

## **Questions and Answers about ASPREE Trial**

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## Q&A for ASPREE website (US)

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### What is the ASPREE Trial?

ASPREE (**AS**pirin in **R**educing **E**vents in the **E**lderly) is an international randomized, double-blind, placebo-controlled trial in 19,114 older people (16,703 in Australia and 2,411 in the United States). There were approximately 9,500 people in both the aspirin group and the placebo group. The study started in 2010 and enrolled participants mostly aged 70 years and older. The trial finished in 2017. We are now reporting the results.

### The trial was randomized, double-blind and placebo-controlled. What does this mean?

- Randomized means that people were asked to take either aspirin or placebo purely by chance, as with the toss of a coin.
- Placebo-controlled means that people were asked to take either low-dose aspirin or an identically appearing but inactive tablet.
- Double-blind means that neither the research staff nor the participant knew whether they were taking aspirin.
- This approach is considered the scientific gold standard for testing the effects of a treatment.

### What was the goal of this trial?

The main goal of the study was to study the value of daily low-dose aspirin in healthy older people. In particular, we wanted to see if aspirin would increase survival free of persistent physical disability or dementia in healthy older people. ASPREE is the first clinical trial to do this.

Current guidelines recommend daily, low-dose aspirin for people who have had a heart attack or stroke to help prevent that event from re-occurring. The ASPREE study did not evaluate the use of low-dose aspirin for this purpose.

Many previous studies in middle-aged people have shown that low-dose aspirin reduces the risk of a first heart attack or stroke. Results from those studies have been applied to older people, in the absence of direct evidence in that age group.

Millions of people around the world take aspirin to prevent the onset of heart disease, stroke and possibly other conditions as well. Many of these people have never had a heart attack or stroke, but we didn't know whether aspirin could help healthy older people live longer and healthier lives by delaying the onset of illnesses. In addition, aspirin is known to have adverse effects, such as bleeding and reduced blood clotting, which may offset any benefits.

### What were the major results from ASPREE?

The study did not find a significant difference between the aspirin and placebo groups on the primary outcome of survival free of persistent physical disability or dementia. The results showed that daily low-dose aspirin, taken for approximately four and a half years by healthy older people enrolled in ASPREE, had no discernible benefit. Across the

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population studied, daily low-dose aspirin had no measured benefits in preventing heart disease, physical disability, dementia, or stroke.

ASPREE results also showed that daily low-dose aspirin increases the risk of bleeding, which is a well-known side effect of aspirin. This finding was expected and was consistent with results from many other aspirin studies.

### What do we know now that we didn't know before the trial began?

Based on these results, we know that for healthy people over age 70, like the ones enrolled in ASPREE, daily use of low-dose aspirin does not extend healthy life span.

### If I'm taking aspirin now, should I stop? Do the ASPREE results mean that older healthy people who are currently taking aspirin to prevent heart disease should stop taking it?

ASPREE's results apply primarily to starting aspirin use rather than continuing aspirin use. Only 11 percent of ASPREE participants had been taking aspirin before the study started. ASPREE does not provide definitive evidence about health effects of stopping vs. continuing low-dose aspirin in healthy older persons who are currently taking it.

Healthy older people who have or had been regularly using aspirin for preventing disease should consult their physicians, who can provide individuals with advice based on their risks for cardiovascular and other diseases, as well as other factors.

### To whom do the ASPREE results apply?

ASPREE participants were healthy persons age 70 or older, and these findings apply to that group.

The very small size of the U.S ASPREE group age 65-69 (Hispanics and African Americans) who were enrolled in the trial prevents us from making firm conclusions about effects of aspirin in this age range.

It is important to remember that the ASPREE results do not apply to older people who are taking aspirin because they have cardiovascular disease, for example those who have had a heart attack or stroke or suffer from angina. Current clinical guidelines support the use of aspirin, or another anti-platelet agent, for preventing further cardiovascular events in this group (who were not included in ASPREE).

### Do the ASPREE findings mean that healthy people over 70 should not take low-dose ASPIRIN for disease prevention?

Overall, ASPREE found that there was no evidence of benefit for healthy persons over the age of 70 years to take daily, low-dose (100mg/day) aspirin. ASPREE's findings are

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based on averaged results from a very large group of diverse individuals who differed in many factors.

Doctors are best to give advice on their patients' health care including the use of aspirin. They will consider ASPREE's results along with an individual's health risks and medical history to assess whether or not to initiate or continue aspirin use.

### What about the use of aspirin occasionally to treat pain or reduce fever?

These results apply to regular (daily) low-dose aspirin use only. They do not apply to the occasional use by adults of aspirin for other reasons such as to reduce fever or treat pain.

### What's next for ASPREE participants?

Trial participants have been mailed a letter and notified of the study results and which medication they were taking. They are aware that there are a lot of analyses of the extensive ASPREE data still to be conducted and results reported.

Trial participants have also been invited to enroll in a long-term study of continuing surveillance of their health, following the cessation of trial medication. The study staff will continue to report any clinical measures collected during this follow-on study.

### How many people participated in this trial?

ASPREE participants included a little over 19,000 participants. 16,703 people from Australia and 2,411 people from the United States participated. Study participants were monitored for just over 4 ½ years during the intervention phase and will continue to be monitored.

### Who was eligible to participate in ASPREE? Were there restrictions on eligibility?

ASPREE enrolled participants aged 70 years and above, except for Hispanic and African American groups in the U.S., for whom the minimum age of entry was 65 years. In Australia, the minimum age was 70. There was no upper age limit.

People were excluded from enrolling in the trial if they had:

- a history of a diagnosed cardiovascular event or a serious illness likely to cause death within the next 5 years, such as terminal cancer or obstructive airways disease
- a current or recurrent condition with a high risk of major bleeding, such as bleeding ulcer or cerebral aneurysm
- a medical reason to be taking aspirin or another anti-platelet drug or anticoagulant
- anemia
- a history of dementia
- an allergy to aspirin

## What were the characteristics of the U.S. and Australian groups?

### **U.S. participants**

- ASPREE was conducted through 34 clinical trial centers in the U.S.
- Recruitment began in March 2010 and closed in December 2014.
- The study was led by Professor Anne Murray, M.D., M.S. of the Berman Center for Outcomes and Clinical Research, part of the Hennepin Healthcare Research Institute in Minneapolis.
- The trial included 2,411 people in the U.S. (12.6 percent of the total study population). African-American or Hispanic participants were age 65 or older at study enrollment, representing approximately half of the U.S. participants.

### **Australian participants**

- ASPREE was primarily conducted through general practices in south-eastern Australia and 16 study sites.
- Recruitment began in 2010 and closed in December 2014.
- The study was led by Professor John McNeil MBBS, PhD of Monash University in Melbourne.
- The Australian cohort included 16,703 people age 70 and older (87.4 percent of the total study population).
- Nearly 50% of Australian participants were from regional and rural areas.
- In Australia, several ancillary studies are investigating the effect of aspirin on specific diseases, including age-related macular degeneration, cancer, osteoarthritis, bone fractures, severe infection, sleep apnea, age-related hearing loss, and microvascular changes in the brain.