FULL-LENGTH ARTICLE NPub.org/wn3t9a

Randomized placebo-controlled trial of the effects of aspirin on dementia and cognitive decline

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Study objective

To investigate the effects of low-dose aspirin on the risks of incident all-cause dementia, Alzheimer disease (AD), mild cognitive impairment (MCI), and cognitive decline in older individuals.

Classification of evidence: Class II.

What is known and what this paper adds

Observational studies suggest that NSAIDs can reduce the risk of cognitive decline and dementia in the elderly. This clinical trial did not find such effect.

Participants and setting

Secondary analysis of data from 19,114 people in the US and Australia enrolled in the Aspirin in Reducing Events in the Elderly (ASPREE) trial who were ≥70 years old (or ≥65 years old in the case of minorities in the US); free of cardiovascular disease, physical disability, and dementia; and expected survival ≥5 years at baseline.

Design, size, and duration

Patients randomized to aspirin (100 mg daily) or placebo had a cognitive screen at baseline and every 2 years including tests for global cognition (3 MS), episodic memory (HVLT-R), language and executive function (COWAT), and psychomotor speed (SDMT). If the screen was abnormal, patients were considered to reach a dementia "trigger" (DeTr) and had testing with the ADAS-Cog, Color Trails, Luria overlapping figures, and the ADCS-ADL scale. Dementia was diagnosed using DSM-IV criteria and classified as probable or possible AD using 2011 NIA-AA core criteria. MCI was diagnosed when a DeTr, but not dementia criteria, was met. Cox proportional-hazards models were used for between-group comparisons of cognitive outcomes.

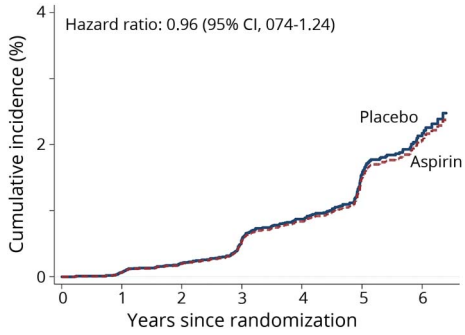
Primary outcome measures

The primary outcome was the association of aspirin use and incident AD, MCI, and cognitive decline.

Main results and the role of chance

The trial was stopped early for futility. After a median of 4.7 years (IQR, 3.6–5.7 years), 488 patients on aspirin and 476 on placebo (11.6/1,000 person-years [PY] vs 11.3/1,000 PY) reached the DeTr (HR 1.03, 95% CI 0.91–1.17). Dementia was diagnosed in 575 patients (41% AD; 6.7/1,000 PY vs 6.9/1,000 PY) and MCI in 389 participants (22% MCI due to AD.) There was no difference in the risk of probable AD (HR, 0.96; 95% CI, 0.74–1.24), MCI (HR, 1.12; 95% CI, 0.92–1.37), or cognitive decline (HR, 1.04; 95% CI, 0.94–1.14).

Figure Cumulative incidence plot for probable AD in the aspirin (red) and placebo (blue) groups



Harms

The aspirin group had a greater risk of major bleeding (HR, 1.38; 95% CI, 1.18–1.62) and higher mortality rate (HR, 1.14; 95% CI, 1.01–1.29).

Bias, confounding, and other reasons for caution

Relatively few cases of incident MCI and dementia occurred.

Study funding/potential competing interests

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Trial registration number

NCT01038583 on ClinicalTrials.gov.

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