# the PRUDENT prescriber

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### Aspirin to Prevent CV Disease: USPSTF Guideline Update

Since 1989, when the United States Preventative Services Task Force (USPSTF) first recommended that clinicians "consider" aspirin prophylaxis for **primary** cardiovascular prevention in men 40 years or older with coronary risk factors and low bleeding risk, the trajectory of aspirin preventive advice has been tortuous.

In the April 26, 2022, issue of *JAMA*, the USPSTF reports its newest recommendation. The pendulum has swung further away from aspirin prophylaxis for primary prevention.

| Population | Recommendation | Grade |
|---|---|---|
| Adults aged 40 to 59 years with the 10% or greater 10-year cardiovascular disease risk. | The decision to initiate low-dose aspirin use for primary prevention of CVD in adults ages 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. **The net benefit in this group is small.** | C |

| | | |
|---|---|---|
| Adults 60 years and older | The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older. | D |

C = "Selectively offer this service to individual patients based on professional judgment and patient preferences."
D = "Do NOT offer this service."

**Supporting Data**

- The basis for these new recommendations is an updated review that included 13 randomized trials (n=161,680) of low dose aspirin (dose of 100 mg/d or less) for primary prevention.
- The review demonstrated a range of benefits/harms from taking aspirin over 4- 10 years in the various studies. The *absolute* differences across trials ranged from 2.5 fewer to 1.2 more events per 100 aspirin users. The number needed to take prophylactic aspirin for 5-7 years to prevent **one cardiovascular event would be 40 at best, with the possibility that as few as 1 in 80 aspirin users might experience an additional CV event.**
- The number needed to harm **(NNH)** for major bleeding events was 100 or more.
- **The USPSTF also reviewed colorectal cancer outcomes with aspirin prophylaxis and found that the evidence was inadequate to include prevention of colorectal cancer in the benefit-harm assessment.**
- An important development between the 2016 and the current recommendations was the publication in 2018 (an era of more aggressive lipid and BP management and decreased prevalence of smoking) of three large placebo-controlled randomized clinical trials of primary prevention with aspirin that involved a total of more than 47,000 patients with 5 to 7 years of follow-up.
    - ARRIVE included people 55 years or older with multiple risk factors (but not diabetes) and an estimated 10-year cardiovascular risk of 17%; it found NO evidence of cardiovascular benefit and a small statistically significant increase in gastrointestinal bleeding.
    - ASPREE included people 65 years or older (with or without cardiovascular risk factors); it found NO significant cardiovascular benefit, a significant 0.7 percentage-point increase in mortality, and a one percentage-point increase in major bleeding.
    - ASCEND exclusively included people with diabetes (40 years or older); it found a one percentage-point decrease in cardiovascular events and a one percentage-point increase in major bleeding.
    - Taken together, these more recent trials cast doubt about the net benefit for aspirin prophylaxis in current practice.


Two aspects of the new USPSTF recommendation statement are of concern:

First, clinicians are left without explicit guidance about management of the many patients (28% of those over 40 years) already taking aspirin for primary prevention. The USPSTF authors offer "for patients who have initiated aspirin use… it may be reasonable to consider stopping aspirin use around age 75 years."

Second, the decision to start aspirin therapy in people aged 40 to 59 years is heavily dependent on 10-year risk for cardiovascular events. Recall that the risk calculator significantly **over-predicts** cardiovascular risk. Conversely there is some evidence to suggest **underprediction in disadvantaged communities.** Plugging data into the ACC/AHA calculator creates a sense of certainty that is just not present on an individual patient basis.

Assisting individual patients with decision making on this USPSTF "C" recommendation requires a detailed discussion that leads to a false perception we can reliably predict whether a specific patient will benefit from aspirin. The benefits of initiating aspirin use are greater for individuals at higher risk for CVD events (e.g., those with >15% or >20% 10-year CVD risk).

In 2021, European guidelines favored individualized decision-making for prophylactic low dose aspirin for apparently healthy adults younger than 70 years who were without diabetes, yet at high or very high cardiovascular risk.

## Long COVID

Definitions:

- Long COVID is also referred to as "post-COVID conditions" and "post-acute sequelae of SARS-Cov-2 infection." (PASC)
- Acute COVID-19: Symptoms of COVID-19, new or persistent, for four weeks or more following the onset of illness.
- Post-COVID-19 condition: Broad range of symptoms that develop during or after COVID-19.
- Whether long COVID represents a new syndrome unique to COVID-19 or if there is overlap with the recovery from other infectious illnesses is unknown.
- The studies evaluating the prevalence and severity of post-COVID-19 symptoms have significant limitations: lack of a control populations (observational studies), reporting biases, short durations, and small "Ns."

Prevalence:

- Several observational studies of hospitalized patients **describe more than one-third of COVID-19 patients experiencing more than one long COVID symptom. In a CDC study of COVID-19 patients with mild-severe illness, 13.3% had symptoms at one month or longer after infection; 2.5% of all patients had symptoms at three months or longer based on self-reporting.**
- New data from the Household Pulse Survey (Census Bureau and CDC) showed that 40% of adults in the United States reported having COVID-19 in the past and nearly 1 in 5 of those (19%) are currently still having symptoms of long COVID. The data were collected from June 1- June 13, 2022. The data show:
    - Overall, 1 in 13 adults in the US (7.5%) have long COVID symptoms.
    - Older adults are less likely to have long COVID than younger adults.
    - Nearly three times as many adults ages 50 to 59 currently have long COVID than those age 80 and older.
    - Women are more likely than men to currently have long COVID (9.4% versus 5.5%).
- The UK Office for National Statistics survey through May 2022 estimated that 2 million people in the UK had self-reported long COVID. Of these people, 72% reported having long COVID for at least 12 weeks, 42% for at least one year, and 19% for at least two years.
- There are data suggesting a shorter recovery (e.g., two weeks) for those with mild disease and a longer recovery (e.g., 2 to 3 months or longer) for those with more severe disease. But there is a wide variability in time to symptom resolution.

Symptoms:

- Common physical symptoms: cough (17% to 34%), chest pain (12% to 44%), fatigue (13%–87%) and dyspnea (10% to 71%). Most of those with altered taste and smell have resolution in one month. Neuropsychiatric symptoms include difficulty thinking or concentrating (brain fog), headache, sleep problems, depression, and anxiety.
- Olfactory dysfunction is a common symptom of COVID-19. Its reported rates are as high as 70%. The symptom can be associated with mild COVID-19, mostly occurs within five days after symptom onset and can persist for a few days to several months after infection resolution. In a study reported in JAMA on August 9, 2022, the researchers found that individuals with mild COVID-19 infected during the Gamma (42%) and Omicron (6%) waves had lower likelihood of reporting of olfactory dysfunction than individuals infected during the period of original lineages (53%).
- Patients can develop long COVIDeven if their initial infection was asymptomatic.
- Depression, anxiety, PTSD, memory issues and “brain fog” were more common in hospitalized COVID-19 patients than in those with mild illness.
- In an observational study including over 97,000 vaccinated individuals in the United Kingdom, infection with the Omicron variant was associated with a lower risk of developing persistent symptoms compared with Delta (4.5 versus 10.8 percent) Lancet. 2022;399(10343):2263

Protection against long COVID

- **Vaccines**: A large observational cohort study from Italy totaling 2560 patients with mild COVID-19 reported that compared with unvaccinated individuals, the prevalence of long COVID decreased in vaccinated individuals in a dose-dependent fashion: 42% in unvaccinated patients versus 30% in patients with one vaccine dose, 17% in patients with two vaccine doses and 16% in patients with three doses. Research Letter in the July 1, 2022, JAMA.
- **Physical fitness** confers benefit in those infected with COVID-19. In a South African study performed in over 65,000 people participating in a physical activity rewards program, those with >150 minutes/week of activity suffered substantially lower morbidity from complications of COVID-19 infection than those with <60 minutes/week of activity. Patients with high activity levels prior to becoming infected experienced lower rates of hospitalization, intensive care unit admission, mechanical ventilation, and death. These findings emphasize the importance of maintaining exercise programs during the pandemic. Br J Sports Med. 2022;56(10):568.
- **Long COVID is less common in children and adolescents.**

Susceptibility to long COVID

- More common in those with more severe COVID disease
- Older age, higher body mass index, and comorbidities such as allergies and obstructive lung disease were associated with increased risk of PASC.
- There is wide variability in time to symptom resolution.
- As of July 2021, long COVID can be considered a disability under the Americans with Disabilities Act (ADA)


- Although my angst about being hospitalized or dying from COVID-19 has lessened, my concern for developing long COVID remains.

- Health and Human Services divisions, including the National Institutes of Health and the CDC, have pledged urgent research to unravel the biological mechanisms of long COVID and develop treatments. Paint me skeptical.

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