# Optimizing the risk-benefit profile of hormone therapy in women aged 50-64 years:

*Findings from a cohort of 225,000 US women*

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# The Research Question

Are the odds of venous thromboembolism (VTE) from menopausal hormone therapy (MHT) exposure mitigated or exacerbated by formulation, delivery route, statin use, or interactions with other risk factors?

# Research Design and Method

- Study Design and Analysis: Nested case-control study
- Data Set: Optum deidentified Clinformatics® Data Mart Database
- Population: Commercially-insured women aged 50-64 in the U.S.
- Outcome measures:
  - VTE cases were defined by ICD-10 diagnoses plus treatment (anticoagulation or IVC filter) or death within 30 days.
  - Controls were matched on date and age 10:1.
- Exposure: Exposure to hormone therapy in the prior 60 days.
- Analysis: Odds ratios (OR) for VTE risk were estimated using logistic regression models for HT by formulation and route with/without 90d statin exposure and common VTE risk factors. Two-way interactions were tested between hormone exposure and VTE risk factors.

# What the Research Found

- The risk-benefit profile of hormone therapy is influenced by route and formulation of hormones.
  - Oral conjugated equine estrogen formulations convey higher odds of VTE compared to oral estradiol formulations.
    - **OR 1.19,** 95%CI 0.99-1.43 (estrogen-only regimens)
    - **OR 1.33,** 95%CI 1.02-1.72 (estrogen-progestogen regimens)
  - Oral delivery of any estrogen confers higher odds of VTE than transdermal delivery
    - **OR 1.90,** 95%CI 1.56-2.32
- Concurrent statin use may partially mitigate VTE risks from hormone therapy.
  - **OR=0.82,** 95% CI 0.71-0.94 (MHT with statin compared to MHT without statin)
  - **OR=0.69,** 95% CI 0.50-0.95 (MHT with high-intensity statin versus MHT without statin)
- MHT did not exacerbate other common VTE risk factors (smoking, history of stroke, varicose veins, hypercoagulable conditions, trauma, hospitalization, surgery, cancer, coronary artery disease, higher comorbidity burden, and higher age)

# What this means for Clinical Practice

- The risk-benefit profile of menopausal hormone therapy can be optimized through the choice of hormone formulation and delivery route, with transdermal estradiol conferring the lowest odds of venous thromboembolism (VTE).
- The VTE risk associated with menopausal hormone therapy may be further mitigated through concurrent treatment with statins, especially high-intensity statins.

# References


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# Funding


- Texas Academy of Family Physicians