

*Menopause research:***Randomized clinical trials 1 – The WHI**

Designed in the early 1990s, the US Women's Health Initiative (WHI) randomized trials considered hormone therapy, calcium and vitamin D supplements and dietary modification vs placebo in healthy postmenopausal women aged 50–79.

**Hormone therapy trial**

- Conjugated equine estrogen 0.625 mg (CEE) alone (10,739 women) and combined with medroxyprogesterone acetate 2.5 mg (MPA) (16,608 women), taken once daily

**Original key findings**

- Compared with placebo, combined therapy reduced fractures and increased invasive breast cancer risk
- Estrogen alone reduced fractures and invasive breast cancer incidence and death

**18-year follow-up**

- Hormone therapy with CEE plus MPA for a median of 5.6 years or with CEE alone for a median of 7.2 years was not associated with risk of all-cause, cardiovascular or cancer mortality during a cumulative follow-up of 18 years

Over 2,000 publications have reported results from the WHI.

**Calcium and vitamin D trial**

- **Intervention** Calcium carbonate with 1000 mg elemental calcium combined with vitamin D3 400 IU per day, taken in two divided doses daily, or placebo, taken as one pill twice a day (36,282 women)
- **Findings** After 7 years, calcium with vitamin D supplementation resulted in a small but significant improvement in hip bone density, did not significantly reduce hip fracture, did not reduce the incidence of colorectal cancer and increased the risk of kidney stones

**Dietary modification trial**

- **Intervention** Low-fat dietary pattern compared with a usual dietary pattern (48,835 women)
- **Findings** After 8 years, no significant benefit on any outcome (risk of breast or colorectal cancers or coronary heart disease) was found

**Further information**

EMAS (2025). CareOnline. Health at menopause and beyond <https://emas-online.org/guidelines-and-education/#emas-care-online>

Women's Health Initiative <https://www.whi.org>