



Is one oral estrogen formulation safer than another for menopausal women?

Yes. Women using estradiol had a lower risk of incident venous thromboembolism than women using conjugated equine estrogens (CEE), according to this population-based, case-control study from Washington State. They also had a lower risk of myocardial infarction (MI), although this difference did not achieve statistical significance.

The odds ratio (OR) for venous thrombosis was 2.08 for women using CEE, compared with women using estradiol (95% confidence interval [CI], 1.02–4.27; $P = .045$). The OR for MI was 1.87 for women using CEE, compared with women using estradiol (95% CI, 0.91–3.84; $P = .09$).

FAST TRACK

The risks of venous thromboembolism and myocardial infarction were higher for women using oral CEE than for those using oral estradiol, but the risk of ischemic stroke was similar between groups

Smith NL, Blondon M, Wiggins KL, et al. Lower risk of cardiovascular events in postmenopausal women taking oral estradiol compared with oral conjugated equine estrogens [published online ahead of print September 30, 2013]. JAMA Intern Med. doi:10.1001/jamainternmed.2013.11074.

► **EXPERT COMMENTARY**

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Although numerous investigators, including the Women's Health Initiative (WHI) team, have compared cardiovascular risks in women using menopausal hormone therapy (HT) versus nonusers, few researchers have addressed the comparative safety of different oral estrogen formulations.

In this case-control study, Smith and colleagues compared the safety of oral estradiol

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WHAT THIS EVIDENCE MEANS FOR PRACTICE

Although the risk of VTE appears to be higher among users of oral estrogen than among those using a transdermal formulation,¹ many menopausal women prefer oral estrogen for its convenience and because patch adherence can sometimes be an issue.

Oral estradiol and oral CEE appear to be equally effective in relieving menopausal symptoms. However, there is a significant cost differential: A 1-month supply of 1-mg estradiol tablets costs \$4 at some chain pharmacies, whereas 0.625-mg tablets of CEE cost \$84.92 (according to goodrx.com). Therefore, for menopausal women who elect to use an oral estrogen formulation, estradiol appears to be a wise choice for both safety and economy.

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and CEE in menopausal members of a large US Health Maintenance Organization who were using these oral estrogens between 2003 and 2009.

Details of the study


Cases were women diagnosed with deep venous thrombosis, including pulmonary embolism; myocardial infarction; or ischemic stroke. Women in the control group had no history of cardiovascular events. The endogenous thrombin potential-based normalized activated protein C sensitivity ratio (nAPCsr), which has been shown to predict venous thromboembolism (VTE) in the setting of estrogen therapy, was measured in the control group.

Between 2003 and 2009, incident VTE, MI, and stroke were diagnosed in 68, 67, and 49 cases, respectively, and 201 controls were identified. Cases were more likely than

controls to have cardiovascular risk factors.

More than 90% of participants were white, with a mean age ranging from 63.2 to 67.6 years.

Among women in the control group, those using oral estradiol had slightly more cardiovascular risk factors than those using CEE, although age, body mass index, and the recency of HT initiation were similar among women using the two oral estrogens.

Although the ORs for VTE and MI were elevated among CEE users, the risk for ischemic stroke was similar for estradiol and CEE users. Women using CEE had higher nAPCsr ($P < .001$), however, suggesting a greater tendency to clot. 

Reference

1. Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. Committee Opinion #556. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2013;121(4):887-890.

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