ASPIRIN IN THE HEALTHY ELDERLY, IS THE RISK WORTH THE BENEFIT?

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LEARNING OBJECTIVE

- Discuss the risks of cardiovascular (CV) disease and major bleeding associated with aspirin use in the healthy elderly

BACKGROUND

- Current guidelines have noted that there is limited evidence regarding the use of aspirin for primary prevention of CV disease in the elderly
- Aspirin is a well-established therapy for the secondary prevention of CV events
- Low-dose aspirin is among the most widely used agents for reduction of CV disease and stroke

McNeil, J. et al. (2018).*NEJM*. 379(16):1509-1518.

EFFECT OF ASPIRIN ON CARDIOVASCULAR EVENTS AND BLEEDING IN THE HEALTHY ELDERLY.

NEJM. 2018 379(16): 1509-1518.

Purpose: Evaluate the effect of low-dose aspirin in community-dwelling older adults

Intervention: Randomized 1:1 to either aspirin 100mg daily or placebo

Outcomes: Major hemorrhage and cardiovascular disease

- Secondary endpoints of ASPREE trial (ClinicalTrials.gov number, NCT01038583.)

McNeil, J. et al. (2018).*NEJM*. 379(16):1509-1518.

METHODS

Inclusion Criteria

- 70 years and older (≥ 65 years if Hispanic or black)

Exclusion Criteria

- Anticoagulant or antiplatelet use
- Cardiovascular disease
- Dementia
- Disability
- Contraindication to aspirin
- SBP ≥180 mm Hg and/or DBP ≥105 mm Hg
- Presence of condition likely to result in death within 5 years

McNeil, J. et al. (2018).*NEJM*. 379(16):1509-1518.

METHODS

Prespecified end points

- Cardiovascular disease
  - Fatal coronary heart disease
  - Nonfatal myocardial infarction
  - Fatal or nonfatal stroke
  - Hospitalization for heart failure
- Major hemorrhage
  - Hemorrhagic stroke
  - Symptomatic intracranial bleeding
  - Clinically significant intracranial bleeding

Non-prespecified end point

- Major adverse cardiovascular event
  - Fatal coronary heart disease (excluding death from heart failure)
  - Nonfatal myocardial infarction
  - Fatal or nonfatal ischemic stroke

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RESULTS

- 19,411 total participants
  - Aspirin: 9,525
  - Placebo: 9,589
- Similar CV risk profiles
- Median age: 74 years
- Median follow-up: 4.7 years

Table 1. Demographic Characteristics, Cardiovascular Risk Factors, and Treatment of the Participants at Randomization.*

Variable	Aspirin (N = 9525)	Placebo (N = 9589)
	no. (%)	
Male sex	4152 (44)	4179 (44)
Age ≥74 yr	4806 (50)	4766 (50)
Black race†	451 (5)	450 (5)
Obese‡	2820 (30)	2857 (30)
Smoking		
Current	352 (4)	383 (4)
Former	3909 (41)	3890 (41)
Never	5264 (55)	5316 (55)
Diabetes§	1027 (11)	1030 (11)
Hypertension¶	7065 (74)	7148 (75)
Dyslipidemia‖	6159 (65)	6308 (66)
Chronic kidney disease**	2456 (26)	2464 (26)
Number of cardiovascular risk factors††		
0 or 1	2935 (31)	2885 (30)
2	3968 (42)	4049 (42)
3 or 4	2622 (28)	2655 (28)
Previous regular aspirin use‡‡	1053 (11)	1041 (11)
Statin use at trial entry§§	3244 (34)	3226 (34)
Use of nonsteroidal antiinflammatory drug at trial entry	1371 (14)	1342 (14)
Use of H_2-receptor blocker at trial entry	189 (2)	183 (2)
Use of proton-pump inhibitor at trial entry	2340 (25)	2374 (25)

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RESULTS

End Point	Aspirin (per 1000 person-years)	Placebo (per 1000 person-years)	Hazard Ratio (95% CI)	P value	
CV Disease	10.7	11.3	0.95 (0.83 - 1.08)	---	NNT= 418
Major CV Events	7.8	8.8	0.89 (0.77 - 1.03)	---	NNT= 236
Major Hemorrhage	8.6	6.2	1.38 (1.18 - 1.62)	< 0.001	NNH= 97

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DISCUSSION

- Primary endpoint of the ASPREE trial failed to show a significant survival benefit
- Secondary endpoints have demonstrated there is no significant reduction of CV disease or major CV events but, a significant increase in major hemorrhage associated with aspirin therapy
- Major hemorrhagic events primarily attributed to upper gastrointestinal bleeding and intracranial hemorrhage.
- The observed rate of CV disease was approximately half of the anticipated rate.
  - Likely due to the relatively good health of the participants
- Results are compatible with recent meta-analysis of 8 primary prevention trials which demonstrated higher risk of serious bleeding in the aspirin group
- Limitation:
  - Only approximately 2/3 of the participants were still taking the assigned trial intervention at completion

McNeil, J. et al. (2018).*NEJM*. 379(16):1509-1518.
Guirguis, B. et al. (2016).*Ann Intern Med.* 164(12):804-13.

DISCUSSION

AMERICAN COLLEGE of CARDIOLOGY

Arnett et al.
2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

4.6. Aspirin Use

Recommendations for Aspirin Use Referenced studies that support recommendations are summarized in Online Data Supplements 17 and 18.		
COR	**LOE**	**Recommendations**
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (S4.6-1–S4.6-8).
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age (S4.6-9).
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding (S4.6-10).

CONCLUSIONS

- Low-dose aspirin did not result in significantly lower risk of CV disease or major CV adverse events
- Low-dose aspirin was associated with significantly higher risk of major bleeding
- The common practice of using aspirin for primary prevention, is now questioned in light of this data

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ASSESSMENT QUESTION

- True or False?

The use of low-dose aspirin in the healthy elderly significantly lowers the risk of CV disease compared to placebo.

FALSE