cognitive decline
 - Some cancers (bowel & prostate)
 - VS
 - Hemorrhage & anaemia

- Will Rx extend the duration of healthy, non-disabled, non-institutionalised life

Other Cohort Studies



International

- Rotterdam 1989; 7,983
- US Nurses I 1976; 122,000
- US Nurses II 1989; 116,686
- ARIC 1987; 15,792

Australian

- MCCS 1990; 41,528
- Dubbo 1987; 2,805
- NSW 45 & up 2006 250,000

Issues

- Sample size of other studies
- Ageing population