



Cochrane
Library

Cochrane Database of Systematic Reviews

Hormone therapy for preventing cardiovascular disease in post-menopausal women (Review)

Boardman HMP, Hartley L, Eisinga A, Main C, Roqué i Figuls M, Bonfill Cosp X, Gabriel Sanchez R, Knight B

Boardman HMP, Hartley L, Eisinga A, Main C, Roqué i Figuls M, Bonfill Cosp X, Gabriel Sanchez R, Knight B.

Hormone therapy for preventing cardiovascular disease in post-menopausal women.

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD002229.

DOI: 10.1002/14651858.CD002229.pub4.

www.cochranelibrary.com

Hormone therapy for preventing cardiovascular disease in post-menopausal women

Henry MP Boardman¹, Louise Hartley², Anne Eisinga³, Caroline Main⁴, Marta Roqué i Figuls⁵, Xavier Bonfill Cosp⁶, Rafael Gabriel Sanchez⁷, Beatrice Knight⁸

¹Department of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK. ²Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK. ³UK Cochrane Centre, Oxford, UK. ⁴Cancer Research UK Clinical Trials Unit (CRCTU), School of Cancer Sciences, University of Birmingham, Birmingham, UK. ⁵Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB Sant Pau), CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain. ⁶Iberoamerican Cochrane Centre - Biomedical Research Institute Sant Pau (IIB Sant Pau), CIBER Epidemiología y Salud Pública (CIBERESP) - Universitat Autònoma de Barcelona, Barcelona, Spain. ⁷Instituto de Investigación IdiPAZ, Red Española de Investigación Cardiovascular RD/12/0042/0008, Hospital Universitario de la Paz, Universidad Autónoma de Madrid, Madrid, Spain. ⁸NIHR Exeter Clinical Research Facility, University of Exeter Medical School, Exeter, UK

Contact address: Henry MP Boardman, Department of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, OX3 9DU, UK. Harry.Boardman@cochrane.nhs.uk, hboardman@doctors.org.uk.

Editorial group: Cochrane Heart Group.

Publication status and date: Edited (no change to conclusions), comment added to review, published in Issue 8, 2015.

Citation: Boardman HMP, Hartley L, Eisinga A, Main C, Roqué i Figuls M, Bonfill Cosp X, Gabriel Sanchez R, Knight B. Hormone therapy for preventing cardiovascular disease in post-menopausal women. *Cochrane Database of Systematic Reviews* 2015, Issue 3. Art. No.: CD002229. DOI: 10.1002/14651858.CD002229.pub4.

Copyright © 2015 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Evidence from systematic reviews of observational studies suggests that hormone therapy may have beneficial effects in reducing the incidence of cardiovascular disease events in post-menopausal women, however the results of randomised controlled trials (RCTs) have had mixed results. This is an updated version of a Cochrane review published in 2013.

Objectives

To assess the effects of hormone therapy for the prevention of cardiovascular disease in post-menopausal women, and whether there are differential effects between use in primary or secondary prevention.

Secondary aims were to undertake exploratory analyses to (i) assess the impact of time since menopause that treatment was commenced (≥ 10 years versus < 10 years), and where these data were not available, use age of trial participants at baseline as a proxy (≥ 60 years of age versus < 60 years of age); and (ii) assess the effects of length of time on treatment.

Search methods

We searched the following databases on 25 February 2014: Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, MEDLINE, EMBASE and LILACS. We also searched research and trials registers, and conducted reference checking of relevant studies and related systematic reviews to identify additional studies.

Selection criteria

RCTs of women comparing orally administered hormone therapy with placebo or a no treatment control, with a minimum of six months follow-up.

Data collection and analysis

Two authors independently assessed study quality and extracted data. We calculated risk ratios (RRs) with 95% confidence intervals (CIs) for each outcome. We combined results using random effects meta-analyses, and undertook further analyses to assess the effects of treatment as primary or secondary prevention, and whether treatment was commenced more than or less than 10 years after menopause.

Main results

We identified six new trials through this update. Therefore the review includes 19 trials with a total of 40,410 post-menopausal women. On the whole, study quality was good and generally at low risk of bias; the findings are dominated by the three largest trials. We found high quality evidence that hormone therapy in both primary and secondary prevention conferred no protective effects for all-cause mortality, cardiovascular death, non-fatal myocardial infarction, angina, or revascularisation. However, there was an increased risk of stroke in those in the hormone therapy arm for combined primary and secondary prevention (RR 1.24, 95% CI 1.10 to 1.41). Venous thromboembolic events were increased (RR 1.92, 95% CI 1.36 to 2.69), as were pulmonary emboli (RR 1.81, 95% CI 1.32 to 2.48) on hormone therapy relative to placebo.

The absolute risk increase for stroke was 6 per 1000 women (number needed to treat for an additional harmful outcome (NNTH) = 165; mean length of follow-up: 4.21 years (range: 2.0 to 7.1)); for venous thromboembolism 8 per 1000 women (NNTH = 118; mean length of follow-up: 5.95 years (range: 1.0 to 7.1)); and for pulmonary embolism 4 per 1000 (NNTH = 242; mean length of follow-up: 3.13 years (range: 1.0 to 7.1)).

We performed subgroup analyses according to when treatment was started in relation to the menopause. Those who started hormone therapy less than 10 years after the menopause had lower mortality (RR 0.70, 95% CI 0.52 to 0.95, moderate quality evidence) and coronary heart disease (composite of death from cardiovascular causes and non-fatal myocardial infarction) (RR 0.52, 95% CI 0.29 to 0.96; moderate quality evidence), though they were still at increased risk of venous thromboembolism (RR 1.74, 95% CI 1.11 to 2.73, high quality evidence) compared to placebo or no treatment. There was no strong evidence of effect on risk of stroke in this group. In those who started treatment more than 10 years after the menopause there was high quality evidence that it had little effect on death or coronary heart disease between groups but there was an increased risk of stroke (RR 1.21, 95% CI 1.06 to 1.38, high quality evidence) and venous thromboembolism (RR 1.96, 95% CI 1.37 to 2.80, high quality evidence).

Authors' conclusions

Our review findings provide strong evidence that treatment with hormone therapy in post-menopausal women overall, for either primary or secondary prevention of cardiovascular disease events has little if any benefit and causes an increase in the risk of stroke and venous thromboembolic events.

PLAIN LANGUAGE SUMMARY

Hormone therapy for preventing cardiovascular disease in both healthy post-menopausal women and post-menopausal women with pre-existing cardiovascular disease

Hormone therapy is used for controlling menopausal symptoms. It has also been used for the prevention of cardiovascular disease in post-menopausal women. The present review assessed the effects of using hormone therapy for six months or more. Nineteen randomised controlled trials (involving 40,410 women) compared oral hormone therapy (oestrogen, with or without progestogen) with placebo. Most participants were from the United States (US), and the mean age in most studies was over 60 years. The length of time women were on treatment varied across the trials from 7 months to 10.1 years. The studies were generally well conducted with overall low risk of bias.

Overall, results showed no evidence that hormone therapy provides any protective effects against death from any cause, death specifically from cardiovascular disease, non-fatal heart attack or angina, either in healthy women or women with pre-existing heart disease.

Rather, in post-menopausal women hormone therapy increased the risk of stroke and obstruction of a vein by a blood clot (venous thromboembolism).

We are confident that the results of are review are close to the true effects for most of the outcomes we looked at. The studies were large, well-designed and the results were generally consistent across the studies.