Can aspirin slow cognitive decline and the onset of dementia? The ASPREE study.

Mark Nelson on behalf of ASPREE Investigators
• Randomized, double-blind, placebo-controlled trial for extending healthy active life in the elderly (70+ years, 65+ years US minorities).
• 19,000 subjects randomised to daily 100 mg enteric-coated aspirin or placebo and followed for 5 years.
• 16,000 in Australian general practice, 3,000 in USA community (mainly minorities of African-American and Hispanic).
• Proposed 16,000 Australian participants (+ 3000 US = 19,000)
• Currently 10,997 Australian participants (+ 1747 US = 12,744)
• ANBP2 6,083 Australian participants
• FIELD 6,051 Australian participants (+ 2,351 NZ + 1,393 Finland = 9,795)
• LIPID 5,958 Australian participants (+ 3,056 NZ = 9,014)
Million dollar sponsors

• (NHFA)
• Bayer Healthcare
• NHMRC
• NIH (NIA)
• Victorian state government
• CSIRO
• NCI
Screening and monitoring methods for the detection of cognitive decline and incident dementia

<table>
<thead>
<tr>
<th>Measurement/Activity</th>
<th>Lifestyle Profile &amp; Screening (Visit 1)</th>
<th>Assessments &amp; Eligibility (Visit 2)</th>
<th>Follow-up (1yr)</th>
<th>Follow-up (2yr)</th>
<th>Follow-up (3yr)</th>
<th>Follow-up (4yr)</th>
<th>Follow-up (5yr)**</th>
<th>Follow-up (6yr)**</th>
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<tr>
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<td>Dispense study medication</td>
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<td>Assess medication compliance</td>
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<td>Concomitant medications</td>
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<td>Blood pressure &amp; heart rate, height, weight &amp; abdominal circumference</td>
<td>X&lt;sup&gt;a&lt;/sup&gt;, X&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>X&lt;sup&gt;ac&lt;/sup&gt;, X&lt;sup&gt;ac&lt;/sup&gt;</td>
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<td>Laboratory testing:</td>
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<td>X&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>- Fasting blood: total cholesterol, HDL, LDL, triglyceride, glucose, creatinine &amp; hemoglobin&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>- Urine: albumin:creatinine ratio and microalbuminurea</td>
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<td>Quality of Life</td>
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<td>- SF-12</td>
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<td>Assess cognitive function</td>
<td>X&lt;sup&gt;a&lt;/sup&gt;</td>
<td>X&lt;sup&gt;b&lt;/sup&gt;</td>
<td>X&lt;sup&gt;a&lt;/sup&gt;</td>
<td>X&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>- 3MS&lt;sup&gt;a&lt;/sup&gt;, CES-D&lt;sup&gt;b&lt;/sup&gt;, SDMT&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>- HVLT-R&lt;sup&gt;b&lt;/sup&gt; &amp; COWAT&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Assess physical disability</td>
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<td>- KATZ ADLs</td>
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<td>Assess physical function</td>
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<td>- Walk test and grip strength</td>
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<td>Clinical event reporting</td>
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<td>- Questionnaire &amp; medical record review</td>
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<td>Retinal Vascular Imaging</td>
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</table>
Cognitive Measurements

- **3MS – Modified Mini-Mental State Examination**
  - Cognition and memory

- **CES-D – Center for Epidemiologic Studies - Depression**
  - Assessment of depression

- **SDMT – Symbol-Digit Modalities Test**
  - Language-independent cognition

- **HVLRT-R – Hopkins Verbal Learning Test**
  - Verbal learning and memory (recognition and recall)

- **COWAT – Controlled Oral Word Association**
  - Verbal processing ability and verbal fluency
**Dementia Assessment**

Regular cognitive function tests in ASPREE subjects
- 3MS, Hopkins VLT, SDMT, COWAT, CES-D

- **3MS < 78 or drop of 10 points**
  - ASPREE Neuropsychologist:
  - Additional cognitive tests & IADL testing (>6 weeks)
  - (ADAS-COG, Color Trails, visual agnosia, CAM + ADCS-ADL with surrogate)

- **3MS > 78**
  - Continue in study

**Dementia positive**
- Adjudication Committee (DSM-IV criteria)
  - Continue in study

**Dementia negative**
- **PRIMARY ENDPOINT**
- **MCI (SECONDARY ENDPOINT)**
  - Continue in study
  - Medication records
  - Order labs & CT/MRI
Alzheimers Dementia Assessment

Probable AD vs probable non-AD
(using McKhann et al criteria)

Current ASPREE dementia assessment process addresses the 4 main criteria to separate probable AD from probably non-AD:

A. Insidious onset (non-AD)

B. Worsening (standardised evidence of decline with 3MS and other tests)

C. Cognitive deficits (amnestic presentation (ADAS-cog & HVLT), learning & recall, language (ADAS-cog & COWAT), visuospatial (Lurian figs & pentagon in 3MS), executive dysfunction (Color trails & 3MS)

D. Exclusions (dementia assessment, CT scan, patient records, labs, neuropsychologist detection of parkinsonism).
### Baseline characteristics the first 10,000 participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All 10000</th>
<th>Australia 8465 (85)</th>
<th>US 1540 (15)</th>
</tr>
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<tbody>
<tr>
<td>N (%)</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
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<td>4241 (42)</td>
<td>5759 (58)</td>
<td>3737 (44)</td>
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<tr>
<td>Age (years)</td>
<td>75.3 (4.5)</td>
<td>75.6 (4.6)</td>
<td>75.5 (4.4)</td>
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<tr>
<td>Cognition 3MS* scores</td>
<td>92.9 (4.8)</td>
<td>94.1 (4.5)</td>
<td>92.9 (4.7)</td>
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<tr>
<td>78 – 84 N (%)</td>
<td>293 (7)</td>
<td>246 (4)</td>
<td>251 (7)</td>
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<tr>
<td>85 – 89 N (%)</td>
<td>599 (14)</td>
<td>614 (10)</td>
<td>538 (14)</td>
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<tr>
<td>90 – 94 N (%)</td>
<td>1454 (34)</td>
<td>1700 (30)</td>
<td>1300 (35)</td>
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<tr>
<td>≥ 95 N (%)</td>
<td>1895 (45)</td>
<td>3199 (56)</td>
<td>1648 (44)</td>
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<tr>
<td>Lifestyle factors N (%)</td>
<td></td>
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<tr>
<td>Live alone</td>
<td>865 (20)</td>
<td>2506 (44)</td>
<td>756 (20)</td>
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<tr>
<td>Residential care</td>
<td>11 (0.3)</td>
<td>37 (1)</td>
<td>9 (0.2)</td>
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</table>
ASPREE Healthy Ageing Biobank
ENVIS-ion
SNORE-ASA
ALSOP
ASPREE Healthy Ageing Biobank

- To study factors in the blood and urine that may contribute to health or disease in older Australians.

- Collect biospecimens (10,000 volunteers) before the onset of disease and store until future testing of novel predictors of disease or health.
• Provide high quality data & biospecimens for applied health sciences & epidemiology for many years to come
• Future case-control studies
• Identification of new predictive biomarkers
• Better targeting of existing prevention strategies
• Unique database to guide health and social policy in older Australians

Improving the health of older Australians
BIOBUS

BIOBANK
ENVIS-ion

Aspirin for the prevention of cognitive decline in the Elderly: a Neuro-Vascular Imaging Study

- Neuro-imaging sub-study of ASPREE
- NHMRC funded
- 300 in Melbourne, 300 in Canberra
- Brain MRI, retinal VI at baseline and 3 yr
- Anatomical correlates and explanation for aspirin benefit on cognitive decline
SNORE-ASA

A Study of Neurocognitive Outcomes, Radiological and retinal Effects of Aspirin in Sleep Apnoea

• NHMRC funded (2012 – 2016)
• 3300 Apnealink + additional neurocognition tests + sleep questionnaire
• 365 neuro-imaging in Melbourne (brain MRI + RVI)
ALSOP
ASPREE Longitudinal Study of Older Persons

- Questionnaires focused on
  - Medical
  - Social Health
  - Health Services
- Cohort study – Framingham / Rotterdam
- Epidemiology – factors influencing health and disease outcomes