

Differential Effects of Type, Route and Dose of Menopausal Hormone Therapy on survival, cancer, cardiovascular and dementia risks in 10 million women age over 65: a retrospective case-control study

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Abstract

Objectives: To examine the variation in patient's health outcomes across different type, route, and strength of menopausal hormone therapy (HT). **Design:** Retrospective case-control study **Setting:** United States 2007-2020 **Population:** 10 million women aged 65 or more in US Medicare. **Methods:** Cox regression models with time-varying type, route, and strength of HT as well as patient characteristics. **Main Outcome(s):** all-cause mortality; 5 cancers- breast, lung, endometrial, colorectal, ovarian cancers; 6 CV conditions- ischemic heart diseases, heart failure, venous thromboembolism, stroke, atrial fibrillation, acute myocardial infarction; and dementia. **Results** Estrogen monotherapy (ET) exhibited a significant, 19% (HR=0.81; 95% CI 0.79-0.82), relative risk reduction on mortality. The reduction was greater with estradiol and vaginal/transdermal than conjugated estrogen and oral preparations. ET also exhibited significant risk *reductions* for all study cancers; breast (15%), lung (13%), endometrial (29%), colorectal (13%) and ovarian (14%). All ET preparations except low-dose slightly increased risk of ischemic heart diseases (1-4%). Both combination therapy and progestogen monotherapy exhibited significantly *increased* risk of breast cancer (7-14%). Oral ET exhibited moderately increased risk of stroke (6%) and dementia (2%). **Conclusions:** Among senior Medicare women, the effect of menopausal HT varies by type, route, and strength. The use of estradiol, vaginal/transdermal, and low/medium for menopausal care is safer than its counterparts.

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