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## Aspirin Following Anticoagulation Therapy Prevents Recurrent VTE

### Clinical Question

Does aspirin prevent recurrent venous thromboembolism (VTE) in patients who have completed an initial course of anticoagulation therapy?

### Bottom Line

Although this ASPIRE study was underpowered to detect a difference in the primary outcome, when the results were combined with those of the WARFASA trial, the data show that daily low-dose aspirin prevents recurrent VTE as well as major vascular events without increasing bleeding in patients who have completed anticoagulation therapy for an initial, unprovoked VTE. (Level of Evidence = 1b)

### Synopsis

Following a protocol identical to that of the WARFASA trial, investigators recruited 822 patients who had completed anticoagulation therapy for an initial, unprovoked VTE. Each patient received 100 mg of aspirin daily or placebo. Patients were a mean age of 54 years, and the majority of each group had received anticoagulation for six to 12 months before randomization into the study. After a median follow-up of 37 months, there was no significant difference detected between the groups for the primary outcome of recurrent VTE. However, this study was underpowered to detect such a difference if it truly exists. Patients in the aspirin group had a lower rate of major vascular events, defined as the composite of VTE, myocardial infarction, stroke, or cardiovascular death (5.2% vs. 8% per year; number needed to treat [NNT] = 36;  $P = .01$ ). In addition, there was no significant increase in bleeding events in the aspirin group. Because of slow recruitment and lack of power, the investigators decided a priori to combine the data of this study with those of the WARFASA trial. The combined

results showed that daily low-dose aspirin, as compared with placebo, reduced the risk of recurrent VTE (NNT = 19; hazard ratio = 0.68; 95% confidence interval, 0.51 to 0.90;  $P = .007$ ) as well as the risk of major vascular events (NNT = 16; hazard ratio = 0.66; 95% confidence interval, 0.51 to 0.86;  $P = .002$ ) without increasing bleeding.

### Reference

Brighton TA, Eikelboom JW, Mann K, et al.; ASPIRE Investigators. Low-dose aspirin for preventing recurrent venous thromboembolism. *N Engl J Med*. 2012;367(21):1979-1987.

**Study design:** Randomized controlled trial (double-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Outpatient (any)

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## Daily Multivitamins Do Not Reduce Major Cardiovascular Events in Men and Do Not Affect Mortality

### Clinical Question

Do daily multivitamin supplements reduce the risk of cardiovascular disease and subsequent mortality in adult men?

### Bottom Line

Daily multivitamin supplementation does not reduce the risk of major cardiovascular events in men. The risks of cardiovascular-related mortality and all-cause mortality were also not reduced by multivitamin supplementation. (Level of Evidence = 1b-)

### Synopsis

As part of the Physicians' Health Study, which evaluated various health interventions, including aspirin, vitamin E, and beta carotene, these investigators analyzed separate data on the potential value of daily ►

multivitamin supplements in reducing major cardiovascular disease events. Eligible men (n = 14,641) 50 years or older randomly received (uncertain allocation concealment) a common daily multivitamin supplement (Centrum Silver) or a matched placebo. Of these, 5.1% had a history of cardiovascular disease and 9.0% had a history of cancer. Approximately 40% were former smokers, and only 3.6% were current smokers. Individuals masked to treatment group assignment assessed outcomes, including all cancer and mortality end points. Complete follow-up occurred for more than 98% of participants for a median of 11.2 years.

Using intention-to-treat analysis, the authors report no significant effect of a daily multivitamin on major cardiovascular events, including total myocardial infarction, stroke, or cardiovascular-related mortality. There was also no significant difference in all-cause mortality. Results were similar for the subset of patients with a history of cardiovascular disease.

## Reference

Sesso HD, Christen WG, Bubes V, et al. Multivitamins in the prevention of cardiovascular disease in men. *The Physicians' Health Study II randomized controlled trial*. *JAMA*. 2012;308(17):1751-1760.

**Study design:** Randomized controlled trial (double-blinded)

**Funding source:** Government

**Allocation:** Uncertain

**Setting:** Population-based

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## Vitamin D + Calcium = Placebo for Cognitive Decline

### Clinical Question

Does calcium plus vitamin D prevent cognitive decline in older women?

### Bottom Line

Calcium plus vitamin D is no better than placebo in preventing cognitive decline in women older than 65 years. (Level of Evidence = 1b)

## Synopsis

These authors used data from the Women's Health Initiative to compare cognitive outcomes in 2,034 women older than 65 years who received calcium (1,000 mg daily) plus vitamin D (400 IU daily) vs. 2,109 women who received placebo. The women were primarily non-Hispanic whites. The researchers assessed each woman's cognition at baseline and then annually for an average of eight years. The researchers used many cognitive assessment measures, including Consortium to Establish a Registry for Alzheimer's Disease (CERAD) tests, the Modified Mini-Mental State Examination, the Digit Span Forward and Backward test, the Primary Mental Abilities Vocabulary test, the Card Rotation test, the California Verbal Learning test, the Benton Visual Retention test, and the Finger Tapping test. CERAD test results were used to classify the primary outcome: probable dementia, mild cognitive impairment, or cognitively normal. The secondary outcome, the patient's global function, was assessed using the other tools. At the end of the study interval, using intention-to-treat analysis, the percentage of women who developed dementia or mild cognitive impairment was similar in each group (4.8% vs. 5.1% in the intervention and control groups, respectively). If one excludes nonadherent women from the analysis, the rates remain comparable (3.1% vs. 2.9% in the intervention and control groups, respectively). Because this latter approach tends to bias data in favor of interventions, it strengthens the conclusion that calcium plus vitamin D is no better than placebo in preventing cognitive decline.

## Reference

Rossum RC, Espeland MA, Manson JE, et al. Calcium and vitamin D supplementation and cognitive impairment in the Women's Health Initiative. *J Am Geriatr Soc*. 2012;60(12):2197-2205.

**Study design:** Randomized controlled trial (double-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Population-based

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