Baptist Health
HEART INSTITUTE

Antithrombotics: Where Has All the Aspirin Gone?

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Disclosures: None

LEARNING OBJECTIVES

- Review current evidence on aspirin use in prevention and treatment
- Discuss changes in recommendations for antithrombotic therapy
- Select appropriate antithrombotic strategies in different patient scenarios

SCOPE

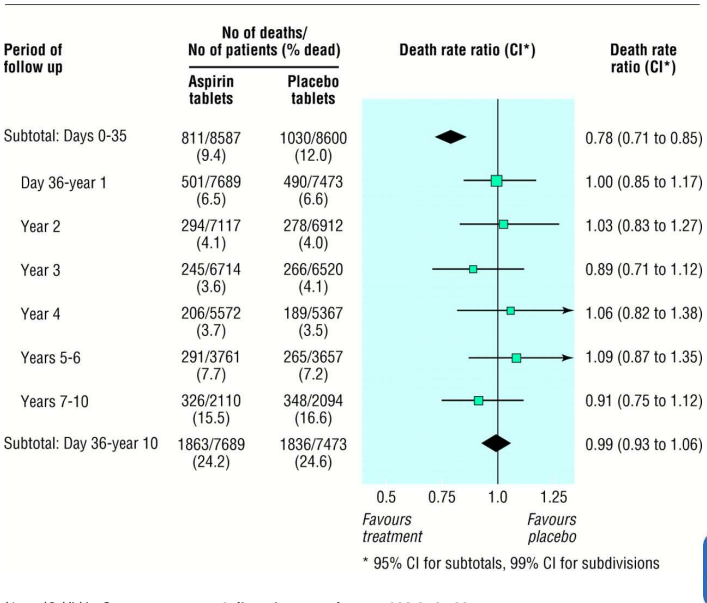
- Cardiovascular disease (CVD) is leading cause of death in US
  - Accounts for > ¼ deaths
  - ~ 605,000 have first MI
  - ~ 610,000 have first stroke

JAMA (2022), *327* (16), 1577-1584

KEY STUDIES IN ASPIRIN HISTORY

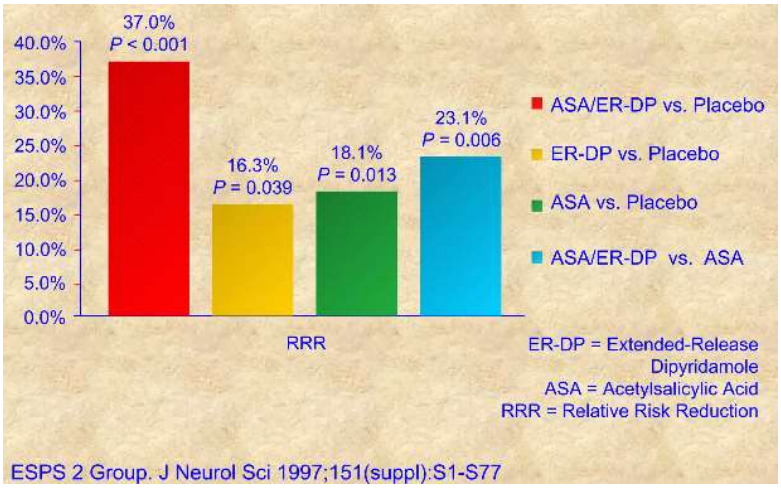
- ISIS-2
  - Significant reductions in vascular death, reinfarct, and stroke in patients with acute MI
- ESPS-2
  - Showed ASA effectiveness at secondary prevention of ischemic stroke
- Women's Health Study
  - Low-dose ASA for primary prevention in females > 65 and former/never smokers
- ASPREE
  - Bleeding risks > benefits for primary prevention in older adults without established CVD

Proportional effects of aspirin on death during days 0-35 and day 36 to 10 years



Colin Baigent et al. BMJ 1998;316:1337

ESPS-2



WOMEN'S HEALTH STUDY

Table 3. Incidence and Relative Risk of Cardiovascular Events, According to Baseline Characteristics.*

Group	Total No.	Major CV Event				Stroke				Ischemic Stroke				Myocardial Infarction			
		Asp	Pla	RR (95% CI)	P Value	Asp	Pla	RR (95% CI)	P Value	Asp	Pla	RR (95% CI)	P Value	Asp	Pla	RR (95% CI)	P Value
		no.				no.				no.				no.			
Age																	
45–54 yr	24,025	163	161	1.01 (0.81–1.26)	0.92	77	90	0.85 (0.63–1.16)	0.31	57	71	0.80 (0.57–1.14)	0.21	69	56	1.23 (0.87–1.75)	0.25
55–64 yr	11,754	183	186	0.98 (0.80–1.20)	0.84	76	90	0.84 (0.62–1.14)	0.26	60	75	0.80 (0.57–1.12)	0.19	88	75	1.17 (0.86–1.59)	0.32
≥65 yr	4,097	131	175	0.74 (0.59–0.92)	0.008	68	86	0.78 (0.57–1.08)	0.13	53	75	0.70 (0.49–1.00)	0.05	41	62	0.66 (0.44–0.97)	0.04
Smoking status																	
Current	5,235	157	127	1.30 (1.03–1.64)	0.03	63	58	1.14 (0.80–1.63)	0.48	50	46	1.14 (0.76–1.70)	0.52	76	53	1.50 (1.06–2.13)	0.02
Past or never	34,605	319	392	0.80 (0.69–0.93)	0.003	157	207	0.75 (0.61–0.92)	0.006	119	174	0.67 (0.53–0.85)	0.001	122	139	0.87 (0.68–1.10)	0.25

ASPREE

Cause of Death	Overall (N=19,114)	Aspirin (N=9525)	Placebo (N=9589)	Hazard Ratio (95% CI)
	no. of deaths	*no. of deaths (%)*		
Any	1052	558 (5.9)	494 (5.2)	1.14 (1.01–1.29)
Cancer†	522	295 (3.1)	227 (2.3)	1.31 (1.10–1.56)
Cardiovascular disease, including ischemic stroke‡	203	91 (1.0)	112 (1.2)	0.82 (0.62–1.08)
Major hemorrhage, including hemorrhagic stroke§	53	28 (0.3)	25 (0.3)	1.13 (0.66–1.94)
Other¶	262	140 (1.5)	122 (1.3)	1.16 (0.91–1.48)
Insufficient information‖	12	4 (<0.1)	8 (0.1)	—

ASPIRIN INDICATIONS

- 1980s – FDA authorized ASA for patients with ischemic stroke
- 1985 – FDA approved ASA for treatment of acute MI and for secondary prevention
- 1998 – FDA approved low-dose ASA for high-risk patients for secondary prevention of MI or ischemic stroke

JAMA (2022), *327* (16), 1577-1584

JAMA Network

From: **Aspirin Use to Prevent Cardiovascular Disease: US Preventive Services Task Force Recommendation Statement**
JAMA. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983

What does the USPSTF recommend?	**For adults aged 40 to 59 years with an estimated 10% or greater 10-year cardiovascular disease (CVD) risk:** The decision to initiate low-dose aspirin use for the primary prevention of CVD in this group should be an individual one. **Grade: C** **For adults 60 years or older:** Do not initiate aspirin for the primary prevention of CVD. **Grade: D**
To whom does this recommendation apply?	This recommendation applies to adults 40 years or older without signs or symptoms of CVD or known CVD and who are not at increased risk for bleeding (eg, no history of gastrointestinal ulcers, recent bleeding, or other medical conditions, or taking medications that increase bleeding risk).
What's new?	• The USPSTF has changed the age ranges and grades of its recommendation on aspirin use. • The USPSTF currently recommends considering initiating aspirin in persons with an estimated 10% or greater CVD risk at a younger age: 40 years instead of 50 years. • Aspirin should be initiated selectively based on individual decision-making rather than routinely for all persons in the recommended age and CVD risk group. • 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.
How to implement this recommendation?	• Consider the patient's age. • **For adults aged 40 to 59 years:** Estimate CVD risk using a CVD risk estimator. • In patients whose estimated CVD risk is 10% or greater, use shared decision-making, taking into account potential benefits and harms of aspirin use, as well as patients' values and preferences, to inform the decision about initiating aspirin. • For patients initiating aspirin use, it would be reasonable to use a dose of 81 mg/d. • **For adults 60 years or older:** Do not initiate aspirin for primary prevention of CVD.
What additional information should clinicians know about this recommendation?	• Age is one of the strongest risk factors for CVD. • Males have a higher prevalence of CVD than females. Among both sexes, Black persons have the highest prevalence of CVD. • Aspirin reduces the risk of cardiovascular events, but it increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. • Both CVD risk and risk for gastrointestinal bleeding, intracranial hemorrhage, and hemorrhagic stroke (with or without aspirin use) increase with age. • For patients who are eligible and choose to start taking aspirin, the benefits become smaller with advancing age, and data suggest that clinicians and patients should consider stopping aspirin use around age 75 years.
Why is this recommendation and topic important?	CVD is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths. Each year, an estimated 605 000 Americans have a first heart attack and about 610 000 experience a first stroke.
What are additional tools and resources?	• The Million Hearts initiative provides information on improving cardiovascular health and preventing heart attack and stroke at https://millionhearts.hhs.gov/ • The Centers for Disease Control and Prevention have resources related to risk of heart disease and the prevention of heart disease for patients and health professionals at https://www.cdc.gov/heartdisease/index.htm • The National Heart, Lung, and Blood Institute has patient resources related to coronary heart disease at https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

Figure Legend:
Clinician Summary: Aspirin Use to Prevent Cardiovascular Disease

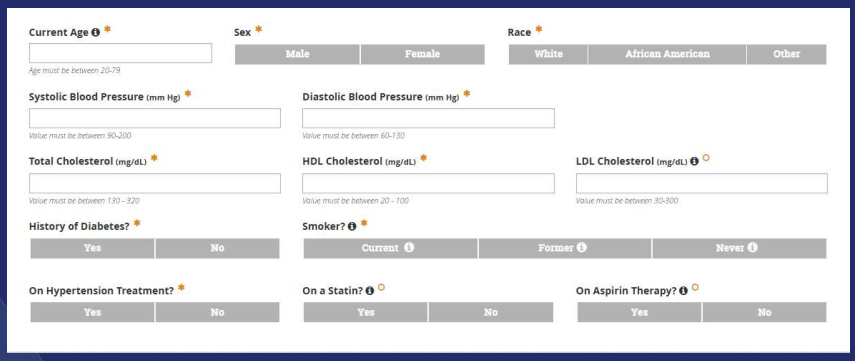
JAMA Network

From: **Aspirin Use to Prevent Cardiovascular Disease: US Preventive Services Task Force Recommendation Statement**
JAMA. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983

	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)

Figure Legend:
Quality-Adjusted Life-Years and Life-Years Gained: Lifetime Net Benefit of Initiating Aspirin Use for Women and Men With Lifetime UseYellow shaded cells indicate persons to whom the C grade recommendation applies. CVD indicates cardiovascular disease; QALY, quality-adjusted life-year.

WHO IS AT RISK?



ASCVD Risk Estimator Plus

2019 ACC/AHA GUIDELINE FOR PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

- Low-dose aspirin might be considered for primary prevention of ASCVD in select higher ASCVD adults aged 40-70 years who are not at increased bleeding risk.
- Low-dose aspirin should not be administered on a routine basis for primary prevention of ASCVD among adults >70 years.
- Low-dose aspirin should not be administered for primary prevention among adults at any age who are at increased bleeding risk.

JACC; 2019; March 17:[Epub ahead of print]

2023 AHA/ACC/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease

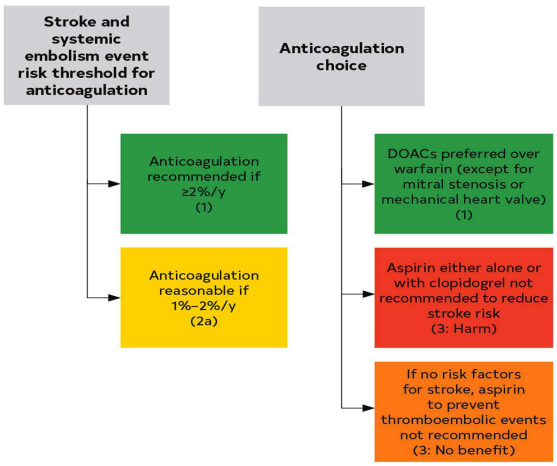
- Aspirin 81 mg recommended to reduce atherosclerotic events (1A)
- Dual antiplatelet therapy (DAPT) consisting of ASA + clopidogrel for 6 months post PCI, followed by single antiplatelet therapy (SAPT) (1A)
- When oral anticoagulation is indicated post PCI, DAPT x 1-4 weeks followed by clopidogrel monotherapy, in addition to OAC
- Low atherothrombotic risk, OK to DC ASA after 1 year and continue on OAC only, after PCI

JACC (2023), 82 (9), 833-955

2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease

COR	LOE	Recommendations
1	A	1. In patients with symptomatic PAD, single antiplatelet therapy is recommended to reduce the risk of MACE.[1-4]
1	B-R	2. In patients with symptomatic PAD, single antiplatelet therapy with clopidogrel alone (75 mg daily) is recommended to reduce the risk of MACE.[4]
1	C-LD	3. In patients with symptomatic PAD, single antiplatelet therapy with aspirin alone (range, 75-325 mg daily) is recommended to reduce the risk of MACE.[1-3]
1	A	4. In patients with symptomatic PAD, low-dose rivaroxaban (2.5 mg twice daily) combined with low-dose aspirin is effective to reduce the risk of MACE and MALE.[5,6]
1	B-R	5. After endovascular or surgical revascularization for PAD, antiplatelet therapy is recommended.[1,7-9]
1	A	6. After endovascular or surgical revascularization for PAD, low-dose rivaroxaban (2.5 mg twice daily) combined with low-dose aspirin is recommended to reduce the risk of MACE and MALE.[7]
2a	C-LD	7. After endovascular revascularization for PAD, dual antiplatelet therapy with a P2Y12 antagonist and low-dose aspirin is reasonable for at least 1 to 6 months.[8-11]
2a	C-LD	8. After endovascular or surgical revascularization in patients with PAD who require full-intensity anticoagulation for another indication and are not at high risk of bleeding, adding single antiplatelet therapy is reasonable.[12,13]
2a	C-EO	9. In patients with asymptomatic PAD, single antiplatelet therapy is reasonable to reduce the risk of MACE.
2b	B-R	10. In patients with symptomatic PAD without recent revascularization, the benefit of dual antiplatelet therapy is uncertain.[14,15]
2b	B-R	11. In patients with symptomatic PAD, the benefit of vorapaxar added to existing antiplatelet therapy is uncertain.[16]
2b	B-R	12. After surgical revascularization for PAD with a prosthetic graft, dual antiplatelet therapy with a P2Y12 antagonist and low-dose aspirin may be reasonable for at least 1 month.[17]
3: Harm	A	13. In patients with PAD without another indication (eg, atrial fibrillation), full-intensity oral anticoagulation should not be used to reduce the risk of MACE and MALE.[18-20]

2023 ACC/AHA/ACCP/HRS GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF ATRIAL FIBRILLATION



JACC (2023), 83 (1), 109-279

JAMA Network

From: **Aspirin vs Clopidogrel for Long-term Maintenance After Coronary Stenting in Patients With Diabetes: A Post Hoc Analysis of the HOST-EXAM Trial**

JAMA Cardiol. 2023;8(6):535-544. doi:10.1001/jamacardio.2023.0592

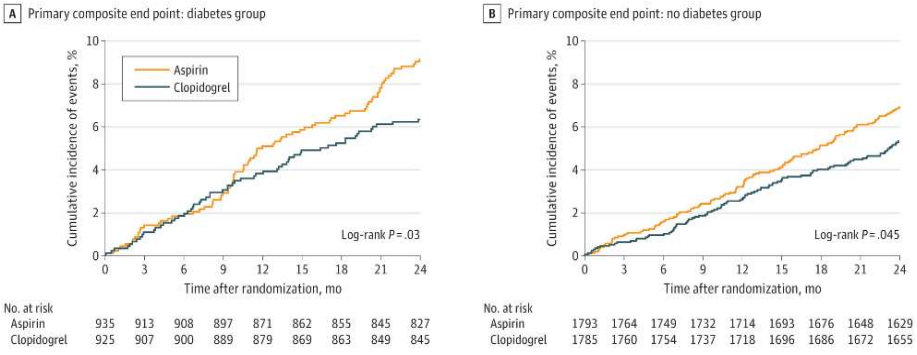
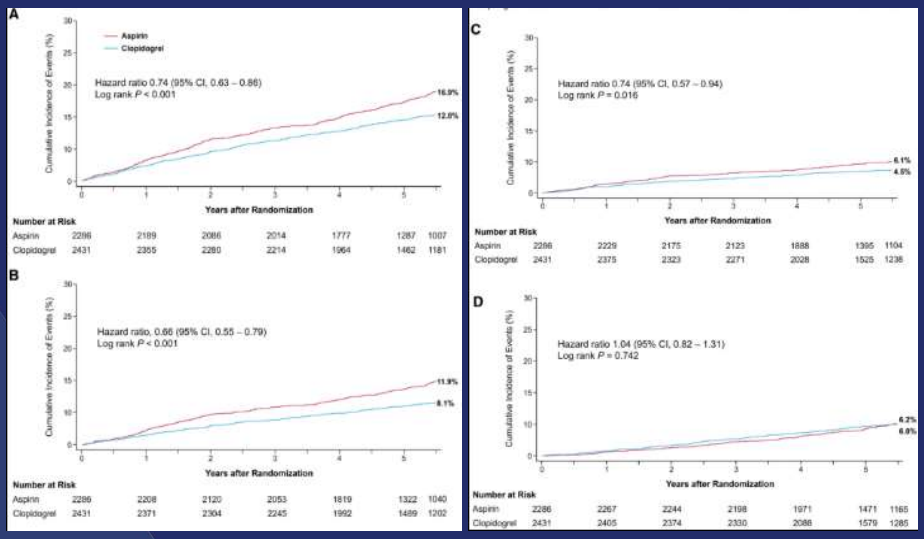


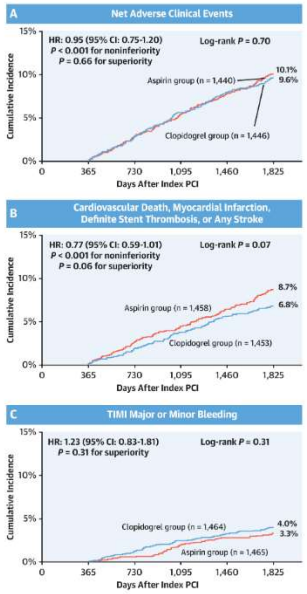
Figure Legend:

Cumulative Incidence of Primary Composite End Point in Diabetic and Nondiabetic Subgroups The primary composite end point consisted of all-cause death, myocardial infarction, stroke, readmission due to acute coronary syndrome, and major bleeding.

HOST-EXAM



CENTRAL ILLUSTRATION: Time-to-Event Curves for the Landmark Analysis Beyond 1 Year



Watanabe H, et al. J Am Coll Cardiol. 2024;83(1):17-31.

Thank You