Menopausal hormone therapy for the primary prevention of chronic conditions: a systematic review to update the US Preventive Services Task Force recommendations

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CRD summary

Postmenopausal therapy using oestrogen with progestin or oestrogen alone decreased risk of fractures but increased risks of stroke, thromboembolic events, gallbladder disease and urinary incontinence. Oestrogen plus progestin increased risks of breast cancer and probable dementia. Oestrogen-only decreases the risk of breast cancer. The conclusions were based on the evidence presented and appear reliable.

Authors' objectives

To update evidence about the effectiveness of hormone therapy in reducing risk of chronic conditions and adverse effects, and to examine whether outcomes vary among women in different subgroups (see Other Publications of Related Interest).

Searching

Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (third quarter 2011), MEDLINE (2002 to 30 November 2011) and Scopus were searched for studies in English. Relevant reference lists from previous reviews were searched.

Study selection

Randomised placebo-controlled trials of postmenopausal therapy versus placebo for prevention of chronic conditions for postmenopausal women were eligible for inclusion. Women with known thrombotic disorders, hormone sensitive cancer or coronary heart disease were excluded.

The review was concerned with primary prevention of new conditions rather than effects on pre-existing conditions. Outcomes of interest were coronary heart disease, stroke, deep vein thrombosis, pulmonary embolism, cancer (breast, colon, lung, endometrium or ovaries), fracture at various sites, cognition and dementia, disease-specific and all-cause mortality and any new findings reported by the trials. Intervention drugs included conjugated equine oestrogen with or without medroxyprogesterone acetate, estradiol valerate, 17-beta estradiol plus norethindrone and unopposed transdermal estradiol. The main analysis was based on participants aged 60 to 69.

More than one reviewer selected the studies.

Assessment of study quality

Two reviewers independently evaluated individual trials (good, fair or poor). Any disagreements were resolved by consensus.

Data extraction

Where trials included women with pre-existing conditions, the reviewers used data for all outcomes except pre-existing and related conditions.

Two reviewers extracted data. Any disagreements were resolved by discussion.

Methods of synthesis

Differences between the included trials precluded meta-analysis. Instead the results from Women's Health Initiative trials (which included main trials, the Women’s Health Initiative Memory Study and Women’s Health Initiative Study of Cognitive Aging) were used as the main estimates for each outcome for several reasons including sample size and applicability. The results were presented as hazard ratios (HR) and difference in events per 10,000 women-years, each with 95% confidence intervals (CIs).

Planned subgroup analyses were: premature menopause or women with surgical menopause; age of use; doses and

modes of delivery of hormone; and presence of comorbidities.

Results of the review

Nine randomised placebo controlled trials were included in the review. The longest follow-up was 11 years (Women's Health Initiative trials). All trials were rated of fair quality. The most common problems across the trials were high attrition and low adherence.

Oestrogen plus progestin reduced fractures (HR 0.76, 95% CI 0.69 to 0.83) but increased invasive breast cancer (HR 1.25, 95% CI 1.07 to 1.46), stroke (HR 1.34, 95% CI 1.05 to 1.71), deep venous thrombosis (HR 1.88, 95% CI 1.38 to 2.55), pulmonary embolism (HR 1.98, 95% CI 1.36 to 2.87), lung cancer death (HR 1.71, 95% CI 1.16 to 2.52), gallbladder disease (HR 1.61, 95% CI 1.30 to 2.00), probable dementia (HR 2.05, 95% CI 1.21 to 3.48) and urinary incontinence (HR 1.39, 95% CI 1.27 to 1.52). There were no statistically significant reductions in colorectal cancer, lung cancer, endometrial, ovarian and cervical cancers, coronary heart disease, pulmonary embolism, all-cause mortality, probable dementia and mild cognitive impairment.

Oestrogen-only therapy reduced fractures (HR 0.70, 95% CI 0.63 to 0.79), invasive breast cancer incidence (HR 0.77, 95% CI 0.62 to 0.95) and breast cancer death (HR 0.37, 95% CI 0.13 to 0.91) but increased stroke (HR 1.36, 95% CI 1.08 to 1.71), deep venous thrombosis (HR 1.47, 95% CI 1.06 to 2.05), gallbladder disease (HR 1.79, 95% CI 1.44 to 2.22) and urinary incontinence (HR 1.53, 95% CI 1.37 to 1.71). There were no statistically significant reductions in diabetes, colorectal cancer, lung cancer, coronary heart disease, pulmonary embolism, all-cause mortality, probable dementia and mild cognitive impairment.

Among the subgroup analyses, there were no consistent differences by age and comorbidities. Other subgroup analyses were not performed due to lack of data.

Authors' conclusions

Postmenopausal therapy using oestrogen with progestin or oestrogen alone decreased risk of fractures but increased risks of stroke, thromboembolic events, gallbladder disease and urinary incontinence. Oestrogen plus progestin increased risks of breast cancer and probable dementia. Oestrogen-only decreased the risk of breast cancer.

CRD commentary

The review addressed a clear question and was supported by appropriate inclusion criteria. Several relevant data sources were searched. The review was restricted to studies in English (the authors reported that they did not identify any relevant trials from journals in other languages). Study quality was assessed. The authors appropriately highlighted weaknesses in the evidence such as high drop-out rates and differential adherence rates. Two reviewers were involved in study selection, data extraction and quality assessment, which minimised potential for error and bias. The restriction of results to those of the Women's Health Initiative trials appeared justified.

The conclusions were based on the evidence presented and appear reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies were needed to investigate long-term outcomes such as cancer and death and understand the effects on health outcomes of hormonal agents other than those investigated in this review. Research should look at the women in the transition period of the menopause or immediately post menopause.

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