# Low-Dose Aspirin Does Not Prevent Venous Thromboembolism in Healthy Women

*Glynn RJ, Ridker PM, Goldhaber SZ, Buring JE. Effect of low-dose aspirin on the occurrence of venous thromboembolism: a randomized trial. Ann Intern Med 2007;147:525–33.*

## Study Overview

Objective. To determine whether long-term aspirin use reduces the risk of venous thromboembolism (VTE) in healthy adult women.

Design. Secondary analysis of data from the Women's Health Study [1], a randomized, double-blind, placebo-controlled trial conducted over a 10-year period.

Setting and participants. 39,876 female health professionals aged ≥ 45 years who had no known major chronic diseases, had not used anticoagulants, and had not used aspirin or nonsteroidal anti-inflammatory drugs > once per week. Patients who did not adhere to the medication regimen during a 3-month run-in period were excluded. Women were randomized to receive either 100 mg aspirin or placebo on alternate days.

Main outcome measure. VTE (deep venous thrombosis or pulmonary embolism), determined by patient self-report and confirmed by examination of patients' medical records.

Main results. 482 women had VTE during a median follow-up period of 10.2 years. The incidence of VTE did not differ significantly between the treatment groups (1.18/1000 person-years for aspirin vs. 1.25/1000 person-years for placebo; hazard ratio, 0.95 [95% confidence interval, 0.79–1.13]). Subgroup analyses among higher-risk patients (genetic factors or personal history of VTE) did not reveal any significant differences between treatment with aspirin versus placebo. The incidence of gastrointestinal bleeding, peptic ulcers, hematuria, easy bruising, and epistaxis were significantly higher in patients taking aspirin, with hazard ratios ranging from 1.06 to 1.44.

Conclusion. Long-term use of aspirin has no effect on the incidence of VTE in healthy women but does raise the risk of several adverse events.

## Commentary

Among healthy women, the incidence of VTE is nearly equal to the incidence of stroke and slightly exceeds the incidence of myocardial infarction [2]. Prior meta-analyses of antiplatelet therapy (predominantly aspirin use) in high-risk patients have shown a protective effect against VTE [3,4], and a randomized trial of short-term aspirin use after orthopaedic surgery demonstrated a reduction of 43% in the relative risk of VTE [5]. However, no randomized trial of aspirin use in low-risk, healthy individuals has been conducted.

The current study by Glynn and colleagues provides new evidence to guide the use of aspirin in adult women who do not have a short-term elevated risk of VTE. This large-scale, long-term trial showed no protective effect of aspirin use, and this lack of protection extended even to subgroups of women who had genetic risk factors for VTE. The study was well-designed, with careful monitoring of patients' adherence to aspirin as well as monitoring of nontrial aspirin use. Sensitivity analyses to account for nonadherence did not change the study's results. Although the study dose of aspirin was low (100 mg), previous research by the study investigators demonstrated that this dose was sufficient to achieve the same degree of platelet inhibition as higher doses [6].

This study has some important limitations. First, as a retrospective secondary analysis of data from the Women's Health Study, any statistically significant differences could be questioned on the grounds of multiple hypothesis testing. However, because there was no significant difference in the incidence of the primary endpoint (ie, occurrence of VTE), this concern is less important. Second, the study may have been underpowered to detect small but clinically important effects on the incidence of VTE. In post hoc power analysis, the authors point out that the 95% confidence interval for the protective effect of aspirin excluded a 25% reduction in the incidence of VTE. Finally, participants in the Women's Health Study may differ systematically from patients in the general population. This is especially true because nonadherent patients were excluded prior to randomization. However, the null findings of this study make the likelihood of dissimilar effects in the less-adherent general population unlikely.

## Applications for Clinical Practice

Long-term daily aspirin use does not lower the risk of VTE among healthy adult women. Anticoagulation remains the

standard of care for the prevention of VTE [7].

*—Review by Mark W. Friedberg, MD, MPP*

## References


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