

Aspirin Use to Prevent Cardiovascular Disease

US Preventative Services Task Force Recommendation Statement

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Cecilia Mathis, MD

Brigette Schuman, DO

Family Medicine Residency Spokane (Providence Health)

Objectives

- Understand the new USPSTF recommendations on aspirin use in primary prevention of CVD.
- Understand how the new recommendations differ from the 2016 recommendations.
- Discuss the changes in recommendations to aspirin use in CRC.
- Discuss how to apply these recommendations to clinical practice including when to stop aspirin therapy.

Introduction

- New recommendations change long-time primary care practice
- Cardiovascular disease (CVD) is the leading cause of mortality in the US
 - More than 1 in 4 deaths
- Colorectal Cancer is the third leading cause of death.
- Each year, an estimated 605,000 people in the US have a first myocardial infarction
- Each year, an estimated 610,000 experience a first stroke.

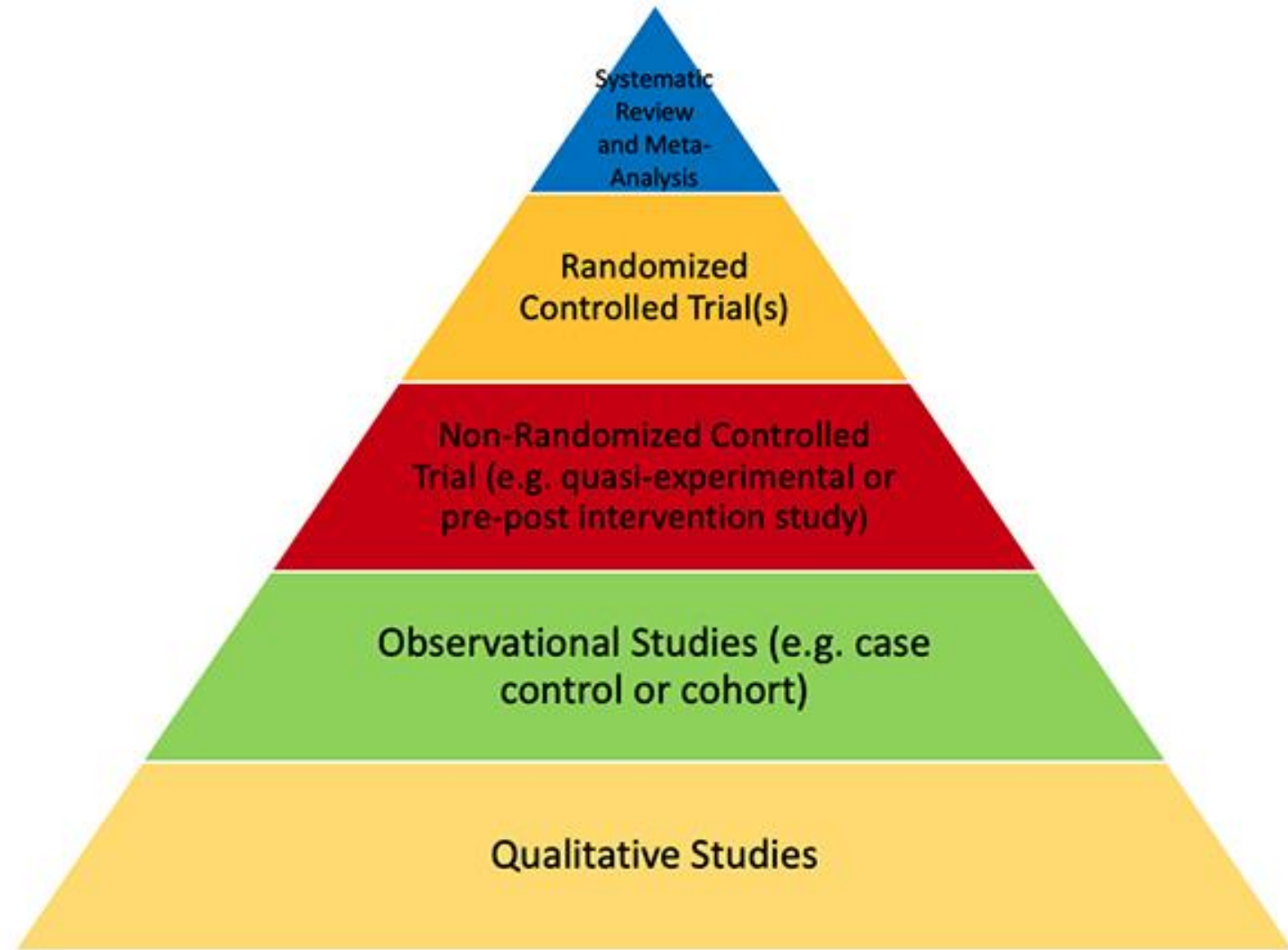
Population

- Adults 40 years or older without signs or symptoms of CVD or known CVD
 - Including history of myocardial infarction or stroke
 - Who are not at increased risk for bleeding
- Increased risk of bleeding includes:
 - History of gastrointestinal ulcers
 - Recent bleeding
 - Use of medications that increase bleeding risk
- Populations not included:
 - < 40yrs of age
 - ASCVD risk < 5%

Methods

- USPSTF completed a systematic review on the effectiveness of aspirin to reduce the risk of CVD events (MI and stroke), cardiovascular mortality, all-cause mortality, CRC incidence and mortality.
- Included 13 randomized controlled trials (RCTs) involving 161,680 participants that reported on the benefits of aspirin use for the primary prevention of cardiovascular morbidity and mortality.
- Most trials used:
 - Low-dose aspirin of 100 mg/d or less or aspirin every other day
 - Included a balanced number of male and female participants
 - Broad distribution of ages (mean age ranging from 53 years in the Physicians' Health Study to 74 years in the Aspirin in Reducing Events in the Elderly (ASPREE) trial)

Methods



Methods

- A decision analysis of the data was completed using a microsimulation model.
 - Assess the net benefits and harms of aspirin
- Peto Odds Ratio
- Outcomes: Net Quality Adjusted Life Years (QALYs) and net life years gained or lost.

Results

- Adults ages 40 to 59 yrs of age:
 - 10% or greater 10yr ASCVD risk
 - Small net benefit of aspirin use in this group.
 - Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit. **(C recommendation)**
- Adults >60yrs of age:
 - Recommends against initiating low-dose aspirin use for the primary prevention of CVD **(D recommendation)**
- The evidence is unclear whether aspirin use reduces the risk of colorectal cancer incidence or mortality.

Results

- Low dose aspirin was associated with 12% decreased risk of nonfatal MI: OR 0.88 [95% CI, 0.80-0.96) (statistically significant)
- Low dose aspirin was associated with 12% decreased risk of ischemic stroke: OR 0.88 [95% CI, 0.78-1.00] P = 0.046
- Not associated with statistically significant effect on fatal MI, fatal stroke, CVD mortality, or all cause mortality

Case 1

- 50 yo M with a 10% 10 yr ASCVD risk, no prior history of CVD nor at increased risk for GI bleed, what would be his adjusted 10-year risk of having a heart attack if he was started on aspirin?

Results

- Aspirin use was associated with a 58% increase in major GI bleeding: OR 1.58
- Aspirin use was associated with a 31% increase in intracranial bleeds: OR 1.31

Case 2

- 50 yo M with a 0.05% risk of major bleed, how much would his risk of GI bleeding increase if he was started on aspirin?

Case 2

- 70 yo M with a 0.22% risk of major bleed, how much would his risk of GI bleeding increase if he was started on aspirin?

Case 2

- 80 yo M with a 0.6% risk of major bleed, how much would his risk of GI bleeding increase if he was started on aspirin?

Figure 2. Quality-Adjusted Life-Years and Life-Years Gained: Lifetime Net Benefit of Initiating Aspirin Use for Women and Men With Lifetime Use

	Mean (95% CI)				
	Initiation age 40-49 y	Initiation age 50-59 y	Initiation age 60-69 y	Initiation age 70-79 y	
Women					
Net life-years per 1000 persons					
10-y CVD risk, %					
7.5	-2.6 (-10.0 to 4.7)	-11.8 (-18.7 to -5.0)	-20.2 (-25.6 to -14.9)	-15.4 (-19.0 to -11.8)	
10	11.4 (3.2 to 19.7)	-6.5 (-13.6 to 0.7)	-13.5 (-18.7 to -8.4)	-16.6 (-20.0 to -13.2)	
15	17.7 (9.8 to 25.5)	7.5 (0.9 to 14.1)	-7.2 (-12.3 to -2.1)	-17.9 (-21.9 to -14.0)	
20	24.2 (15.7 to 32.7)	16.9 (9.7 to 24.1)	-1.6 (-6.8 to 3.6)	-14.8 (-18.6 to -11.0)	
Net QALYs per 1000 persons					
10-y CVD risk, %					
7.5	19.6 (12.3 to 26.8)	10.4 (3.9 to 16.9)	-5.8 (-10.9 to -0.7)	-6.4 (-10.0 to -2.8)	
10	35.1 (27.3 to 43.0)	17.1 (10.2 to 24.0)	2.3 (-2.7 to 7.4)	-6.1 (-9.4 to -2.7)	
15	43.0 (35.4 to 50.5)	30.8 (24.5 to 37.2)	11.6 (6.9 to 16.4)	-6.9 (-10.7 to -3.0)	
20	50.4 (42.3 to 58.5)	41.6 (34.8 to 48.5)	19.1 (14.2 to 24.1)	-4.4 (-8.1 to -0.7)	
Men					
Net life-years per 1000 persons					
10-y CVD risk, %					
7.5	16.2 (9.0 to 23.5)	0.4 (-6.1 to 6.9)	-6.7 (-11.5 to -1.9)	-10.1 (-13.4 to -6.8)	
10	36.1 (28.1 to 44.1)	4.2 (-2.3 to 10.8)	-3.0 (-8.0 to 1.9)	-6.9 (-10.5 to -3.4)	
15	37.9 (29.6 to 46.2)	18.6 (11.7 to 25.4)	-2.2 (-7.2 to 2.9)	-7.6 (-11.3 to -3.9)	
20	52.4 (43.9 to 60.9)	33.9 (26.9 to 40.9)	4.9 (-0.1 to 10.0)	-5.5 (-8.8 to -2.2)	
Net QALYs per 1000 persons					
10-y CVD risk, %					
7.5	29.1 (22.3 to 36.0)	12.5 (6.5 to 18.5)	2.6 (-1.9 to 7.2)	-4.6 (-7.7 to -1.5)	
10	48.0 (40.6 to 55.5)	18.0 (12.0 to 24.0)	7.0 (2.2 to 11.8)	-1.1 (-4.4 to 2.2)	
15	52.3 (44.5 to 60.1)	32.3 (26.2 to 38.5)	8.3 (3.5 to 13.0)	-1.9 (-5.4 to 1.6)	
20	66.2 (58.2 to 74.1)	48.4 (41.9 to 54.8)	16.3 (11.4 to 21.1)	0.9 (-2.2 to 3.9)	

Yellow shaded cells indicate persons to whom the C grade recommendation applies. CVD indicates cardiovascular disease; QALY, quality-adjusted life-year.

What's new from USPSTF?

- Changed the age ranges and grades of its recommendation on aspirin use.
- Current recommendations consider initiating aspirin in persons with an estimated 10% or greater CVD risk at a younger age: 40 years instead of 50 years.
- There is a new recommendation not to initiate aspirin in adults 60 years or older for primary prevention.
- The evidence is unclear whether aspirin use reduces the risk of colorectal cancer incidence or mortality.

When to stop:

- Risk for bleeding increases modestly with advancing age.
- For persons who have initiated aspirin use, the net benefits continue to accrue over time in the absence of a bleeding event.
- When looking at net lifetime benefit of continuous aspirin use until stopping at age 65, 70, 75, 80, or 85 years, modeling data suggested that there is generally little incremental lifetime net benefit in continuing aspirin use beyond the age of 75 to 80 years.
- The net benefits become progressively smaller with advancing age because of an increased risk for bleeding, and modeling data suggest that it may be reasonable to *consider stopping aspirin use around age 75 years.*

Discussion

- What is the difference between starting age for aspirin and the patient's current age?
- What about secondary prevention?

Colorectal Cancer Summary

- Four studies conducted in primary CVD prevention populations found no association between aspirin use and CRC incidence (10 yr follow-up).
- WHS (n=39,876) reported on the effect of low dose aspirin beyond 10 years with posttrial observational follow-up. Initially reported a lower incidence of CRC (OR 0.82), recent data showed that this effect did not persist from 17.5 to 26 years of follow-up.
- ASPREE trial reported higher CRC mortality at 4.7 years with aspirin use
- Thrombosis Prevention Trial (n=5085), statistically significant lower risk of CRC mortality at 18.3 years of follow-up (OR 0.62)

Additional Information:

- Age is one of the strongest risk factors for CVD.
- For patients who are eligible and choose to start taking aspirin, the benefits become smaller with advancing age.
- Males have a higher prevalence of CVD than females. Among both sexes, Black persons have the highest prevalence of CVD.
- Current research shows that 23.4% of individuals > 40 yrs old are currently on aspirin, and of that group, 22.8% started without physician recommendation.

Research Needs and Gaps

More research is needed to evaluate the following:

- Improving the accuracy of CVD risk prediction in all racial and ethnic and socioeconomic groups.
- Investigating the gastrointestinal bleeding risk associated with aspirin use in populations representative of the US primary CVD prevention population.
- Developing bleeding risk calculator.
- The effects of low-dose aspirin use on CRC incidence and mortality over the long term (10 to 20 years and longer) in primary prevention populations and in the context of current CRC screening practices.