Reassessment of the cost-effectiveness of hormone replacement therapy in Sweden: results based on the Women's Health Initiative randomized controlled trial

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The analysis considered the use of hormone replacement therapy (HRT) for women with menopausal symptoms. Those women with an intact uterus received HRT that consisted of combination therapy, whilst those women who had previously undergone a hysterectomy received HRT that consisted of oestrogen alone.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of Swedish women with menopausal symptoms. The study population was analysed in six groups depend on age (50, 55 or 60 years) and uterine status (intact uterus or hysterectomy).

Setting
The setting was the community. The economic study was carried out in Stockholm, Sweden.

Dates to which data relate
Most of the effectiveness data were extracted from studies published between 2000 and 2004. The age-specific annual mortality rates for the general population in Sweden were obtained from a source available online. The cost information came from published and unpublished studies between 1997 and 2002. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from published literature, augmented by authors' assumptions when necessary.

Modelling
A published Markov model (Zethraeus et al. 1999, see 'Other Publications of Related Interest' below for bibliographic details) was adapted to estimate the long-term impact of treatment with HRT on costs and effects. The health states of the original model were coronary heart disease (CHD), breast cancer and fracture outcomes (hip fracture, vertebral fracture and wrist fracture). This model was extended to include, stroke, venous thromboembolic events (VTE) and colorectal cancer, thus allowing all relevant effects of HRT to be captured. The cycle length of the model was 1 year and the time horizon was 50 years.
Outcomes assessed in the review
The following model parameters were assessed within the review of the literature:

the relative risk (RR) and age-specific population risks of CHD, VTE, stroke, breast cancer, colorectal cancer, hip fracture, vertebral fracture and other osteoporotic fracture;

the age-specific annual mortality rates for the general population; and

the age-specific mortality rates from hip fractures and clinical vertebral fractures.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Approximately five primary studies were reviewed for the estimation of model parameters.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The following estimates used within the model were reported.

For women with an intact uterus on combination therapy, the RR was 1.29 for CHD, 1.41 for stroke, 2.11 for VTE, 1.26 for breast cancer, 0.63 for colorectal cancer, 0.66 for hip fracture and vertebral fracture, and 0.77 for osteoporotic fracture.

For women with a hysterectomy on oestrogen-only therapy, the RR was 0.91 for CHD, 1.39 for stroke, 1.33 for VTE, 0.77 for breast cancer, 1.08 for colorectal cancer, 0.61 for hip fracture, 0.62 for vertebral fracture, and 0.70 for osteoporotic fracture.

Details of other parameters used within the model were reported in a working paper (Zethraeus et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details).

Methods used to derive estimates of effectiveness
The authors made some assumptions when literature-based estimates were not available.

**Estimates of effectiveness and key assumptions**
The authors assumed that 30% of the observed excess mortality after a hip or vertebral fracture was associated with the fracture event. In addition, they assumed that the gain in quality of life due to HRT was equal to 0.29, which was equal to the average of a women with menopausal symptoms.

**Measure of benefits used in the economic analysis**
The summary measures of benefits were the life-years gained and the quality-adjusted life-years (QALYs) gained. Both of the measures were estimated through the use of a Markov model that determined the long-term effects of treatment with HRT.

**Direct costs**
The quantity/cost boundary adopted in the economic study was that of society. The costs included were those borne by the hospital, patients and society, such as initial and annual intervention costs (including drug costs and costs of hospital and physician visits), direct fracture costs, and the cost-savings and costs incurred because of changes in morbidity due to HRT treatment. The resource use and the unit costs were not presented separately. All costs were discounted at an annual rate of 3%. The price year was 2003.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
Indirect costs due to fracture were included in the economic study. The costs were discounted at an annual rate of 3%. The price year was 2003.

**Currency**
Swedish kroner (SEK).

**Sensitivity analysis**
One-way sensitivity analyses and a threshold analysis were conducted to test the robustness of the results. The variables included the effects of HRT, remaining effects of HRT, size of the quality of life improvement, treatment duration, intervention cost, and the discount rates of costs and benefits.

**Estimated benefits used in the economic analysis**
The authors reported the life-years gained and QALYs gained for each of the six groups, compared with no treatment. The benefits were discounted at a rate of 3%.

For women with a hysterectomy on oestrogen-only therapy, HRT resulted in a gain from 0.006 to 0.03 in life-years and a gain from 1.2 to 1.3 in QALYs.

For women with an intact uterus on combination therapy, HRT resulted in a gain from 0.02 to 0.03 in life-years and a gain from 1.2 to 1.3 in QALYs.

**Cost results**
The costs with no HRT and with HRT for 50-year-old women with an intact uterus were SEK 804,024 and SEK
819,266, respectively. The difference was SEK 15,242. The costs for 55-year-old women were SEK 1,312,432 (no HRT) and SEK 1,325,282 (HRT), and the difference was SEK 12,850. The costs for 60-year-old women were SEK 1,925,364 (no HRT) and SEK 1,936,097 (HRT), and the difference was SEK 10,733.

The costs with no HRT and with HRT for 50-year-old women with a hysterectomy were SEK 805,706 and SEK 815,813, respectively. The difference was SEK 10,107. The costs for 55-year-old women were SEK 1,314,143 (no HRT) and 1,323,882 (HRT), and the difference was SEK 9,739. The costs for 60-year-old women were SEK 1,925,986 (no HRT) and SEK 1,939,631 (HRT), and the difference was SEK 13,645.

Synthesis of costs and benefits
Compared with no therapy, the cost per QALY gained for women with an intact uterus were SEK 12,807 for 50-year-old women, SEK 10,844 for 55-year-old women and SEK 9,159 for 60-year-old women.

Compared with no therapy, the costs per QALY gained for women with a hysterectomy were SEK 8,266 for 50-year-old women, SEK 7,960 for 55-year-old women and 11,043 for 60-year-old women.

For women with both intact uterus and hysterectomy, the cost-effectiveness results were stable to all but one of the alternative scenarios. The results were sensitive to whether the therapy had a positive effect on menopausal symptoms or not.

The threshold analysis revealed that HRT was cost-effective for women with or without a hysterectomy if the gain in quality of life exceeded 0.013 units.

Authors' conclusions
There was a high probability that hormone replacement therapy (HRT) was a cost-effective strategy for women with menopausal symptoms.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator strategies was clear. They represented current options in the authors' setting. You should consider whether these health technologies apply to your own setting.

Validity of estimate of measure of effectiveness
The authors identified a variety of studies to determine the model parameters. However, most of the parameter values were estimated from the clinical findings in two WHI studies. Given that the purpose was to reassess the situation in light of these new findings, it seems reasonable that the authors have derived their effectiveness data directly from these studies, although some assessment of the quality and internal validity of the WHI studies might have proved useful. However, for the other model parameters it was not clear that a systematic review was performed. For full details the reader should refer to Zethraeus et al. 2004.

Validity of estimate of measure of benefit
Life-years gained and QALYs gained were used as the summary benefit measures. This was appropriate since they capture the impact of the intervention on life expectancy and quality of life. Discounting was applied. Both measures were comparable with the benefits of other health care interventions. Extensive sensitivity analyses were carried out.

Validity of estimate of costs
It appears that all the cost categories relevant to the societal perspective have been included. A breakdown of the cost items was not provided, nor was there any information on the unit costs and quantities of resources used. Much of the costing was taken from the earlier publication (Zethraeus et al. 2004), which again makes a judgement on quality and validity difficult. Details were not reported in full, thereby reducing the possibility of replicating the study. Discounting
was conducted and the price year was reported, which aids reflation exercises in other settings.

**Other issues**
The authors compared their findings with other published studies and found that they were similar. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of their analysis. The modelling methods employed appear to have been appropriate for the analysis undertaken.

**Implications of the study**
The authors suggest that further studies are required to examine the cost-effectiveness of HRT in other population (e.g. women with a high risk of fracture).

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

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