Cost effectiveness of hormone therapy in women at high risks of fracture in Sweden, the US and the UK: results based on the Women's Health Initiative randomised 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.

CRD summary
This study compared the costs and effects of hormone therapy with no therapy in postmenopausal women with no menopausal symptoms, but at increased risk of fracture. The authors concluded that hormone therapy was a cost-effective approach for certain women with osteoporosis, specifically, those with hysterectomies or those with an intact uterus and prior vertebral fracture. The methods and results were appropriate and were mostly well-reported. Overall, the authors’ conclusions appear to be reasonable.

Type of economic evaluation
Cost-utility analysis

Study objective
The goal was to compare, by means of a state transition model, the costs and effects of hormone therapy in postmenopausal women at high risk of fracture in Sweden, the USA and the UK.

Interventions
Hormone therapy, administered for three years for postmenopausal women on the threshold of osteoporosis, was compared with no therapy. The therapy consisted of conjugated equine oestrogen (CEE, 0.625mg) alone in hysterectomised women, and medroxyprogesterone acetate (2.5mg) with CEE (0.625mg) in women with an intact uterus. Women in the hypothetical cohorts were assumed to be aged 60 years, without menopausal symptoms, with an osteoporosis femoral neck T-score under -2.5, and located in Sweden, the USA or the UK.

Location/setting
Sweden/primary care.

Methods
Analytical approach:
A Markov individual state transition model, which kept track of disease history, was developed and used to synthesise published and national data estimates. A 40-year time frame was used (until the women reached 100 years or died). The analyses were subcategorised by uterus status (intact or removed) and by previous or no previous fracture. The authors stated that a societal perspective was adopted.

Effectiveness data:
The data on the effectiveness of the hormone therapy were derived from a single randomised controlled trial (The Women’s Health Initiative, WHI, Study, Anderson et al. 2004, Rossouw et al. 2002, and Jackson et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). National and inpatient registries and published literature were used for country-specific disease risks and mortalities. The clinical outcomes in the analysis were treatment-related adverse events (hip, vertebral, and wrist fractures, breast and colorectal cancers, and cardiovascular diseases) and deaths. To derive the model parameters, some assumptions were made and these were clearly justified and supported with references where relevant.

Monetary benefit and utility valuations:
The utilities for each adverse event were based on several published studies, all of which used the EuroQol-5D (EQ-5D) questionnaire, except for stroke where the utility estimates were based on a meta-analysis using various estimation
methods. The utility estimates were assumed to be the same for each of the three countries.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs), which were discounted at a rate of 3%.

Cost data:
All the direct medical costs for therapeutics, morbidity, and mortality were included. The prices were derived from more than 20 country-specific reports published from 1996 to 2006. Drug prices were selected for drugs which were comparable across the three countries. The costs were divided into short-term (within one year) and long-term (if the event persisted for several years). The model used tracking and memory features to account for the long-term costs and effects of adverse events. The indirect costs for the UK and the USA were calculated, based on Swedish data and using purchasing power parities. Prices were adjusted to 2006 US dollars ($) using country-specific inflation rates. All costs were discounted at a rate of 3%.

Analysis of uncertainty:
Threshold and sensitivity analyses tested for the effects of changes in key parameters including fracture risks, cohort ages, treatment duration, duration of effectiveness in fracture prevention, reduction in risk of breast cancer, criteria for osteoporosis status, and inclusion of the indirect costs of longer survival. A probabilistic sensitivity analysis was also performed, and the results were reported using cost-effectiveness acceptability curves.

Results
The discounted additional costs for hormone therapy ranged from $107 to $1,439 compared with no therapy, across the three countries and four patient groups.

The discounted QALYs gained ranged from 0.013 to 0.083 for hysterectomised women and from 0.019 to 0.032 for women with an intact uterus and with a previous fracture. However, losses in QALYs in the range 0.018 to 0.039 occurred for women with an intact uterus and with no previous fracture.

The incremental cost-effectiveness ratios ranged from $2,054 to $49,539 per QALY gained for hormone therapy for hysterectomised women, or women with an intact uterus and with a previous fracture. Hormone therapy produced losses in QALYs and higher costs than no therapy for women with an intact uterus and with no previous fracture, and was therefore an inferior option to no therapy.

The results were sensitive to variations in treatment effect estimates, the age at initiation of therapy, cut-off criteria for osteoporosis status, and the duration of the treatment effect. The cost-effectiveness ratios were lower for older women, shorter treatment duration, and women with a previous fracture, irrespective of uterus status and risk of fractures.

The probability sensitivity analyses indicated that, at a willingness to pay of $75,000, for hysterectomised women at 60 years, with a previous fracture, hormone therapy was cost-effective in 99% of simulations for all countries.

Authors’ conclusions
The authors concluded that hormone therapy was cost-effective for asymptomatic menopausal women at high risk of fracture and with an intact uterus, and for all asymptomatic menopausal women with a hysterectomy irrespective of baseline risk of fracture. Hormone therapy was not cost-effective in asymptomatic menopausal women with an intact uterus and fracture risk equal to that of the general population.

CRD commentary
Interventions:
The two strategies and the profile of the intended population were clearly described. The composition of the hormone therapy was the same as that used in the WHI Study, but the authors’ stated that these drugs may have been different to those currently used in clinical practice. The ‘no therapy’ option may also have been inappropriate because new therapies designed to reduce fracture risks were available and may have been suitable as comparison options.

Effectiveness/benefits:
The effectiveness data were derived from various published studies which appear to be of high quality. However, the methods used to identify and select these studies were not stated. The authors focused on reporting the QALYs gained and did not report the results of the additional health outcomes (fractures, cancers, and cardiovascular events). These results might have been useful given that the outcomes can cause mortality and therefore they are an important link between hormone therapy and life-years gained. The use of utilities from published studies, which all used the EQ-5D (except for stroke), is a strength of the study. However, the use of the same utilities across the three countries may have introduced bias.

Costs:
The costs appear to reflect those applicable to a health-system perspective rather than the societal perspective reported by the authors. Productivity costs, which are usually included for a societal perspective, were omitted and the only indirect cost which was included was that of additional survival time. This could be categorised as a (delayed) health system cost. The costing methods, cost sources and references were reported in detail and clearly. The costs were adjusted for inflation, but the resource quantities were not reported separately from their costs.

Analysis and results:
An illustration of the model structure was presented and a thorough description of the cohort and model features was provided. The health outcomes and net costs were synthesised into incremental cost-effectiveness ratios. The model structure is likely to be valid as it extended models from previous work. The model parameter distributions used for the probabilistic sensitivity analyses were not reported, so it is not possible to judge their suitability. However, the authors did provide very detailed results of their sensitivity analyses. Additionally, the authors identified and discussed a number of limitations to their study and gave detailed explanations of differences between countries.

Concluding remarks:
The study methods and results were comprehensive and, in most cases, were transparently reported. The authors’ conclusions appear to be a fair assessment of the analysis undertaken.

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Other publications of related interest


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