Evidence base for deprescribing in older adults – evidentiary limitations and controversies

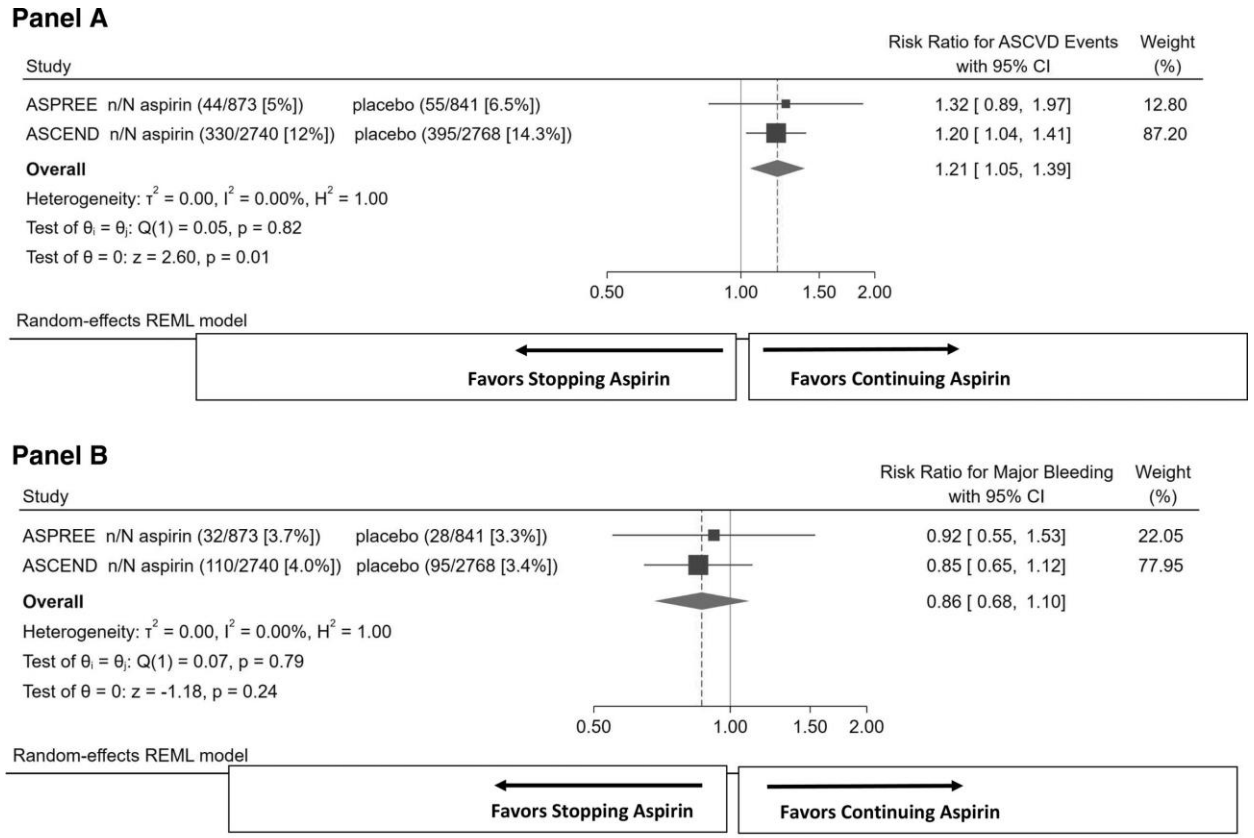
Michael W. Rich, MD, FACC, AGSF
Professor of Medicine
Washington University School of Medicine
St. Louis, Missouri

No disclosures

Can Specific Medications Be Safely Discontinued in Older Adults?

- Aspirin
- Statins
- PPIs

Meta-analysis of Aspirin Discontinuation: ASPREE and ASCEND



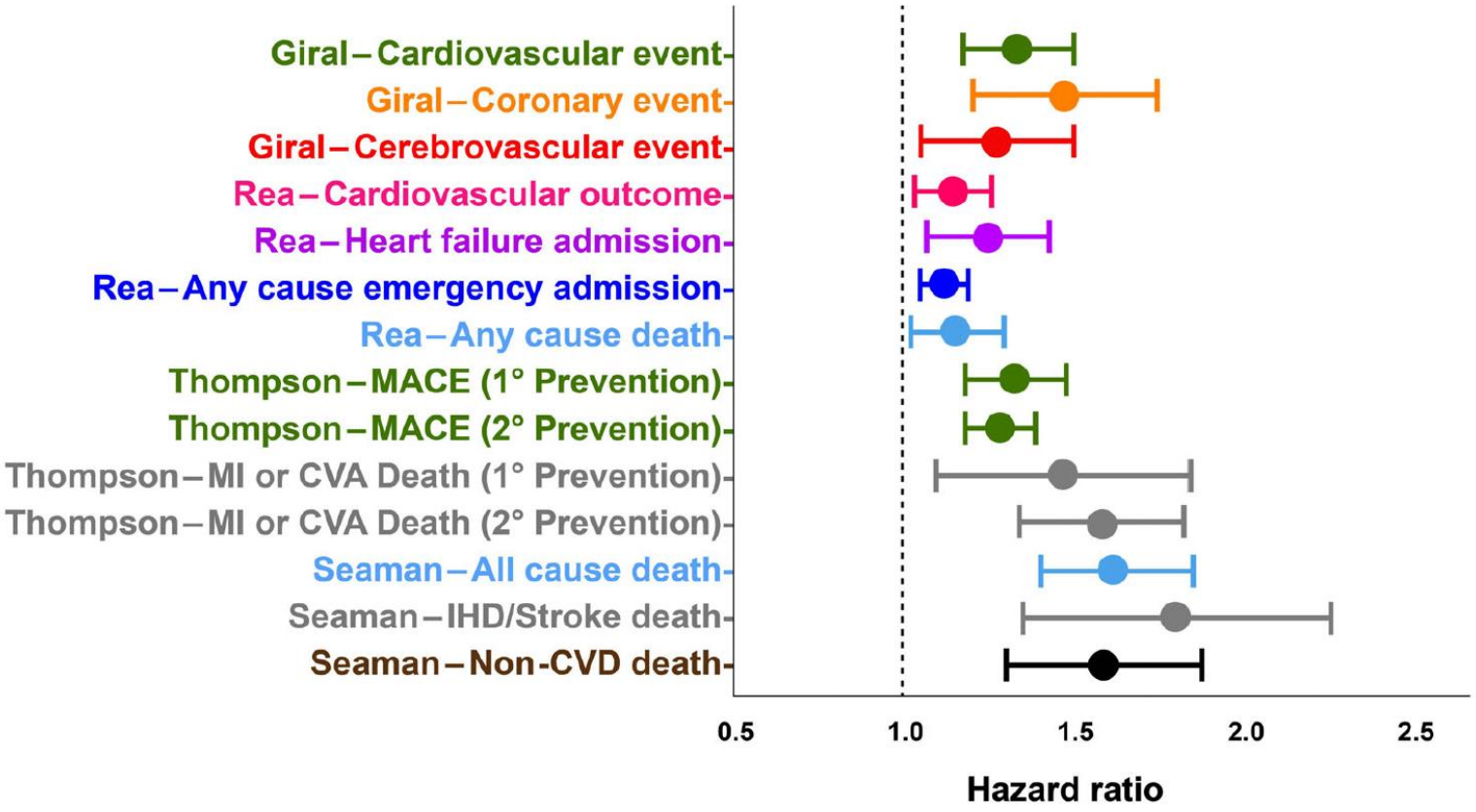
FOOTNOTE- *Panel A: ASCVD was defined as a composite of fatal coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal stroke, or hospitalization for heart failure in ASPREE and a composite of nonfatal myocardial infarction, nonfatal stroke (excluding confirmed intracranial hemorrhage) or transient ischemic attack, or death from any vascular cause (excluding confirmed intracranial hemorrhage) in ASCEND. Panel B: Major Bleeding was defined as a composite of hemorrhagic stroke, symptomatic intracranial bleeding, or clinically significant extracranial bleeding in ASPREE and as a composite of any confirmed intracranial hemorrhage, sight-threatening bleeding event in the eye, gastrointestinal bleeding, or any other serious bleeding (i.e., a bleeding event that resulted in hospitalization or transfusion or that was fatal) in ASCEND.*

- ASPREE: N=19,114, mean 74 yrs, 56% women, 1714 on ASA at BL
- ASCEND: N=15,480 with DM, mean 63 yrs (23.5% ≥70), 37% women, 5508 on ASA at BL
- Median follow-up 4.7-7.4 years
- ASCVD: 12.5% vs 10.4%, HR 1.21 (1.05-1.39); NNT 48
- Major bleeding: 3.4% vs 3.9%, HR 0.86 (0.68-1.10, p=NS); NNH 200

Circulation 2024;149:722-4

Observational studies of statin deprescribing

- N: 8000 to >100,000
- Median age 75-80 years
- 37%-66% women
- Primary/secondary prevention
- Median F/U 1.7-5.5 years



J Am Geriatr Soc 2023;71(8):2685-2689

Safety of Discontinuing Statins at End-of-Life: A Noninferiority Randomized Trial

- 381 patients with advanced life-limiting illness, mean 74.1 yrs, 45% women
- 58% CVD, 49% cancer, 36% hospice, 22% cognitive impairment
- Randomized to continuation or discontinuation of statins
- Primary endpoint 60-day mortality; multiple secondary endpoints, incl. QoL
- 60-day mortality: 20.3% vs. 23.5%, OR 1.23, p=0.36, failed to meet noninferiority
- Fewer medications, lower cost, better quality of life

JAMA Intern Med 2015;175(5):691-700

Deprescribing PPIs – Cochrane Systematic Review

- 6 RCTs, total N 1758 (range 105-598)
- Age (mean): 48-57 (5 trials), 73 (1 trial with N=105)
- Intervention: on-demand use (5 trials); abrupt cessation (1 trial)
- All trials reported decreased PPI use in intervention arm
- Increased symptoms (RR 1.71, 95% CI 1.31 to 2.21) and decreased patient satisfaction with deprescribing
- In a recent non-randomized trial of 166 pts, mean age 74, no difference in QoL but specific symptoms not reported

Cochrane Database Syst Rev 2017;3(3):CD011969
Drugs Aging 2025;42(12):1169-83

Mechanisms for Adverse Outcomes with Deprescribing: Statins as an Example

- Chronic pathway inhibition → upregulation of compensatory pathways to maintain homeostasis
- Within weeks of statin initiation → marked increase in hepatic HMG-CoA reductase activity
- Stopping statins → rebound increase in serum cholesterol
- Stopping statins → potential increase in inflammation, endothelial dysfunction, other adverse pleiotropic effects
- Thus, chronic use of a medication alters the internal milieu, and stopping the medication could increase risk for adverse outcomes
- TTB when starting a medication ≠ TTH when stopping the medication

J Am Geriatr Soc 2023;71(8):2685-2689

Summary and Implications for Guidelines

- Deprescription of commonly used “low hanging fruit” CV and non-CV medications in older adults may be associated with adverse outcomes, but the quality of evidence is low and additional research is needed.
- Nonetheless, based on the totality of evidence and considering individual patient circumstances and preferences, deprescribing through shared decision-making is a reasonable strategy in selected settings and it would be appropriate to support deprescribing as an option in clinical practice guidelines (most likely COR 2b, LOE B or C pending further research).