Menopause research:

Randomized clinical trials 2 – KEEPS, DOPS, ELITE

Randomized clinical trials with up to about 1,000 women have looked at hormone therapy and menopausal and postmenopausal health.

Kronos Early Estrogen Prevention Study (KEEPS)

- Started in 2005 to study the effect of hormone therapy on subclinical atherosclerosis and cognitive function in 727 healthy women aged 42–58 up to 3 years after menopause
- The continuation study involved 299 women 10 years later
- **Intervention** Oral CEE 0.450 mg daily or transdermal estradiol 50 µg patches twice weekly or placebo (727 women); or oral micronized progesterone 200 mg daily for 12 days each month in estrogen users
- **At 4 years**, no difference in the rate of increase in carotid intima media thickness in the three study arms; hormone use did not affect cognitive performance. **At 10 years**, no evidence of benefits or harms on cardiovascular disease or cognition

Danish Osteoporosis Prevention Study (DOPS)

- Started in 1990 to study the effect of hormone therapy on osteoporotic fractures, death and admission to hospital for myocardial infarction or heart failure in 1,006 women with their last period within the past 2 years
- **Intervention** Sequential MHT with oral estradiol with or without norethisterone acetate (for women with a uterus) or no treatment
- **After 11 years** of treatment, women in the HRT arm had 52% lower risk of death, myocardial infarction or heart failure, an effect that persisted until **16 years** of follow-up

The Early versus Late Intervention Trial with Estradiol (ELITE)

- Started in 2005 to test the timing hypothesis of the effects of hormone use in 643 healthy postmenopausal women without cardiovascular disease
- **Intervention** Oral 17β-estradiol 1 mg per day, plus progesterone 45 mg vaginal gel administered sequentially (i.e. once daily for 10 days of each 30-day cycle) for women with a uterus or placebo (plus sequential placebo vaginal gel for women with a uterus)
- **At 5 years**, estradiol therapy was associated with less progression of subclinical atherosclerosis than placebo when therapy was initiated within 6 years after menopause, but not when it was initiated after 10 or more years. Estradiol initiated within 6 years of menopause did not affect verbal cognition differently than therapy begun 10 or more years after menopause

Further information

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

European Menopause and Andropause Society EMAS