

The cost-effectiveness of the treatment of high risk women with osteoporosis, hypertension and hyperlipidaemia in Sweden

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Abstract

Summary This paper assessed the cost-effectiveness of the treatment of high risk women with osteoporosis, hypertension and hyperlipidaemia in Sweden, using one model and a societal perspective. Cost-effective scenarios were found in all these chronic disorders. These findings are of relevance for decisions on the efficient allocation of health care resources.

Introduction There is a need to assess the cost-effectiveness (CE) of treatment of osteoporosis from a societal perspective and to relate this to the CE of interventions in other

disease areas. This is of relevance for decisions on the efficient allocation of health care resources within and between disease areas. The purpose of the paper was to estimate the CE of the treatment and prevention of osteoporosis and to put that into the perspective of treating hypertension and hyperlipidaemia. The CE was assessed for different high risk female populations aged 50–80 years.

Methods The estimation of CE was based on a model populated with data for Sweden.

Results Compared to no intervention, a 5-year treatment of osteoporosis, hypertension, and hyperlipidaemia, is cost effective for most of the assessed high risk female populations. The cost per gained quality adjusted life year (QALY) for the treatment of a 70-year-old woman never exceeded SEK 330,000 (US\$ 44,000), which is generally judged as an acceptable cost for a gained QALY.

Conclusions The study demonstrates that it is possible to produce reliable estimates of the CE of treatments in different disease areas within the context of a single model.

Keywords Bisphosphonates · Cost · Hydrochlorthiazides · QALY · Statins

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Introduction

There is a vast number of studies that have assessed the cost-effectiveness (CE) of the treatment and prevention of osteoporosis (see e.g., reviews by Zethraeus et al. or Fleurence et al. [1–3]). Since the development of the first CE models at the beginning of the 1980s, the focus has shifted from assessing hormone replacement therapy (HRT) to analysing bone specific interventions such as the bisphosphonates for the treatment and prevention of osteoporosis. To date studies have to a large extent assessed

the CE of different interventions within the osteoporosis area only, and have not systematically compared the CE with that of interventions in other disease areas. Such information is important when discussing the efficient allocation of health care resources within, but also between disease areas.

Information on the CE of interventions in different diseases can be obtained from the literature and assessed by systematic review. The problem with such an approach is that the results of different CE studies may be difficult to compare. There is a risk that different CE results may be a consequence of factors other than the effect of the intervention, such as differences in perspective, data, and model structure. Ideally, a common modelling framework should be adopted to compare the CE of different interventions within and between disease areas.

Recently we undertook a reassessment of the CE of HRT in post-menopausal women based on new medical evidence from the Women's Health Initiative [4, 5] using a societal perspective. The model was populated with data for Sweden and consisted of the following disease states: coronary heart disease (CHD), stroke, venous thromboembolic events (VTE), breast cancer, colorectal cancer, hip fracture, vertebral fracture and wrist fracture [6]. The general structure of the model permits the analysis of the CE of other interventions besides HRT. The model is well suited also for analysing the CE of osteoporosis, antihypertensive and cholesterol lowering therapies.

The purpose of this study was to assess the CE of the treatment and prevention of osteoporosis, hypertension and hyperlipidaemia using one model and a societal perspective [6, 7]. The CE was assessed for different high risk female populations aged 50–80 years.

Methods and data

The CE of the treatment and prevention of osteoporosis, hypertension and hyperlipidaemia was based on the model and data presented in Zethraeus et al. [6, 7]. Costs and QALYs were discounted at a rate of 3%. All costs were expressed in the prices of 2005, and were converted from Swedish Crowns (SEK) to US dollars using the average exchange rate during 2005 of 1US\$=7.5SEK. Where needed, the costs were inflated using the consumer price index from Statistics Sweden.

Indications and patient groups

The CE was estimated for female populations aged 50–80 years with osteoporosis, hyperlipidaemia or hypertension alone or in combination with risk factors such as previous fracture, diabetes and smoking. In total, 48 inde-

pendent patient groups were defined according to different age and risk profile (16 groups in each disease). The base-case age was set to 70 years, i.e., four scenarios for each disease. In the osteoporosis group, patient groups were defined according to T-score level and the presence of a previous fragility fracture (established osteoporosis). In the hypertension group, women were defined according to systolic blood pressure (SBP) in combination with diabetes and smoking. In the hyperlipidaemia group, women were categorised according to the serum level of total cholesterol (TC) and high density lipoprotein (HDL) cholesterol in combination with diabetes and smoking.

Interventions and assumed risk reductions

The CE of a 5-year treatment with cholesterol lowering, antihypertensive and osteoporosis therapy was estimated for the above defined patient groups. The treatments for each patient group were compared with no intervention. The following drugs were selected: alendronate (70 mg weekly), hydrochlorothiazide (25 mg daily), and simvastatin (20 mg daily). These agents were chosen since they were the cheapest within one class of first line drugs. The fracture risk reduction of osteoporosis treatment was taken from a meta-analysis by Stevenson et al. [8]. Risk reductions were set to 44% (CI₉₅ 0.32–0.54), 38% (CI₉₅ 0.02–0.6) and 19% (CI₉₅ 0.03–0.32) for vertebral, hip and wrist fractures. A remaining effect of five years was assumed for fractures, i.e., the relative risk reduction diminished linearly during 5 years after stopping therapy. This is consistent with findings in randomized clinical trials of the effect of bisphosphonates on the overall risk of fracture [9, 10]. The cholesterol lowering therapy was assumed to reduce the risk of CHD by 31% (CI₉₅ 17–43). The risk reduction is based on a randomized trial to evaluate the effectiveness of a reductase inhibitor, pravastatin, in preventing coronary events in men with moderate hypercholesterolemia and no history of myocardial infarction [11]. Treatment was not assumed to affect the risk of stroke. Hypertension therapy was assumed to reduce the risk of CHD by 16% (CI₉₅ 8–23) and stroke by 38% (CI₉₅ 31–45%). The risk reductions are based on a meta analysis of trials of drug therapy (primarily diuretics and β -blockers) for mild to moderate hypertension [12]. These risk reductions were also used in a health technology assessment of hypertension in Sweden [13]. No remaining effects were assumed to exist for hypertension and hyperlipidaemia therapy when treatment was stopped [14, 15].

Design and structure of the model

Our model was based on a merger of two previous models; one for the assessment of the CE of cardiovascular diseases and one for the assessment of osteoporosis [16, 17]. Based

on new findings in the Women's Health Initiative [4, 5], the model was later modified to assess the CE of HRT [6, 7] and was then modified again for this publication. The model is an individual state transition model that follows the patients until 100 years of age or death. The following disease events were incorporated into the model: cardiovascular disease (CHD, stroke, VTE), cancer (breast cancer, colorectal cancer), and fractures (hip fracture, vertebral fracture, wrist fracture). The risks of cancer and VTE were assumed not to be affected by the therapies analysed in this paper and were therefore excluded. The model estimates the costs and quality adjusted life years (QALYs) with and without intervention, which allows for the computation of the incremental CE ratio (costs per QALY gained) of initiating a therapy compared with no therapy. An intervention is modelled by its impact on disease risks during therapy, but also allows for effects after the cessation of therapy, allowing for remaining effects (e.g., in the case of osteoporosis).

Data for the model

The data for the model were based on available evidence for risks, mortality rates, quality of life weights and costs for Sweden. Costs were based on a societal perspective including intervention costs (costs of drugs, consultations and travel and time), disease related direct and indirect costs and costs in added years of life. The study by Zethraeus et al. [6] gives an overview of the model and data, while Zethraeus et al. [7] provides a detailed presentation. Data on fracture costs and quality of life have been updated and are based on two studies by Borgström et al. [18] and Ström et al. [19]. Data on mortality rates and average disease risks in the model were obtained from different Swedish national registers and epidemiological studies.

Baseline and relative risks

To assess the CE of therapies for different female risk populations in Sweden, the base line risks in the model of fracture, stroke and CHD (i.e., the average risk of a Swedish female population) were multiplied by a relative risk that reflected the relative increase in risk compared to an average population. The relative risks for CHD and

stroke were obtained by using the risk equations estimated by Wolf et al. [20] and Wilson et al. [21], who estimated the relation between the risk of stroke and CHD, and risk factors such as smoking, hypertension, hyperlipidaemia, and prevalence of diabetes etc. The relative risk of CHD and stroke, in a defined high risk group, was obtained by dividing the estimated risk of the high risk population (with a specific set of risk factors, see Table 3) given by the equation, with the estimated risk of an average population (with average population values of the risk factors) given by the equation. The baseline values of the risk factors were based on a normal population sample in Stockholm, Sweden [22]. This produced the relative risks of CHD and stroke, which was multiplied with the base line risks in the model. When modeling osteoporosis, the fracture risk in the normal female population was multiplied by different relative risks that reflected the type of fracture, presence of prevalent vertebral fracture, and age. The method used to calculate the relative risk of fractures has previously been described by Kanis et al. and De Laet et al. [23, 24]. The relative risk of fractures due to prevalent vertebral fracture used were adjusted for age, but not for BMD and were therefore down adjusted by 10% [25, 26]. It should be noted that the risks associated with different blood pressures, cholesterol levels and T-scores are estimates of the risk at that particular threshold, not a group with a value below or above the indicated threshold (i.e., TC=7.25 rather than above 7.25).

The baseline risks, relative risks, and risk categories used are shown in Tables 1, 2 and 3. Each disease was divided into four different risk populations based on previously published risk factors for disease events.

– Hypertension

Thresholds of a SBP of 140 and 160 mm Hg were used since they are defined as stage I and stage II hypertension in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [27]. Both smoking and diabetes are risk factors for both stroke and CHD and were therefore included to define additional high risk populations [20, 21].

– Hyperlipidaemia

The cut-offs for increased risk of CHD and stroke (TC=7.25 mmol/L and HDL=1.3 mmol/L) were taken from

Table 1 Baseline annual risk of events per 10,000 women in different ages

Age	AMI	Angina	Cor. insuff.	Stroke	Hip fracture	Vertebral fracture	Wrist fracture
50	6	12	5	10	6	16	40
60	17	31	12	20	14	25	52
70	46	60	23	66	46	64	82
80	103	84	29	173	182	114	114

Source: [7]

Table 2 Relative risk of hip/vertebral/wrist fractures compared to the general female population

Age	T-score=-2.5	T-score=-3	T-score=-2.5 + previous vertebral fracture	T-score=-3 + previous vertebral fracture
50	2.89/2.14/1.61	4.65/2.87/1.91	5.97/8.47/2.03	9.63/11.36/2.40
60	2.11/1.76/1.44	3.40/2.37/1.71	4.19/6.28/1.80	7.45/9.22/2.35
70	1.32/1.32/1.22	2.13/1.36/1.24	2.51/4.21/1.51	4.42/6.11/1.96
80	0.86/1.01/1.05	1.38/1.36/1.24	1.49/2.64/1.27	2.59/3.74/1.63

Source: [24, 39]

Wilson et al. [21] and are similar to those used for the NCEP (National Cholesterol Education Program) III guidelines [28]. Smoking and diabetes were also included to define additional high risk populations [21, 28].

– Osteoporosis

Low T-score and previous fractures are firmly established as important risk factors for osteoporotic fractures. A T-score of -2.5 SD was used as a threshold for osteoporosis and a T-score of -3 SD was arbitrarily used to elevate risk. Previous vertebral fracture was added to these populations to define higher risk groups and established osteoporosis [29].

Intervention costs

The average annual intervention cost of osteoporosis was set to US\$ 795 (the annual drug cost was US\$ 427; consultation cost was US\$ 320; travel and time cost US\$ 48), which reflects an average treatment with alendronate, and includes a physician visit and a bone mineral measurement every second year. The average annual intervention cost of the treatment of hypertension was set to US\$ 377 (annual

drug cost of US\$ 53; consultation cost US\$ 260; travel and time cost US\$ 64), which reflects an average treatment with hydrochlorothiazide, and included two primary care physician visits [13]. The average annual intervention cost of the treatment of hyperlipidaemia was set to US\$ 351 (annual drug cost of US\$ 27; consultation cost US\$ 260; travel and time cost US\$ 64), which reflects an average treatment with simvastatin, and included two primary care physician visits [15]. All drug costs were taken from the Swedish Drug Compendium [30]. The travel and time costs were assumed to be US\$ 32 per visit which corresponds to 25% of the consultation cost for the treatment of hypertension [13].

Definition of cost-effectiveness

To determine whether a therapy (compared with no treatment) is cost-effective the incremental CE ratio is compared with the value of a QALY. If the value exceeds the cost of a gained QALY, the intervention is defined as cost-effective. No exact value of a gained QALY is available. The value is usually found in the range of US\$ 40,000 and US\$ 100,000 [15, 31]. In this paper we use a value of SEK 600,000 per QALY gained (corresponding to US\$ 80,000 using the average exchange rate during 2005 of 1US\$=7.5US\$).

Table 3 Relative risks (RR) of CHD and stroke compared with the general female population for all age groups*

	RR of CHD	RR of stroke
Hypertension		
Stage 1 (SBP=140)	1.30	1.12
Stage 2 (SBP=160)	1.59	1.66
Stage 1 + diabetes	2.21	1.83
Stage 2 + diabetes + smoker	3.30	3.90
Hyperlipidaemia		
TC=7.25	1.38	1.00
TC=7.25 and HDL=1.3	2.12	1.00
TC=7.25 and HDL=1.3 + diabetes	3.62	1.63
TC=7.25 and HDL=1.3 + diabetes + smoker	4.42	2.34

Source: [20–22, 27]

*SBP = systolic blood pressure (mmHg), TC = total cholesterol (mmol/L), HDL = high density lipoprotein (mmol/L)

Stochastic and sensitivity analysis

Simulations of CE ratios were carried out based on the confidence intervals (CI) for the risk reductions for the different therapies. The proportion of the CE ratios being defined cost-effective was then calculated for different values of willingness to pay. The proportions were presented as CE acceptability (CEA) curves for three base-case populations with a given risk profile. It should be noted that the CEA curves only represent uncertainty in estimates of the underlying risk reductions. In a sensitivity analysis the duration of the remaining effect on fractures after the cessation of osteoporosis treatment, was varied between 0 and 10 years, i.e., the relative risk reduction was assumed to diminish immediately and linearly up to 10 years after the cessation of therapy.

Table 4 Cost-effectiveness results for the treatment of osteoporosis, hypertension and hyperlipidaemia for women in different risk groups based on a societal perspective (cost (US\$) per gained quality adjusted life year)*

Age	T-score=-2.5	T-score=-3	T-score=-2.5 + previous vertebral fracture	T-score=-3 + previous vertebral fracture
Osteoporosis (alendronate 70 mg)				
50	97,000	65,000	36,000	25,000
60	61,000	41,000	27,000	20,000
70	44,000	27,000	18,000	9,000
80	25,000	11,000	7,000	cost-saving
Hypertension (hydrochlorothiazide 25 mg)				
Age	SBP=140	SBP=160	SBP=140 + diabetes	SBP=160 + diabetes + smoker
50	79,000	75,000	53,000	28,000
60	56,000	45,000	40,000	25,000
70	40,000	39,000	36,000	29,000
80	45,000	43,000	41,000	37,000
Hyperlipidaemia (simvastatin 20 mg)				
Age	TC=7.25	TC=7.25 and HDL=1.3	TC=7.25 and HDL=1.3 + diabetes	TC=7.25 and HDL=1.3 + diabetes + smoker
50	51,000	33,000	16,000	7,000
60	49,000	33,000	23,000	20,000
70	44,000	39,000	32,000	32,000
80	52,000	47,000	44,000	44,000

*SBP = systolic blood pressure (mm Hg), TC = total cholesterol (mmol/L), HDL = high density lipoprotein (mmol/L)

Results

The cost per gained QALY for the different high risk female populations is presented with (Table 4) and without (Table 5) costs in added years of life. A 5-year treatment of osteoporosis, compared with no therapy was cost-effective in all populations, except for 50-year-old women, since the average fracture risks are relatively low in this age group (Table 4). The CE results for the treatment of osteoporosis varied between cost-savings to US\$ 97,000 per gained QALY. The CE ratios consistently became lower with higher risk of fracture. Further, a 5-year treatment of hypertension was shown to be cost-effective in all the populations compared with no therapy. The CE ratios varied

between US\$ 25,000 and 79,000 per QALY gained. It is evident that the addition of more risk factors (diabetes and smoking) resulted in lower CE ratios. Finally, a 5-year treatment of hyperlipidaemia was also found to be cost-effective in all the defined populations compared with no therapy. The CE ratios ranged between 7,000 and 52,000 US \$ per QALY gained, and became lower when more risk factors were present. Thus, the treatment of osteoporosis, hypertension, and hyperlipidaemia were cost-effective for most combinations of ages and risk profiles. QALYs gained in the populations with lowest risk were 0.065, 0.081, and 0.074 from treatments for osteoporosis, hypertension and hyperlipidaemia, respectively. In the sub-groups with the highest risk 0.18, 0.18, and 0.19 QALYs were gained.

Table 5 Cost-effectiveness results for the treatment of osteoporosis, hypertension and hyperlipidaemia for women aged 70 years in different risk groups (cost (US\$) per gained quality adjusted life year). Costs in added years of life are excluded*

Osteoporosis (alendronate 70 mg)				
T-score=-2.5	T-score=-3	T-score=-2.5 + previous vertebral fracture	T-score=-3 + previous vertebral fracture	
27,000	8,000	cost-saving	cost-saving	
Hypertension (hydrochlorothiazide 25 mg)				
SBP=140	SBP=160	SBP=140 + diabetes	SBP=160 + diabetes + smoker	
16,000	12,000	11,000	4,000	
Hyperlipidaemia (simvastatin 20 mg)				
TC=7.25	TC=7.25 and HDL=1.3	TC=7.25 and HDL=1.3 + diabetes	TC=7.25 and HDL=1.3 + diabetes + smoker	
16,000	8,000	4,000	3,000	

*SBP = systolic blood pressure (mm Hg), TC = total cholesterol (mmol/L), HDL = high density lipoprotein (mmol/L)

An effect of treatments is that CHD, stroke and fracture events are avoided, which result in an increased life expectancy. Each added life year for an average women aged above 70 years is associated with an incremental societal cost since she will consume more (medical and non-medical consumption) than she produces (market production of goods and services). The exclusion of costs in added years of life for women 70 years of age thus implies lower CE ratios, which is shown in Table 5.

The CE improved with age for osteoporosis treatment, but not always for cholesterol lowering and antihypertensive therapy. Cost in added life years created a trend where high age was associated with a cost offset that neutralized the incremental QALY gains usually generated when treating older populations that have high baseline risks. This trend was not as pronounced for osteoporosis. The reasons are that previous vertebral fracture is such a strong risk factor for subsequent fractures and that the long term costs in the years following a hip fracture were substantially higher than for the other events. Thus, saved costs and gained QALYs, both caused by avoided fractures, outweighed the cost in added life years caused by longer life expectancy.

The stochastic analysis was performed for three base-case populations (see figures in bold in Table 4) and are presented as CEA curves in Fig. 1. Given that willingness to pay exceeds 50,000 US\$, the results indicate that all the treatments were markedly cost-effective. Sensitivity analysis of residual treatment effect in the osteoporosis popula-

tion is presented in Fig. 2. The analysis was done for the osteoporotic base-case population (age 70, T-score -2.5 SD, and a previous vertebral fracture) and shows that the incremental CE ratio (cost per gained QALY) was always below US\$ 35,000. When no residual effect on fracture efficacy was assumed after stopping treatment, the cost/QALY was estimated at US\$ 33,000.

Discussion

In this study we have for the first time, using a single model and a societal perspective, estimated the CE of the treatment of osteoporosis, hypertension and hyperlipidaemia compared with no intervention. All these disorders are multifactorial non-communicable diseases that represent a significant burden to society. The CE was assessed for different high risk female populations aged 50–80 years. Using the same model structure, one can use data on risks, mortality rates, costs and quality of life to compare the CE results in the different patient groups. To achieve this we have used a model previously developed for the assessment of the CE of HRT based on the findings in the Women's Health Initiative [6, 7]. The model includes e.g., the risk of fracture, CHD and stroke, which means that the model also can be used to assess other interventions that affect at least one of these disease states.

For many years modelling has played an important role in the assessment of the CE of the treatment and prevention

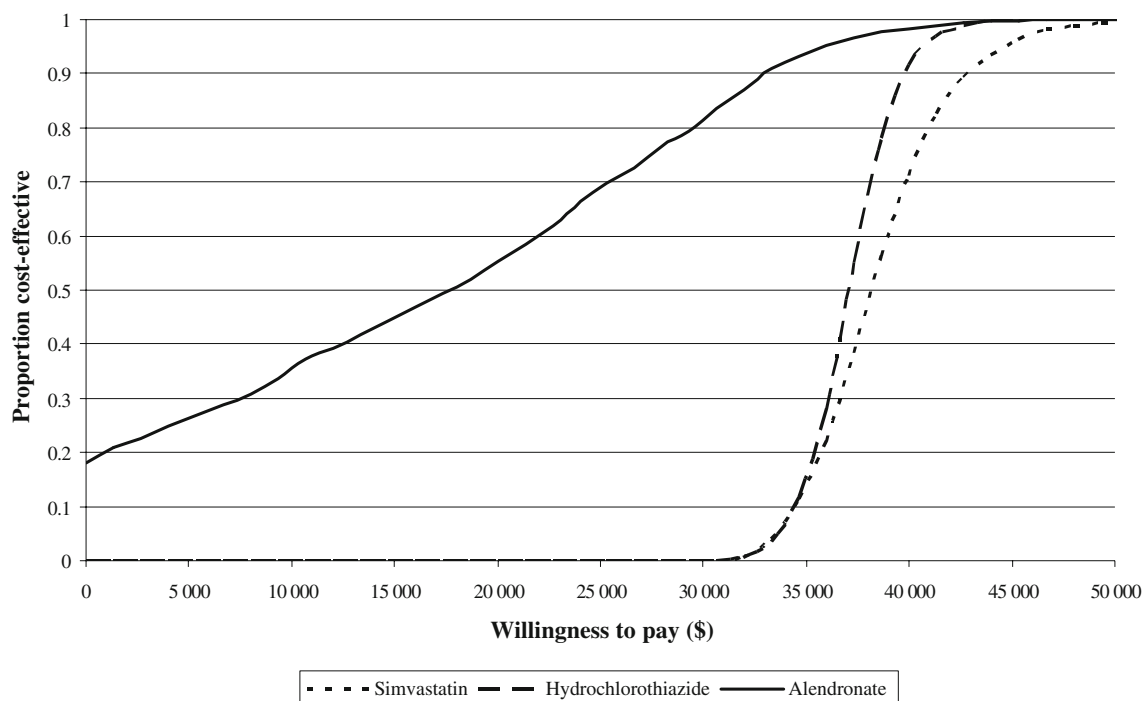


Fig. 1 The proportion of simulations defined as cost effective at different willingness to pay for three base-case populations and treatments (defined by the cost-effectiveness figures in bold in Table 4)

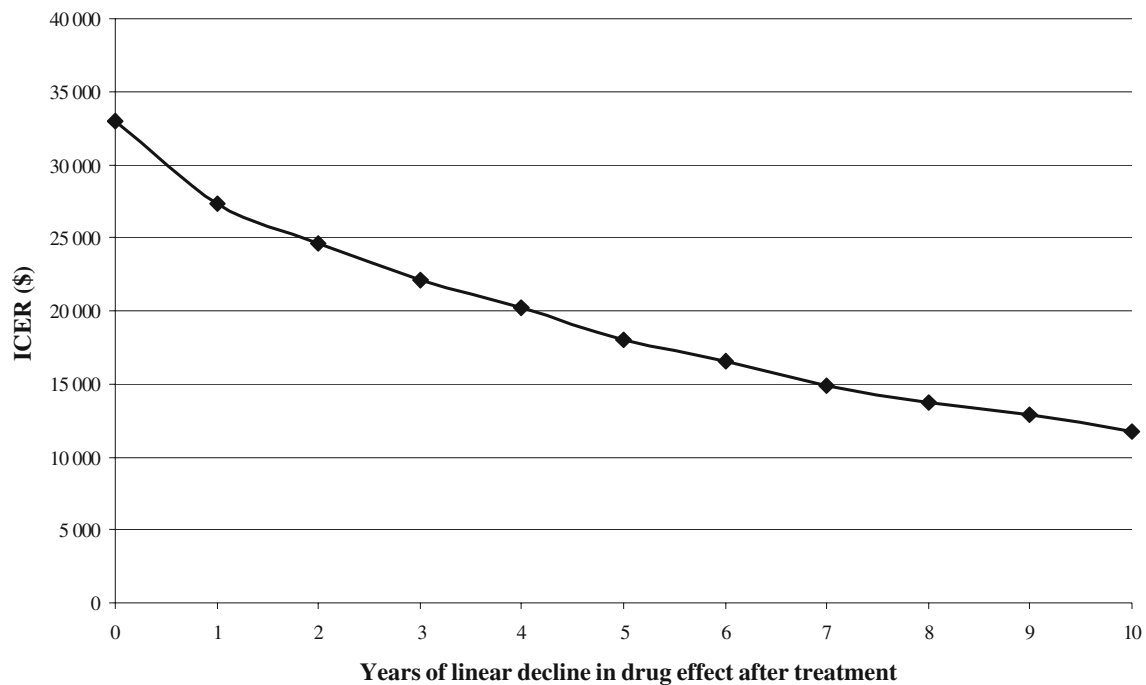


Fig. 2 Sensitivity analysis of residual effect on the incremental cost-effectiveness ratio (ICER) after stopping treatment in 70 years old women with T-score -2.5 and a previous vertebral fracture

of osteoporosis, hypertension and hyperlipidaemia. Modelling, which is a way of integrating the best available data on health effects, risks and costs, is necessary because clinical trials cannot provide all the information that is required for an assessment of the CE in clinical practice. Several models have been developed to assess the CE of health technologies in these fields. Although the models have become more similar over time, they still differ in many respects in terms of data, perspective and validation. This makes it difficult to assess whether the CE results are a consequence of a new model, the adopted perspective, the data, or the technology. In this study we used the same model for the assessment of the CE of the specific treatments and disease areas. The advantage is that the same model structure, perspective and data are used, which increases the comparability, quality and reliability of CE analyses of technologies within and between these disease areas. Thus the user can be more confident that differences in CE reflect the characteristics of the interventions being assessed rather than differences in methodology and data.

The analysis shows that, a 5-year cholesterol lowering, antihypertensive and osteoporosis treatment is cost-effective in nearly all the defined patient groups in a Swedish setting. The CE results largely depend on the level of the benefits of the treatments in terms of avoided costs and increased length and quality of life. It is evident that the presence of additional risk factors favourably affects the CE results. For example, if a population is subject to a

higher risk of fractures, a given risk reduction implies that more fractures are avoided with the result that more costs are saved and that more length and quality of life are gained. The increase in length of life may occasionally have a negative consequence for the CE of the treatment. In particular, for older populations (above the age of 64 years), increases in length of life implies that costs in added life years increases, which increases the CE ratio. Sometimes this negative effect will dominate the positive effect of prolonging life, which causes the CE ratio to increase when age increases. Which effect dominates may differ in different populations.

The results are presented both with and without the inclusion of costs in added years of life. If CE analysis is to be used as a tool for assisting decisions on which treatments maximise the welfare of society, costs in added years of life should be included [32]. This approach is also recommended by the Swedish pharmaceutical benefits board, that decides whether a prescription drug for outpatient care should be reimbursed or not. Nevertheless, the majority of studies do not include these costs, and in order to increase the comparability of our results with other studies, we presented the results with and without costs in added years of life.

The CE of antihypertensive therapy has been reviewed by the Swedish Council on Technology Assessment (SBU) [14]. Hypertension therapy was assumed to reduce the risk of CHD by 16% and stroke by 38%. The results show that for 55-year-old women the CE ratio varies between US\$ 1, 300

and 32,000 depending on therapy, and cardiovascular disease risk. The review showed that antihypertensive therapy generally is a rather cost-effective therapy and that the CE improves if the risk of cardiovascular diseases increases, which are similar to the finding in this study. A drawback with the SBU study is that it only includes direct costs for the health care and excludes indirect costs and costs in added years of life. A consequence is that the CE ratios generally become lower compared to the ones calculated in this study. In a study by Johannesson et al. [33] the CE of the treatment of hypertension was assessed based on a societal perspective also including costs in added years of life. Hypertension therapy was assumed to reduce the risk of CHD by 16% and stroke by 38%. The results showed that for women at least 70 years old the CE ratio is estimated at US\$ 29,000, which is similar to the results found in our study.

The CE of cholesterol lowering therapy has generally focused on secondary prevention strategies in patients with coronary heart disease (see e.g., [34]). The general finding is that cholesterol treatment is cost-effective in this patient population. In a study by Johannesson [15] the coronary risk level was calculated at which cholesterol lowering therapy becomes cost-effective in primary prevention. The treatment was assumed to reduce the annual risk of coronary heart disease by 31% each year in all patient groups. The results showed e.g., that if society is willing to pay \$100,000 to gain a QALY, it was cost-effective to initiate treatment if the 5-year-risk of coronary heart disease exceeded 2% for 50-year-old women, and 5% for 70-year-old women. The 5 year risk of coronary heart disease for 50 and 70-year-old women in our study, was equal to or exceeded these figures, which is consistent with the findings published by Johannesson [15].

The CE of osteoporosis interventions have been assessed in several studies [1–3]. Studies show that it is cost-effective to treat osteoporosis particularly at higher ages and in individuals with a previous fragility fracture. For instance, the cost per gained QALY with bisphosphonates have been estimated at between US\$ 27,000 (age 74 years) and 33,000 (age 71 years) for women with a two-fold increase in the fracture risk, which is similar to the results in this study [35]. Recent economic evaluations have shown that treatment with bisphosphonates is cost-effective in elderly women above the age of 70 years with established osteoporosis [36, 37]. However, some results in this analysis differ markedly from results published by other groups. In a recent economic evaluation commissioned by NICE [38], the CE in UK women with a previous vertebral fracture and a T-score of -2.5 SD was estimated at \$24,000 and \$32,000 at 70 years (converted from £) for alendronate and risedronate, respectively. The NICE analysis was done from a health care perspective and ignored cost in added

life years. The corresponding treatment in the present publication was found to be cost saving. Although CE is generally better in Swedish populations than in the UK, the comparison emphasizes that results may be sensitive to differences in model perspective, structure, assumptions used, modelling horizon, etc.

The CE results are stable to variations in risk reductions as shown in the stochastic analysis. The stochastic analysis considers only the uncertainty in the size of the risk reduction of the different therapies. Thus it should be stressed that we do not analyse the consequences of uncertainty in e.g., disease risks, costs or quality of life and mortality. This is explained by a lack of data on the confidence intervals for the true values of these parameters. However, in a sensitivity analysis we studied the effect of the residual effect after stopping osteoporosis treatment. It shows that changes in the duration of the residual effect, although affecting the cost per gained QALY, do not change the overall conclusions that it is cost-effective to treat 70-year-old women with established osteoporosis.

This study has demonstrated that it is feasible to assess the CE of interventions in different disease areas within the context of one model. By using one model, with the same structure and data, one can produce reliable estimates of the CE, which can be used to inform decision makers about the efficient allocation of resources within and between disease areas.

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Conflicts of interest None.

References

1. Zethraeus N, Borgstrom F, Strom O, Kanis JA et al (2007) Cost-effectiveness of the treatment and prevention of osteoporosis—a review of the literature and a reference model. *Osteoporos Int* 18:9–23
2. Zethraeus N, Ben Sedrine W, Caulin F, Corcaud S et al (2002) Models for assessing the cost-effectiveness of the treatment and prevention of osteoporosis. *Osteoporos Int* 13:841–857
3. Fleurence RL, Iglesias CP, Torgerson DJ (2006) Economic evaluations of interventions for the prevention and treatment of osteoporosis: a structured review of the literature. *Osteoporos Int* 17:29–40
4. Anderson GL, Limacher M, Assaf AR, Bassford T et al (2004) Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 291:1701–1712
5. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ et al (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 288:321–333
6. Zethraeus N, Borgstrom F, Jonsson B, Kanis J (2005) Reassessment of the cost-effectiveness of hormone replacement therapy in Sweden: results based on the Women's Health Initiative randomized controlled trial. *Int J Technol Assess Health Care* 21:433–441
7. Zethraeus N, Borgström F, Jönsson B, Kanis J (2004) A reassessment of the cost-effectiveness of hormone replacement

- therapy in Sweden - results based on the Women's Health Initiative randomised controlled trial. Working Paper Series in Economics and Finance at the Stockholm School of Economics, 2004, Working paper No 571 <http://swopec.hhs.se/hastef/papers/hastef0571.pdf>
8. Stevenson M, Jones ML, Davis S, Beverly C (2005) Extract from DSU report: Osteoporosis - primary prevention. <http://www.nice.org.uk/page.aspx?o=273738>
 9. Black DM, Schwartz AV, Ensrud KE, Cauley JA et al (2006) Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA* 296:2927–2938
 10. Greenspan SL, Emkey RD, Bone HG, Weiss SR et al (2002) Significant differential effects of alendronate, estrogen, or combination therapy on the rate of bone loss after discontinuation of treatment of postmenopausal osteoporosis. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 137:875–883
 11. Shepherd J, Cobbe SM, Ford I, Isles CG et al (2004) Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. 1995. *Atheroscler Suppl* 5:91–97
 12. Hebert PR, Moser M, Mayer J, Glynn RJ et al (1993) Recent evidence on drug therapy of mild to moderate hypertension and decreased risk of coronary heart disease. *Arch Intern Med* 153:578–581
 13. SBU (1994) [The Swedish Council on Technology Assessment in Health Care]. Moderately elevated blood pressure. Report No 121. Stockholm
 14. SBU (2004) [The Swedish Council on Technology Assessment in Health Care]. Moderately elevated blood pressure - a systematic review. Report No 170. Stockholm
 15. Johannesson M (2001) At what coronary risk level is it cost-effective to initiate cholesterol lowering drug treatment in primary prevention? *Eur Heart J* 22:919–925
 16. Johannesson M, Hedbrant J, Jonsson B (1991) A computer simulation model for cost-effectiveness analysis of cardiovascular disease prevention. *Med Inform (Lond)* 16:355–362
 17. Jönsson B, Hedbrant J, Johnell O (1993) A computer simulation model to analyse the cost-effectiveness of fracture prevention of osteoporosis. EFI Research paper Nr 6525
 18. Borgstrom F, Zethraeus N, Johnell O, Lidgren L et al (2006) Costs and quality of life associated with osteoporosis-related fractures in Sweden. *Osteoporos Int* 17:637–650
 19. Strom O, Borgstrom F, Zethraeus N, Johnell O et al (2007) Long term costs and quality of life associated with osteoporosis related fractures in Sweden. accepted in *Acta Orthopaedica* (September)
 20. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB (1991) Probability of stroke: a risk profile from the Framingham Study. *Stroke* 22:312–318
 21. Wilson PW, D'Agostino RB, Levy D, Belanger AM et al (1998) Prediction of coronary heart disease using risk factor categories. *Circulation* 97:1837–1847
 22. Hellenius M, Rosell M, Sandgren J (2000) High prevalence of overweight and metabolic syndrome among 60 year old women and men in Stockholm, Sweden. 12th International Symposium on Atherosclerosis Stockholm
 23. Kanis JA, Johnell O, Oden A, Jonsson B et al (2000) Risk of hip fracture derived from relative risks: an analysis applied to the population of Sweden. *Osteoporos Int* 11:120–127
 24. De Laet CE, van Hout BA, Burger H, Hofman A et al (1997) Bone density and risk of hip fracture in men and women: cross sectional analysis. *BMJ* 315:221–225
 25. Kanis JA, Johnell O, De Laet C, Johansson H et al (2004) A meta-analysis of previous fracture and subsequent fracture risk. *Bone* 35:375–382
 26. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA 3rd, et al (2000) Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 15:721–739
 27. Chobanian AV, Bakris GL, Black HR, Cushman WC et al (2003) Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 42:1206–1252
 28. NCEP (2002) Third report of the National Cholesterol Education Program. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation* 106:3143–3421
 29. WHO (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. WHO Study Group. *World Health Organ Tech Rep Ser* 843:1–129
 30. FASS för förskrivare. Accessed [2006-11-24] <http://www.fass.se>
 31. Hirth RA, Chernew ME, Miller E, Fendrick AM et al (2000) Willingness to pay for a quality-adjusted life year: in search of a standard. *Med Decis Making* 20:332–342
 32. Meltzer D (1997) Accounting for future costs in medical cost-effectiveness analysis. *J Health Econ* 16:33–64
 33. Johannesson M, Meltzer D, O'Connor RM (1997) Incorporating future costs in medical cost-effectiveness analysis: implications for the cost-effectiveness of the treatment of hypertension. *Med Decis Making* 17:382–389
 34. Johannesson M, Jonsson B, Kjekshus J, Olsson AG et al (1997) Cost effectiveness of simvastatin treatment to lower cholesterol levels in patients with coronary heart disease. *Scandinavian Simvastatin Survival Study Group. N Engl J Med* 336:332–336
 35. SBU (2003) [The Swedish Council on Technology Assessment in Health Care]. Osteoporosis - prevention, diagnosis and treatment. Report No 165. Stockholm
 36. Strom O, Borgstrom F, Sen SS, Boonen S et al (2007) Cost-effectiveness of alendronate in the treatment of postmenopausal women in 9 European countries-an economic evaluation based on the fracture intervention trial. *Osteoporos Int* 18:1047–1061
 37. Borgstrom F, Carlsson A, Sintonen H, Boonen S et al (2006) The cost-effectiveness of risedronate in the treatment of osteoporosis: an international perspective. *Osteoporos Int* 17:996–1007
 38. Stevenson M, Lloyd Jones M, De Nigris E, Brewer N et al (2005) A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. *Health Technol Assess* 9:1–160
 39. Kanis JA, Johnell O, Oden A, Sembo I et al (2000) Long-term risk of osteoporotic fracture in Malmo. *Osteoporos Int* 11:669–674