A computer model to analyse the cost-effectiveness of hormone replacement therapy – a revised version

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Abstract

This report presents a computer model for evaluating the cost-effectiveness (CE) of Hormone Replacement Therapy (HRT). The model is an extension of a previous model and includes also the risk of spine and wrist fracture. New Swedish data on risk of coronary heart disease and related mortality are included. The report describes the model's structure and data requirements; it also investigates the impact on the CE results by using the new model and by adding the wrist and spine fractures to the model. We further investigate whether the results are sensitive to the inclusion of Swedish risk and mortality data for CHD instead of using data based on the Framingham study. The results show that the incremental cost-effectiveness ratios (ICERs) are insensitive to the chosen model, to the assumption that the risk of wrist and spine fracture follows that of hip fracture, and to replacing the Framingham data with Swedish CHD risk and mortality data.

Keywords: Computer model, Cost-effectiveness analysis, Hormone replacement therapy.

JEL-classification: D61, I10, I12, I19.

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1. Introduction

This report describes a computer model, which is a revised version of a previous model (Zethraeus et al. 1998, Zethraeus et al. 1999). The revised model also includes the risk of spine and wrist fracture and Swedish data on risk and mortality related to coronary heart disease (CHD). The computer model is designed to analyse the cost-effectiveness (CE) of hormone replacement therapy (HRT)[i] in the prevention/treatment of postmenopausal women's health problem.

At menopause, which occurs on the average at age 50, about 75% of women experience menopausal symptoms such as hot flushes, night sweats and atrophy-related symptoms of the urogenital tract. Menopausal symptoms may substantially decrease a woman's quality of life (Daly et al. 1993, Zethraeus et al. 1997). HRT mitigates or eliminates these symptoms and increases quality of life. HRT offers protection against osteoporosis and related fractures and may also have a cardioprotective effect shown in observational studies (SBU 1996). However, a recent randomised study did not show any reduction in cardiovascular events during a period of 4.2 years (Hulley et al. 1998). Evidence of the effect HRT has on breast cancer is inconclusive; although, the risk is assumed to increase after a long period of treatment (Colditz et al. 1995, OTA 1995, Stanford et al. 1995, SBU 1996, CGHFBC 1997). For non-hysterectomised women taking oestrogen's only, an increased risk of endometrial cancer is evident (SBU 1996). The increased risk of endometrial cancer is decreased or eliminated by the addition of a progestogen (Persson et al. 1989, SBU 1996). Combining oestrogen with a progestogen may induce uterine bleedings; however,

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[i] If nothing else is said HRT refers both to oestrogen only therapy and oestrogen combined with a progestogen.

such bleedings may reduce or vanish if a combined HRT is continuously applied although break through bleeding often occurs in the first few months (Andersson et al. 1992, SBU 1996).

HRT has been used for treating menopausal symptoms for a long time. Also, in the last few years, HRT has been recommended for women at a high risk of osteoporosis-related fractures. Whether HRT can be recommended for asymptomatic women as a preventive treatment has also been discussed (SBU 1996). From a health economic perspective these and other issues may be considered by the use of economic evaluation in a model framework. Modelling in this field is necessary due to the lack of naturalistic prospective randomised studies with a sufficient follow-up period comparing, e.g., HRT with no intervention with respect to costs and health effects (Keeler 1995, Sonnenberg and Beck 1993). The CE of HRT can be studied in a computer model constructed around health states. The model separates data on mortality, quality of life, risks and costs, which implies that CE calculations based on different assumptions can easily be performed. Constructing a model for evaluating an intervention raises the question of which health states to include. Basically, all health states for which the risk is affected by the intervention should be included. To minimise time consuming data collection for transition probabilities, costs, mortality and quality of life, health states associated with small costs and health effects may be excluded. The exclusion of such health states will only slightly affect the CE results. When constructing a computer model for analysing the CE of HRT one question discussed is whether it is required to include other fractures besides hip fracture, such as spine and wrist fracture.

The purpose of this report is to serve as a manual for the user of the model and also to describe the model's structure, data requirements and different outputs it can provide and to compare it with an earlier version of the model described in Zethraeus et al. (1998). First the extended model is compared to the previous one with respect to incremental cost-effectiveness ratios (ICERs). Second we investigate how the ICERs are affected by the assumption that the risk of spine and wrist factors are affected in the same way as the risk of hip fracture. Third we analyse whether the ICERs change by replacing the Framingham data with Swedish CHD risk and mortality data.

2. The design and structure of the model

The computer model is programmed in *C++* and built as a Markov type model around menus in a Microsoft Windows environment (See Appendix 1 for a description of the menus in the computer model). The computer model is developed to analyse the CE of HRT and is based on a model described in an earlier paper (Zethraeus et al. 1998). The revised version of the model also includes spine and wrist fractures and also new CHD risk and mortality data. The model structure is illustrated in Figure 1. The basic health states are: 1. Healthy, 2. Hip fracture first year, 3. Hip fracture following years, 4. Spine fracture first year, 5. Wrist fracture first year, 6. Breast cancer first year, 7. Breast cancer following years, 8. CHD first year, 9. CHD following years, and 10. Death. CHD is divided into five health states (a-e): a) Recognised acute myocardial infarction (AMI (rec.)); b) Unrecognised acute myocardial infarction (AMI (unrec.)), c) Angina pectoris (Angina), d) Coronary insufficiency[ii]; and e) Sudden death. The health states (2-9) are also denoted disease states and their inclusion is motivated from the medical literature showing that HRT

[ii] Coronary Insufficiency or Unstable Angina Pectoris can be used interchangeably.

may affect these disease risks. Each disease state is characterised by age-dependent mortality rates, costs and quality of life weights. Hip fractures, breast cancer and CHD are divided into first and second and following years after a disease event as mortality rates, costs, and quality of life differ strongly among these time periods. Spine and wrist fracture are characterised only by a first year after the events. After the first year the individual moves back to the healthy or death states. When disease events, besides spine and wrist fracture, occurs, the patient will stay in that state or transition until “death”. No transitions between health states after an event are allowed such as CHD to hip fracture or CHD to breast cancer. Solving this problem can be done in two ways: One way is to introduce new states such as hip fracture after CHD. The problem is that the model becomes more complicated due to more health states and difficulties with data arise. An alternative is to adjust the data to the model and to use cost, quality of life and mortality data that account for the possibility of sustaining a hip fracture after CHD. The latter approach has been taken in this model.

Figure 1: The basic model structure for evaluating the CE of HRT.

The basic model structure assumes a healthy cohort of individuals in its initial population group (the cohort size can vary between 1- 100,000); whereby, ‘healthy’ means free from CHD, breast cancer and hip, spine and wrist fractures. At each cycle of the process, the cohort is reallocated to health states according to specified transition probabilities. All transitions are assumed to occur instantaneously halfway through each cycle. In the first cycle the cohort is exposed to disease risks of CHD, breast cancer hip, spine and wrist fractures as well as the risk of dying from other causes. The cohort is followed until age 110. The disease risk function is specified as a logistic distribution function including different risk factors (Gujarati 1988). The disease risk function can be expressed as:

(1)

where (2)

p_i is the risk of the disease during a cycle; are risk factors and are parameters to be estimated. The model can also tabulate the risks, using the risk override menus, instead of using the risk functions.

The ICER formula used in the simulation model can be expressed as:

, (3)

where a subscript 0 (1) denotes no intervention (with intervention).

ΔINT = Intervention costs.

$\Delta MORB$ = Changes in morbidity costs due to the intervention.

$\Delta MORT$ = Changes in mortality costs due to the intervention.

ΔLE = Changes in life expectancy due to the intervention.

ΔLEQ = Changes in quality of life measured in years due to the intervention (where 'quality of life' refers to changes in morbidity and side effects).

$\Delta QLE = \Delta LE + \Delta LEQ$

The numerator in the above formula represents the change in costs resulting from an intervention. The denominator is the change in effectiveness generated by the intervention. The change in costs and effectiveness resulting from the intervention is compared to a baseline alternative, i.e., no intervention. The change in cost is based on the sum of changes in intervention, morbidity and mortality costs generated through the intervention; whereas, the change in effectiveness is based on the sum of changes in life expectancy and a quality of life adjustment factor measured in years due to the intervention. The model permits the ICER to be expressed either as costs per LYG (if ΔLEQ is set to zero) or costs per QALYs gained. As the model incorporates consequences for different diseases, effectiveness measures, such as number of events avoided from an intervention, may not provide meaningful information. Instead a composed outcome measure is needed, which incorporates the interventions effectiveness for different risks.

Intervention costs (ΔINT) are divided into yearly and initial costs. Yearly costs consist of direct and indirect costs. Direct costs for a drug include: cost of drug, costs for services in hospitals (physician visits), primary health care and travelling costs. Indirect costs reflect resources foregone due to the treatment (e.g., production losses). These costs are particularly relevant for primary prevention when healthy time is used for the interventions (e.g., physician visits). Initial costs consist of direct and indirect costs and may, for example, be costs for screening patients to be treated.

Changes in morbidity costs ($\Delta MORB$) consist of costs saved because of reduced morbidity from CHD, hip, spine and wrist fractures and costs added because of increased morbidity from breast cancer. The change in morbidity costs are divided into changes in direct and indirect costs. The model also permits the inclusion of changes in mortality costs ($\Delta MORT$) or costs in added life years. Changes in mortality costs are equal to changes in total consumption minus changes in the total production due to a change in mortality from the intervention (Meltzer 1997). The estimation of consumption and production should in principle be based on a healthy population, free of hip fractures, breast cancer and CHD.

3. Modelling an intervention

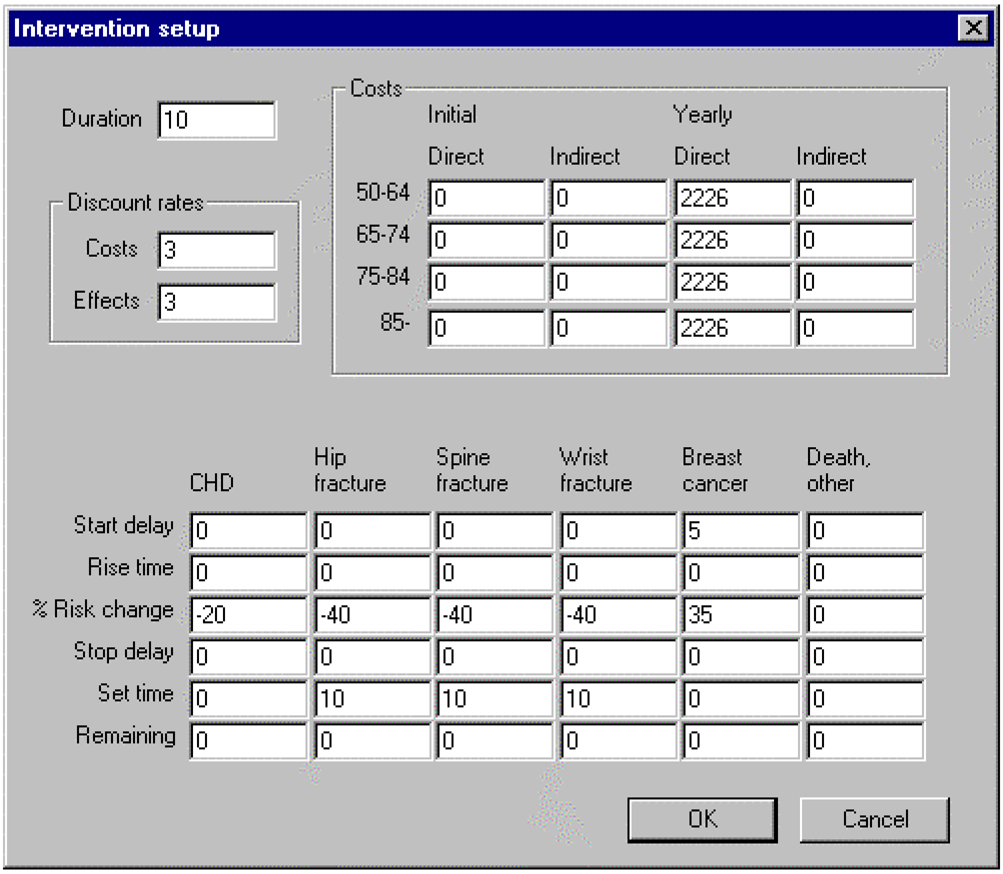
An intervention is modelled by its impact on the disease risks (Figure 2). The example illustrated in Figure 2 assumes that treatment duration lasts 10 years. With treatment, the relative risk (RR) follows the dotted line. The risk reduction is entered as a percentage change in the baseline risk. For example, if the risk of CHD is assumed to be reduced by 40% during HRT, this is equal to multiplying equation (1) for CHD above by 0.6. According to the CHD risk equation, the risk without treatment of CHD for a woman of age 60 years is 6.2 per 1,000 population. The intervention reduces the risk by 40% and the resulting risk of CHD for this woman with treatment is then equal to: .

Figure 2: Modelling an intervention.

Different options are available for the user when modelling disease risks affected by the intervention. Start delay is defined as the time prior to when the intervention affects the risk (2 years in Figure 2). Rise time is defined as the time it takes from the end of the start delay until the risk reduction has reached its maximum value (2 years in the Figure 2). The risk adjustment is specified as a linear function of time. Stop delay and set time are defined analogously to start delay and rise time. The model also permits a remaining effect lasting from the end of set time until the rest of the lifetime.

Figure 3 shows the “Setup” “Intervention” menu for a hypothetical cohort of 50-year-old women. A 10 year treatment duration is modelled with costs and effectiveness discounted at 3%. The risk of CHD is assumed to decrease by 20%, the risk of fractures is supposed to decrease by 40% while the risk of breast cancer is assumed to increase by 35% after 5 years treatment. At treatment cessation the fracture risk reduction gradually adjusts to no risk reduction after 10 years.

Figure 3: The “Setup” and “Intervention” menu.



In Figure 3 there is a yearly direct cost of SEK 2,226. If indirect costs are excluded, the distinction between direct and indirect costs can be used to separate, for example, drug costs and costs for patient management, such as physician visits. Otherwise all direct and indirect costs, initially and annually, must be aggregated before being entered into the model.

4. Data for the model

The model demands data about risks, mortality rates, quality of life weights, and costs.

4.1 Risks

First, the base-case risk of CHD, breast cancer, hip, spine and wrist fractures without treatment needs to be known. Within the model, it is possible to use risks specified as risk functions, risks manually incorporated into tables (“Setup” and “Override” menus) or a combination of both. For example the base-case risk of hip fracture may be extracted from the table and used in the age interval 50-60 years and the risk function for ages above 60. To accomplish this, the table “Hip fracture risk override” in “Setup” and “Override” is set to zero for ages above 60 years of age (the risk function is used for all ages where the risk override is set to zero). For the age’s 50-60 years, the risk values are incorporated into the table. Note that the “Log fcn override” must be marked on the “Setup” and “Conditions” menu. It is also possible to extract the risk with treatment from tables. To accomplish this, you first have to mark the “Risk and iv override” on the “Setup” and “Conditions” menu. Then insert values for the chosen ages in the table from the “Setup”, “Override” and “intervention override” menu. The base-case disease risks can be changed by using “Setup”, “Risks” and the relative risk fields. For example if the risk of hip fracture is assumed to be 50% higher compared with the base risk, 1.5 is plugged into all the age-group fields (“Relative risks” on the “Setup” and “Conditions” menu must be marked). This option makes it easier to analyse cohorts subject to an increased base-case risk, e.g. osteoporotic individuals. For the “Risks” menu, values have to be identified for the risk factors involved in the CHD risk function (if the CHD risk function is used): Cholesterol, diastolic blood pressure, smoking status (fraction between 0 and 1), glucose intolerance (fraction between 0 and 1) and left ventricular hypertrophy (fraction between 0 and 1). These may represent mean values (an average woman) in the population that are subject to analysis. By changing the risk factors, it also becomes possible to analyse cohorts subject to an e.g. increased risk of CHD. Conditional on sustaining a CHD, a table decides the distribution among the CHD disease states. The age-dependent probability of different CHD disease states must, therefore, also be identified. The base case disease risks based on tables can be changed by using the "Setup", "Override" and "Relative risk factors, risk override" (Mark "log fcn override" and "Relative risks" on the "Setup" and "Conditions" menu).

4.2 Mortality rates

Age-specific annual mortality rates have to be specified for CHD (and for all the sub states), breast cancer and hip fractures for the first and second and following years after the disease event. For spine and wrist fracture the age-specific annual mortality for the first year needs to be estimated. Mortality rates need to be stated for all ages between the initial age of the cohort and 110 years.

Age-specific annual mortality rates have to be identified also for death for other causes. To calculate the mortality rate for death other, the risk of dying from CHD, breast cancer and hip fractures are subtracted from the normal mortality rate (normal mortality tables can be combined with tables showing mortality by underlying causes). The mortality rates can be changed by using the "Setup", "Mortality" and "Relative risk factors, mortality" menu (Mark the "Relative risks" on the "Setup" and "Conditions" menu).

4.3 Quality of life weights

Quality of life weight is a number between 0 (dead) and 1 (full health) which reflects health state preference. Age-dependent quality of life weights have to be specified for CHD, breast cancer and hip fractures for the first, second, and following years after an event. Age-dependent quality of life weights need also to be specified for spine and wrist fracture for the first year after an event. Quality of life weights need to be identified for healthy individuals (the quality of life weight may be lower than 1 due to other diseases not included in the model). The model also permits the inclusion of quality of life weights during treatment, which takes into account potential side effects associated with the intervention.

4.4 Costs

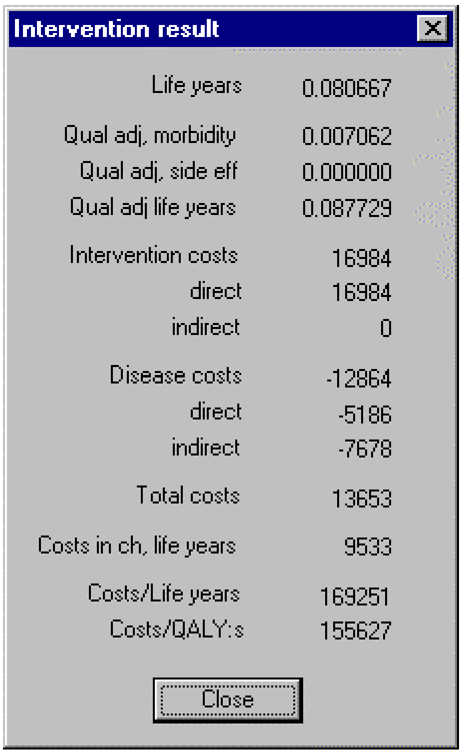
Costs necessary for the model can be divided into: intervention, morbidity and mortality costs. Their inclusion is based on a societal perspective meaning that all costs are incorporated into the analysis no matter who pays the costs. First, the intervention costs, yearly and initial, must be settled for the individual in different age groups. Second, age-specific morbidity costs must be specified for the first, second and following years after a disease event. For spine and wrist fracture only costs for the first year following the event need to be estimated. Finally age-specific costs in added life years may be included (Meltzer 1997).

5. Output from the model

5.1 Cost per gained life-year and QALY

The top of the intervention result menu ("Life years") shows the expected change in life years per patient resulting from the intervention (Figure 4). This change is calculated as the change in expected survival for the cohort generated by the intervention. Subsequently, the quality adjustment factors taking into account potential morbidity and side effects, measured in years, are shown. Adding the change in life expectancy with the quality adjustment factors gives the change in QALYs resulting from the treatment.

Figure 4: The "Display" and "Intervention result" menu showing changes in costs and effectiveness comparing intervention with no intervention.



The intervention and change in morbidity costs (disease costs) together with the mortality costs ("Costs in ch, life years") constitute the change in total costs. At the bottom of the intervention menu the model presents ICERs expressed as costs per gained life years and QALYs. The effectiveness measures allow for the evaluation of interventions affecting only mortality, quality of life, or a combination of quality and quantity of life.

5.2 Lifetime risk and life expectancy

By the use of the "Display" and "Diseases" menu it is possible to calculate the *lifetime risk* of the included diseases for an individual at a certain age. The life-time risk of hip fracture at a certain age is the number of individuals who sustained a hip fracture during the remaining lifetime divided by the number of individuals at risk. These figures may be compared to estimates on lifetime risks in the general population to check the model's credibility. *Life expectancy* ("Display", "Life expectancy" and "Total") is defined as the average future lifetime of the cohort. The total number of life years at a given cycle (year) is calculated as the arithmetic mean of individuals at the beginning and at the end of the cycle. The increased mortality due to CHD, breast cancer and hip fracture are assumed to occur immediately upon the event. The total number of cycles (years) for each health state is divided by the size of the original cohort. The total life expectancy is the sum of life years over cycles divided by the size of the initial cohort. The life expectancy, conditional on a certain disease state, is calculated as the number of years in the disease state divided by the number of women that end up in the disease state, assuming that the cohort starts in the healthy state.

6. The cost-effectiveness of HRT including spine and wrist fractures and Swedish data for CHD risk and mortality

The CE of HRT compared to no treatment was analysed for 6 indications depending on age and uterus status. The study group was asymptomatic (no menopausal symptoms) women at the age of 50, 60 and 70 years with an intact uterus or a hysterectomy. A treatment duration of 10 years was assumed. Oestrogen only treatment is intended for women with a hysterectomy while a combined treatment (oestrogen and progestogen) is intended for women with an intact uterus. For each indication ICERs are calculated for 12 risk scenarios.

A societal perspective is undertaken including intervention costs, morbidity costs and costs in added life years. The intervention costs include costs for the drug, travel/time and physician visits. Morbidity costs include both direct and indirect costs. Reduced morbidity costs occur when the risk of hip, spine, wrist fractures and CHD decrease from using HRT. Increased morbidity costs occur due to increases in the risk of breast cancer from using HRT. Costs in added life years are calculated as the difference between total consumption and total production (Johannesson 1997). The fracture (hip, spine and wrist) risk reduction is assumed, during treatment, to be 40 or 50% (OTA 1995, SBU 1996). The risk of fractures is assumed to gradually adjust to the base-case risk at 10 years after HRT (SBU 1996). The CHD risk reduction is assumed, during treatment, to be 0, 20 or 50% (OTA 1995, SBU 1996, Hulley et al. 1998). The decrease in the risk of CHD is assumed to be the same for oestrogen only treatment and oestrogen combined with a progestogen (Falkeborn et al. 1992). The increase in the risk of breast cancer is assumed to be 0 or 35% respectively (OTA

1995). The increased risk of breast cancer is assumed to start instantaneously after 5 years of HRT and remains elevated for the intervention duration (OTA 1995, SBU 1996). Costs (given in 1995 prices) and effects are discounted at the rate of 3% (Gold et al. 1996). A detailed presentation of all the assumptions made and data used in the analysis for mortality, risks, quality of life and costs are presented in appendix 2.

In Table 1 we calculate the ICERs comparing HRT with no intervention using the previous model (Zethraeus et al. 1998, Zethraeus et al. 1999). In Table 2 we repeat the same calculations based on the same assumptions and data but instead using the new model. No differences are expected. In Table 3 we again repeat the same calculations in the new model but also add the assumption that the risk of spine and wrist factors are affected in the same way as the risk for hip fracture. Finally in Table 4 the same calculations as in Table 3 are repeated with the additional change that the CHD risk and mortality data, based on the Framingham study, are replaced with Swedish data extracted from the National Board of Health and Welfare.

Table 1 demonstrates for the six indications the cost per gained life-year and QALY according to the 12 risk scenarios. Oestrogen only therapy is associated with lower ICERs compared to combined therapy for all ages and risk reductions (see also Tosteson and Weinstein 1991, Daly et al. 1992). This is explained by, ceteris paribus, higher intervention cost associated with the combined therapy. Generally the ICERs become lower when age increases, which is explained by that the risk of disease events increases with age, which means that more events can be avoided for a given risk reduction. Table 1 shows that the ICER is sensitive to changes in the assumptions about the risk reduction in CHD for women at the age of 50. Also note that the ICER is sensitive to the inclusion of breast cancer risk, for 50-year-old women when the risk reduction of CHD is 0 or 20%.

Table 1: Cost (SEK thousand) per life-year gained and QALY (QALY in parenthesis) assuming different risk reductions for coronary heart disease (CHD), hip fracture (Hip) and breast cancer (Cancer). The treatment duration is 10 years for women aged 50, 60 and 70 years. The old version of the model.

	Oestrogen (post hysterectomy)			Oestrogen+Progestogen (intact uterus)		
Risk change	50	60	70	50	60	70
Hip-40%	5430 (1400)	770(440)	200 (180)	7820 (2020)	1170 (670)	300 (270)
Hip-40%, CHD-20%	400 (310)	240 (230)	170 (190)	580 (450)	300 (300)	200 (230)
Hip-40%, CHD-50%	160 (140)	170 (190)	160 (200)	230 (200)	200 (220)	180 (220)
Hip-50%	4090 (1060)	550 (320)	140 (130)	6000 (1550)	870 (500)	220 (200)
Hip-50%, CHD-20%	360 (280)	210 (200)	150 (170)	540 (410)	280 (260)	180 (200)
Hip-50%, CHD-50%	140 (120)	160 (170)	150 (180)	220 (190)	190 (200)	170 (200)
Hip-40%, Cancer+35%	D (D)	D (1220)	230 (160)	D (D)	D (2200)	410 (280)
Hip-40%, CHD-20%, Cancer+35%	D (630)	270 (240)	170 (190)	D (1050)	370 (320)	210 (230)
Hip-40%, CHD-50%, Cancer+35%	180 (130)	180 (180)	160 (200)	320 (230)	210 (220)	180 (220)
Hip-50%, Cancer+35%	D (D)	D (490)	140 (100)	D (D)	D (950)	260 (190)
Hip-50%, CHD-20%, Cancer+35%	D (490)	240 (200)	150 (160)	D (850)	330 (280)	190 (200)
Hip-50%, CHD-50%, Cancer+35%	160 (110)	170 (170)	150 (180)	300 (210)	200 (200)	170 (200)

D = HRT is dominated by the no intervention alternative

Comparing Table 1 with Table 2 shows that the new extended model including spine and wrist fractures produces almost exactly the same ICERs as the previous model. Any observed difference is due to the change in model structure including the risk of spine and wrist fracture.

Table 2: Cost (SEK thousand) per life-year gained and QALY (QALY in parenthesis) assuming different risk reductions for coronary heart disease (CHD), hip fracture (Hip) and breast cancer (Cancer). The treatment duration is 10 years for women aged 50, 60 and 70 years. The new version of the model.

	Oestrogen (post hysterectomy)			Oestrogen+Progestogen (intact uterus)		
Risk change	50	60	70	50	60	70
Hip-40%	5470 (1410)	780 (440)	200 (180)	7870 (2020)	1170 (670)	310 (270)
Hip-40%, CHD-20%	400 (310)	240 (230)	170 (190)	580 (450)	300 (300)	200 (230)
Hip-40%, CHD-50%	160 (140)	170 (190)	160 (200)	230 (200)	200 (220)	180 (220)
Hip-50%	4120 (1060)	560 (320)	140 (130)	6040 (1550)	870 (500)	230 (200)
Hip-50%, CHD-20%	370 (280)	210 (200)	150 (170)	540 (410)	280 (260)	180 (200)
Hip-50%, CHD-50%	140 (120)	170 (170)	150 (180)	220 (190)	190 (200)	170 (200)
Hip-40%, Cancer+35%	D (D)	D (1240)	240 (160)	D (D)	D (2230)	410 (290)
Hip-40%, CHD-20%, Cancer+35%	D (630)	270 (240)	170 (190)	D (1060)	370 (320)	210 (230)
Hip-40%, CHD-50%, Cancer+35%	190 (130)	180 (180)	160 (200)	320 (230)	210 (220)	180 (220)
Hip-50%, Cancer+35%	D (D)	D (490)	140 (100)	D (D)	D (970)	260 (190)
Hip-50%, CHD-20%, Cancer+35%	D (490)	240 (200)	150 (160)	D (850)	330 (280)	190 (200)
Hip-50%, CHD-50%, Cancer+35%	170 (110)	170 (170)	150 (180)	300 (210)	200 (200)	170 (200)

D = HRT is dominated by the no intervention alternative

Comparing Table 3 with Table 2 we note that adding the assumption that the risk of spine and wrist fracture exactly follows that of hip, just slightly alters the ICERs. The reason is that wrist and spine fracture are associated with small costs and health effects. Further, the time is very limited for women in those disease states, only one year, and then they return to the healthy state.

Table 3: Cost (SEK thousand) per life-year gained and QALY (QALY in parenthesis) assuming different risk reductions for coronary heart disease (CHD), fractures (hip spine and wrist) (Fra) and breast cancer (Cancer). The treatment duration is 10 years for women aged 50, 60 and 70 years.

	Oestrogen (post hysterectomy)			Oestrogen+Progestogen (intact uterus)		
Risk change	50	60	70	50	60	70
Fra-40%	6240 (1330)	790 (420)	190 (170)	9000 (1910)	1200 (640)	300 (260)
Fra-40%, CHD-20%	400 (310)	230 (230)	170 (190)	580 (450)	300 (290)	200 (230)
Fra-40%, CHD-50%	150 (130)	170 (180)	160 (200)	230 (200)	200 (220)	180 (220)
Fra-50%	4690 (1000)	560 (300)	140 (120)	6900 (1470)	890 (470)	220 (190)
Fra-50%, CHD-20%	360 (270)	210 (200)	150 (160)	540 (400)	280 (260)	180 (200)
Fra-50%, CHD-50%	140 (120)	160 (170)	150 (180)	220 (190)	190 (200)	170 (200)
Fra-40%, Cancer+35%	D (D)	D (1050)	220 (150)	D (D)	D (1920)	400 (270)
Fra-40%, CHD-20%, Cancer+35%	D (600)	270 (230)	170 (190)	D (1010)	370 (310)	210 (230)
Fra-40%, CHD-50%, Cancer+35%	180 (130)	180 (180)	160 (200)	320 (220)	210 (220)	180 (220)
Fra-50%, Cancer+35%	D (D)	D (430)	130 (90)	D (D)	D (870)	250 (180)
Fra-50%, CHD-20%, Cancer+35%	D (470)	240 (190)	150 (160)	D (810)	330 (270)	180 (200)
Fra-50%, CHD-50%, Cancer+35%	160 (110)	170 (170)	150 (180)	300 (200)	200 (200)	170 (200)

D = HRT is dominated by the no intervention alternative

Comparing Table 4 with Table 3 illustrates that the ICERs are very similar but in general slightly higher using Swedish data instead of US data.

Table 4: Cost (SEK thousand) per life-year gained and QALY (QALY in parenthesis) assuming different risk reductions for coronary heart disease (CHD), hip, spine, wrist fracture (fracture) and breast cancer (Cancer). The treatment duration is 10 years for women aged 50, 60 and 70 years. Using Swedish data for risks and mortality related to CHD.

	Oestrogen (post hysterectomy)			Oestrogen+Progestogen (intact uterus)		
Risk change	50	60	70	50	60	70
Fra-40%	8460 (1350)	950 (430)	210 (170)	12230 (1960)	1470 (670)	330 (270)
Fra-40%, CHD-20%	480 (370)	240 (230)	170 (190)	700 (540)	320 (300)	200 (230)
Fra-40%, CHD-50%	200 (180)	180 (190)	160 (200)	290 (260)	210 (220)	170 (220)
Fra-50%	6330 (1010)	660 (300)	140 (110)	9350 (1500)	1080 (490)	240 (190)
Fra-50%, CHD-20%	440 (330)	220 (200)	150 (170)	660 (480)	290 (270)	180 (200)
Fra-50%, CHD-50%	190 (160)	170 (170)	150 (180)	270 (240)	200 (210)	160 (200)
Fra-40%, Cancer+35%	D (D)	D (1270)	260 (140)	D (D)	D (2380)	500 (280)
Fra-40%, CHD-20%, Cancer+35%	D (1110)	290 (240)	170 (190)	D (1830)	400 (330)	210 (230)
Fra-40%, CHD-50%, Cancer+35%	280 (200)	180 (190)	160 (200)	470 (320)	220 (220)	180 (220)
Fra-50%, Cancer+35%	D (D)	D (460)	130 (80)	D (D)	D (970)	290 (180)
Fra-50%, CHD-20%, Cancer+35%	D (780)	250 (200)	150 (160)	D (1330)	350 (280)	180 (200)
Fra-50%, CHD-50%, Cancer+35%	250 (170)	170 (170)	150 (180)	440 (290)	200 (210)	170 (200)

D = HRT is dominated by the no intervention alternative

If the willingness to pay for producing one more unit of QALYs exceeds the costs the intervention is cost-effective. If we focus on Table 1 and assume that the willingness to pay for a gained QALY is SEK 200,000 (Zethraeus et al. 1998) then one conclusion is that oestrogen only treatment is cost-effective for 70 year old women irrespective of the assumed risk scenario. This conclusion is insensitive to the chosen model structure, including spine and wrist fractures, to the assumption that the risk of spine and wrist fractures exactly follows that of hip fracture, and to replacing US data with Swedish data for CHD risks/mortality.

The computer model is intended to be used for analysing the CE of HRT. The CE of treatments only affecting the risk of spine or wrist fracture or a combination of those should not be calculated using this model as a tool. For such analysis a separate osteoporosis model can be constructed only including the risk of hip, spine and wrist fractures. The reason for not using the model in such cases is that if the risk of spine/wrist fracture is reduced the model predicts a small lost in life years. This is explained by that the spine/wrist fracture are associated with a relative low mortality. If the risk of those events is lowered this will imply that the risk of moving to a more severe disease state associated with high mortality increases. However, if the mortality after a spine/wrist is increased by about 20% the computer model shows an increase in life years. A recent study has shown that compared to women who did not have a vertebral fracture women with one or more vertebral fractures had a 23% greater age-adjusted mortality rate (Kado et al. 1999).

7. Extending the model to other countries

The model may be theoretically used for any population. However, the default data used for the model in empirical applications are assumed to be valid only for Swedish populations. To make accurate conclusions using the model in other countries, the data must be valid for the specific setting to which the model is applied. Below, opportunities and data needs for extending the model to other countries are discussed.

7.1 Direct and indirect costs

Direct and indirect costs must be determined for each country subject to analyse. Using Swedish cost data, multiplied with an appropriate exchange rate, implicitly assumes that the absolute and relative price level is the same as in Sweden. It also assumes that medical and social care patterns are equivalent. These are very strong assumptions and can only be recommended as a very first preliminary analysis. Country-specific costs should ideally be collected. Yearly direct intervention costs, including the costs of pharmaceuticals, physician visits as well as time and travelling costs, can be estimated empirically by following patients during a year of treatment.

Direct and indirect disease costs must be collected for the first 12 months following an event and for the second and following years. Direct morbidity costs are interpreted as the extra costs of the disease compared with no disease occurrence and can be estimated by, for example, subtracting the costs during one year before a disease event from the costs during one year after the disease event (e.g. see Zethraeus et al. 1997). Another alternative is to estimate the costs without the disease by using a matched cohort. The direct costs include all costs associated with the treatment during the initial hospital stay, as well as rehabilitation in aftercare. Indirect morbidity costs can be estimated by subtracting the production value the year after disease onset from its value the year prior to disease.

7.2 Quality of life data

Quality of life weights may differ between countries and the data should be based on empirical studies; however, different methods exist for estimating the quality of life weights (see Drummond et al. 1997). The rating-scale method is commonly used to estimate weights to construct QALYs. To obtain the QALY weight with the rating scale method, the score on the scale is divided by 100 (for a rating scale between 0 and 100) (e.g. if a woman places her current health state on 70 the QALY weight will be 0.7 (70/100)).

An alternative method used to estimate QALY weights is the time trade-off method. This method involves a trade-off between quantity and quality of life such that individuals are asked to state the number of years in full health followed by death that they deem as being equivalent to a specific number of years in the health state being assessed, followed by death. To obtain the QALY weight the number of years in full health is then divided by the number of years in the assessed state. If, for instance, a woman thinks that 20 years in full health followed by death is of equal value to 30 years with mild menopausal symptoms followed by death, the QALY weight for mild menopausal symptoms is 0.67 (20/30).

A third method is the standard gamble method, which requires the individual to make a choice between two alternatives. The first alternative is to live with certainty in a disease state, for a certain time period, followed by death. The other alternative involves a probability (p) of living in full health for a certain period followed by death or a probability of dying immediately ($1-p$). The probability p is varied until the individual is indifferent between the two alternatives. The probability that makes the individual indifferent between the two alternatives determines the QALY weight.

7.3 Risk functions and mortality after event

The risk of disease may differ between countries and should be based on country-specific data. The model permits the default values to be changed for the estimated parameters in the risk equations (“Setup” and “Coefficients” menu). With these changes, it is then possible to estimate country-specific risk equations for the same risk factors and use these parameter estimates in the model. The risk of breast cancer and hip fractures may be estimated using country-specific incidence data. In the absence of such epidemiological data the risk equation of CHD can be extracted from the Framingham Study; whether the results of this study can be extrapolated to other populations is uncertain. Instead of using the risk equations, tabulations may be used. Data on mortality, referring to the first year and subsequent years after a disease event should be based on country-specific empirical studies.

7.4 General mortality

General mortality may be estimated from national registers involving statistics of mortality rates from the general population.

7.5 Comparing interventions

The model in its original setting evaluates a treatment compared to a baseline alternative (i.e. no treatment). However, the model also permits comparisons between two or more treatments. The ICERs between these alternatives must then be calculated. This is made by first calculating the change in costs and effects for the treatments separately (e.g. in the case of two treatments (1 and 2), calculate C_1 - C_0 and E_1 - E_0 for treatment 1 compared with the baseline alternative (0) and then calculate C_2 - C_0 and E_2 - E_0 for treatment 2 compared with the baseline alternative).

The ICER for treatments 1 and 2 is calculated as:

(4)

7.6 Compliance

Compliance is the extent to which the patient follows a physician's treatment recommendations. Non-compliance is present if the patient does not follow these recommendations and may be one of two types. First the patient may not buy the drug the physician has prescribed such that no costs or effects associated with the treatment are present. Second, the patient may buy the drug, but diverge from the physician's recommendations, in which case costs for the drug are incurred and only a fraction of the full effect (or no effect) from using the drug. The second definition of non-compliance necessitates information about how the drug's effect is altered by non-compliance. Note that this type of compliance should be reflected in the estimates of the costs and effects used such that estimates of costs and effects in a clinical trial are based on actual compliance within the trial. To analyse the effect of compliance, which differs from compliance within the trial, this necessitates information on how to adjust the effects.

8. Summary and conclusion

It has been shown that the addition of spine and wrist fracture to the previous computer model analysing the CE of HRT does not change the ICERs. Adding the assumption that the risk of spine and wrist fracture exactly follows that of hip does only slightly change the ICERs. By excluding those disease states time consuming data collection for transition probabilities, mortality, quality of life and costs, is avoided. The estimation of the CE of HRT in Sweden should primarily be based on Swedish data. However, the ICERs are insensitive to replacing the Framingham data with Swedish CHD risk and mortality data. This is in line with a study by Haq et al. (1999) suggesting that the Framingham function is acceptable accurate for northern European populations at least in men. The model, constructed to be as general and flexible as possible, may be theoretically used for any population. To make accurate conclusions using the model in other countries, the data must be valid for the specific setting to which the model is applied. Finally it should be pointed out that the model is not intended to be used for analysing interventions only affecting the risk of spine and/or wrist fracture. For such analyses a separate osteoporosis model is recommended.

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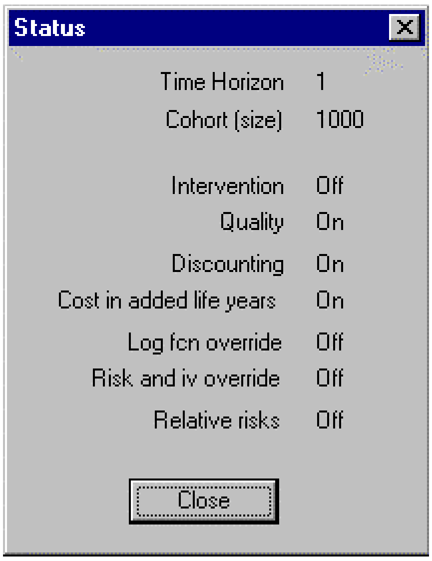
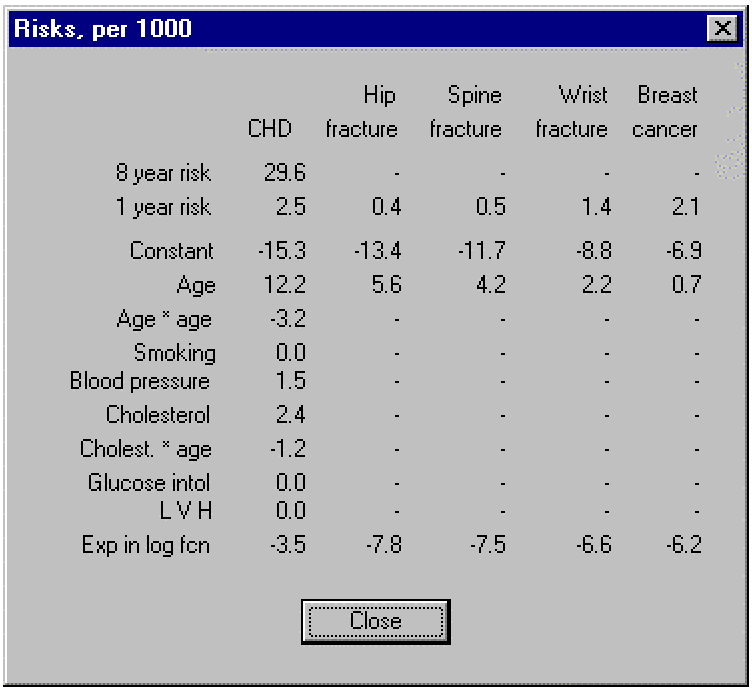
APPENDIX 1 - A DESCRIPTION OF THE MENUS IN THE COMPUTER MODEL

In this appendix a short description of the menus used in the computer model is presented (not demonstrated in the text). The model is built around four main menus: “File”, “Display”, “Setup” and “Help”. From the “File” menu it is possible to open a saved file by “Open” and saving a file by “Save” or “Save As”. The programme is exited by using “Exit”. By using the “Reset” option all changes made in an open file is cancelled and the default values are used. The “Help” menu tells the model version and the copyright of the model. The “Display” menus show the different outputs from the model while the “Setup” menus are used for specifying the conditions for the analysis. Below “Display” and “Setup” menus are shown.

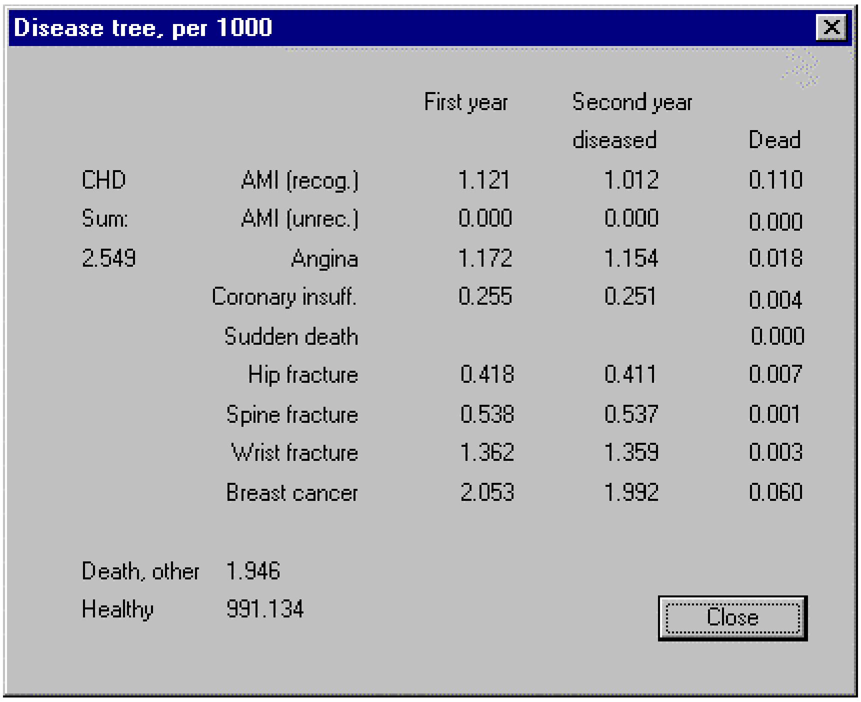
<u>“Display” menus:</u>



“**Status**” menu. Shows the current status (on/off) of the options that have been activated on the “Setup” and “Conditions” menu. It further shows the time horizon (0-60 years) and the chosen cohort size (1-100,000).



“**Risks**” menu. Shows the annual risks per 1000 for CHD, hip, spine, wrist fracture and breast cancer. It also shows the estimated parameters multiplied by the risk factors. “Exp in log fcn” is the value of the estimated exponent in the logistic distribution function.



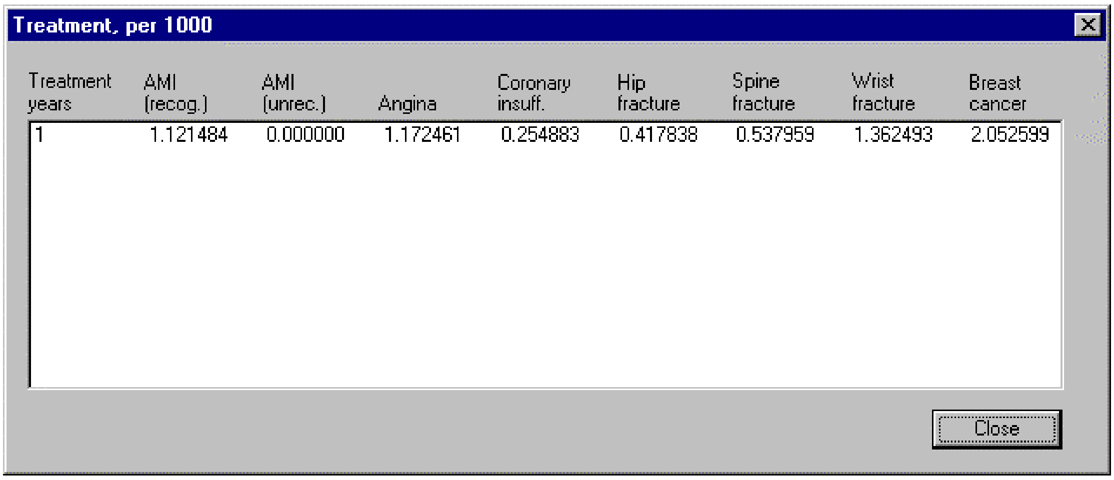
Disease tree, per 1000

		First year	Second year diseased	Dead
CHD	AMI (recog.)	1.121	1.012	0.110
Sum:	AMI (unrec.)	0.000	0.000	0.000
2.549	Angina	1.172	1.154	0.018
	Coronary insuff.	0.255	0.251	0.004
	Sudden death			0.000
	Hip fracture	0.418	0.411	0.007
	Spine fracture	0.538	0.537	0.001
	Wrist fracture	1.362	1.359	0.003
	Breast cancer	2.053	1.992	0.060

Death, other	1.946
Healthy	991.134

Close

"**Diseases**" menu. Shows the cohort distribution in different health states after a specified period of time according to the "Setup", "Conditions" and "Time horizon" field.

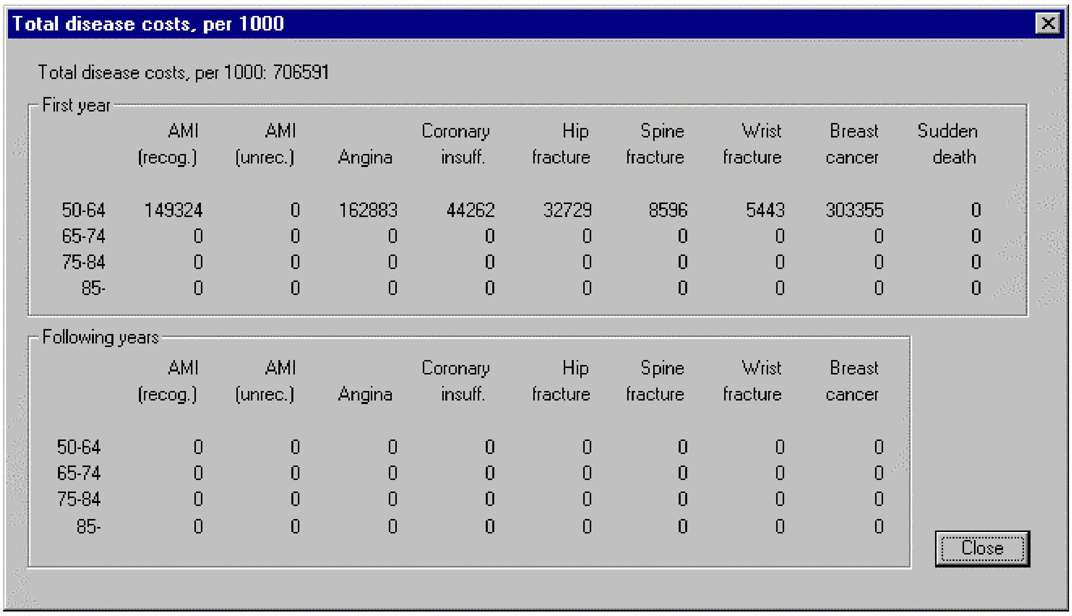


Treatment, per 1000

Treatment years	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Hip fracture	Spine fracture	Wrist fracture	Breast cancer
1	1.121484	0.000000	1.172461	0.254883	0.417838	0.537959	1.362493	2.052599

Close

"**Treatment**" menu. Shows the number of individuals alive in different disease states and the number of cycles (years) the individuals have been in the disease state. It enables the cohort of individuals to be followed through the model by varying the time horizon for the analysis. For example, if a cohort of 50-year-old women is followed and analysed after 1 year ("Time horizon" set to 1 year) the number of women sustaining a hip fracture the first year is equal to the risk of hip fractures for a 50 year old woman multiplied by the number of healthy women at the age of 50 years. Analysing the cohort after two years ("Time horizon" set to 2 years) the number of new hip-fracture patients the first year ("Treatment years 1") is equal to the number of healthy individuals at the age of 51 years multiplied by the risk of hip fracture for a 51 year old woman. The number of women in the second year after a hip fracture ("Treatment years 2") is equal to the number of individuals that sustained a hip fracture the previous year minus the number of hip fracture patients that died during the previous year. Thus, in addition to following the cohort at any time horizon, the menu can be used as an aid for controlling the model's calculations.



Total disease costs, per 1000

Total disease costs, per 1000: 706591

First year

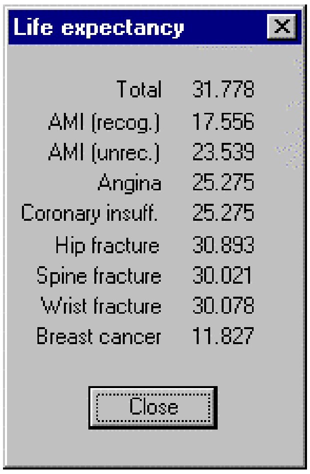
	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Hip fracture	Spine fracture	Wrist fracture	Breast cancer	Sudden death
50-64	149324	0	162883	44262	32729	8596	5443	303355	0
65-74	0	0	0	0	0	0	0	0	0
75-84	0	0	0	0	0	0	0	0	0
85-	0	0	0	0	0	0	0	0	0

Following years

	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Hip fracture	Spine fracture	Wrist fracture	Breast cancer
50-64	0	0	0	0	0	0	0	0
65-74	0	0	0	0	0	0	0	0
75-84	0	0	0	0	0	0	0	0
85-	0	0	0	0	0	0	0	0

Close

"**Disease costs**" and "**Total**" menu. Shows the costs distributed on the disease states at a specified period of time according to the "Setup", "Conditions" and "Time horizon" menu. There are also similar menus for "Direct" and "Indirect" costs.

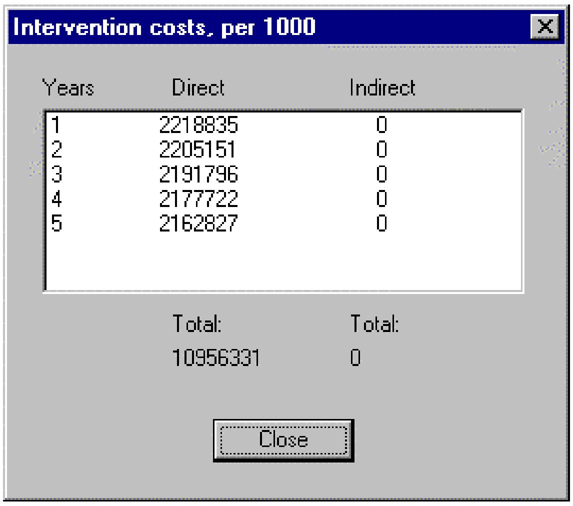


Life expectancy

Total	31.778
AMI (recog.)	17.556
AMI (unrec.)	23.539
Angina	25.275
Coronary insuff.	25.275
Hip fracture	30.893
Spine fracture	30.021
Wrist fracture	30.078
Breast cancer	11.827

Close

"**Life expectancy**" menu. Shows the total life expectancy defined as the average future lifetime of the cohort. Views also the average future life time for women ending up in a certain disease state.



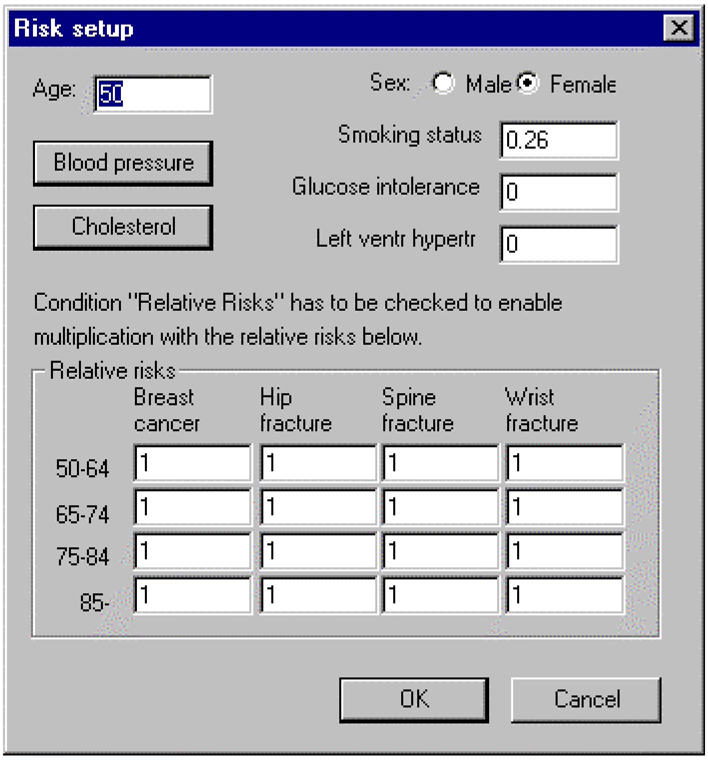
Intervention costs, per 1000

Years	Direct	Indirect
1	2218835	0
2	2205151	0
3	2191796	0
4	2177722	0
5	2162827	0
	Total: 10956331	Total: 0

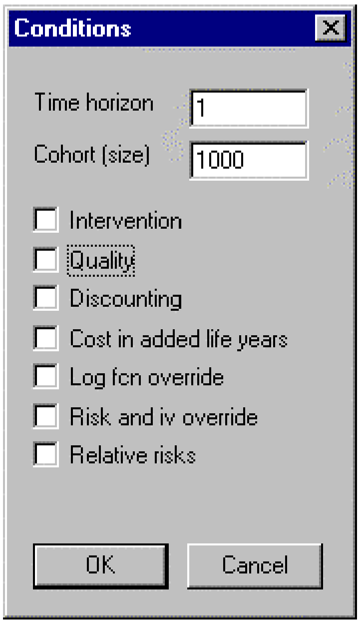
Close

"**Intervention costs**" menu. Shows the annual intervention costs, direct and indirect, during the treatment period (5 years in this case).

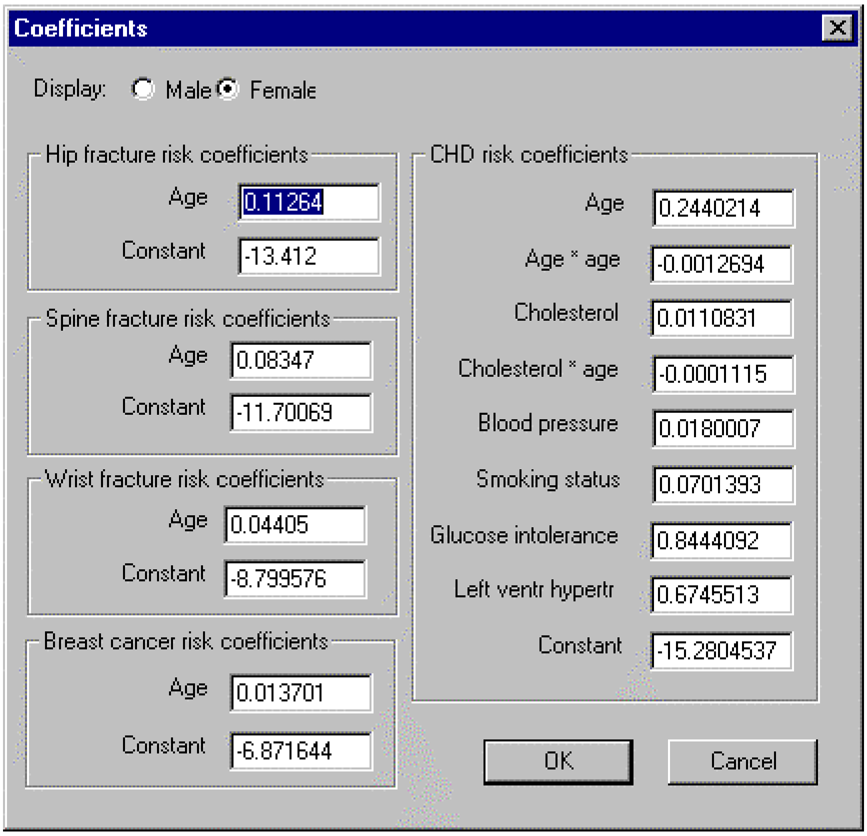
“Setup” menus:



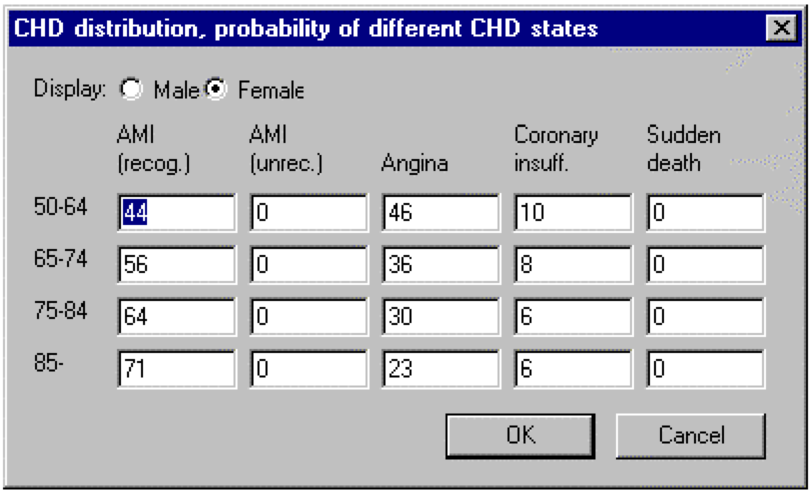
“**Risks**” menu. This menu is used to be able to change the base-case risk (if specified by using the logistic function) of CHD, breast cancer and hip, spine and wrist fractures. The base-case risk of CHD is affected by changing the values on the risk factors in the logistic distribution functions for CHD. The base-case risk of hip, spine, wrist fractures and breast cancer is changed by using the relative risk menus (e.g. if 1.5 is plugged into all the age-group fields of hip fracture this means that the base-case risk of hip fractures is increased by 50%).



“**Conditions**” menu. On this menu the conditions for the analysis is determined. For example the cohort can be analysed with and without intervention.



"**Coefficients**" menu. In this menu it is possible to change the estimated parameter values in the logistic distribution functions.



"**Mortality**" and "**CHD distribution**" menu. Shows the probability of different CHD states. The default values are shown in %. The sum of each rows is equal to 100%.

Hip fracture mortality, first year after fracture (per 1000)

Display: ○ Male ◉ Female

50	17.	63	48.1	76	128.7	89	301.5	102	557.8
51	18.4	64	52.	77	138.2	90	319.1	103	578.
52	20.	65	56.2	78	148.3	91	337.3	104	598.
53	21.7	66	60.8	79	159.	92	356.	105	617.7
54	23.5	67	65.7	80	170.4	93	375.1	106	636.9
55	25.4	68	70.9	81	182.4	94	394.6	107	655.8
56	27.6	69	76.5	82	195.	95	414.5	108	674.2
57	29.9	70	82.6	83	208.3	96	434.7	109	692.
58	32.4	71	89.	84	222.2	97	455.	110	709.3
59	35.	72	96.	85	236.8	98	475.5		
60	37.9	73	103.4	86	252.	99	496.2		
61	41.1	74	111.3	87	267.9	100	516.8		OK
62	44.5	75	119.7	88	284.4	101	537.3		Cancel

"**Mortality**" and "**Hip fracture mortality, first year**". Shows the annual mortality per 1000 the first year after a hip fracture by age. Such a table also exists for the second and following years and for CHD, breast cancer and death other. For spine and wrist fracture there is a mortality table for the first year after event.

Relative Risk Factors, Mortality

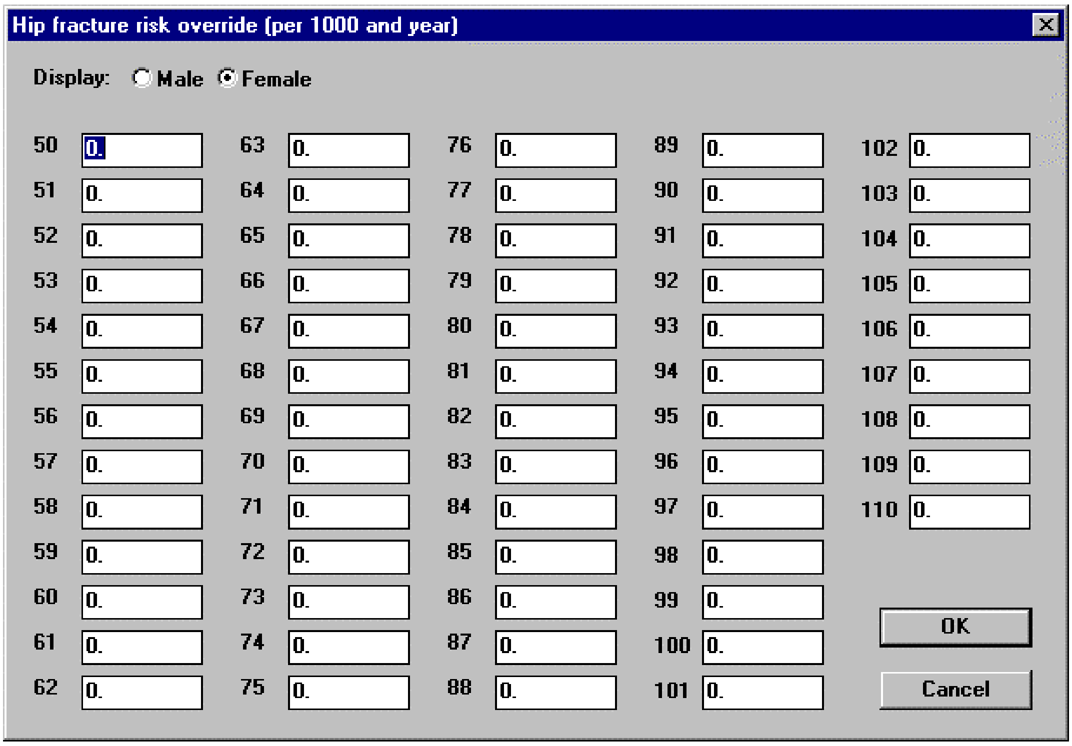
Display: ○ Male ◉ Female

Condition "Relative Risks" has to be checked to enable multiplication with these factors.

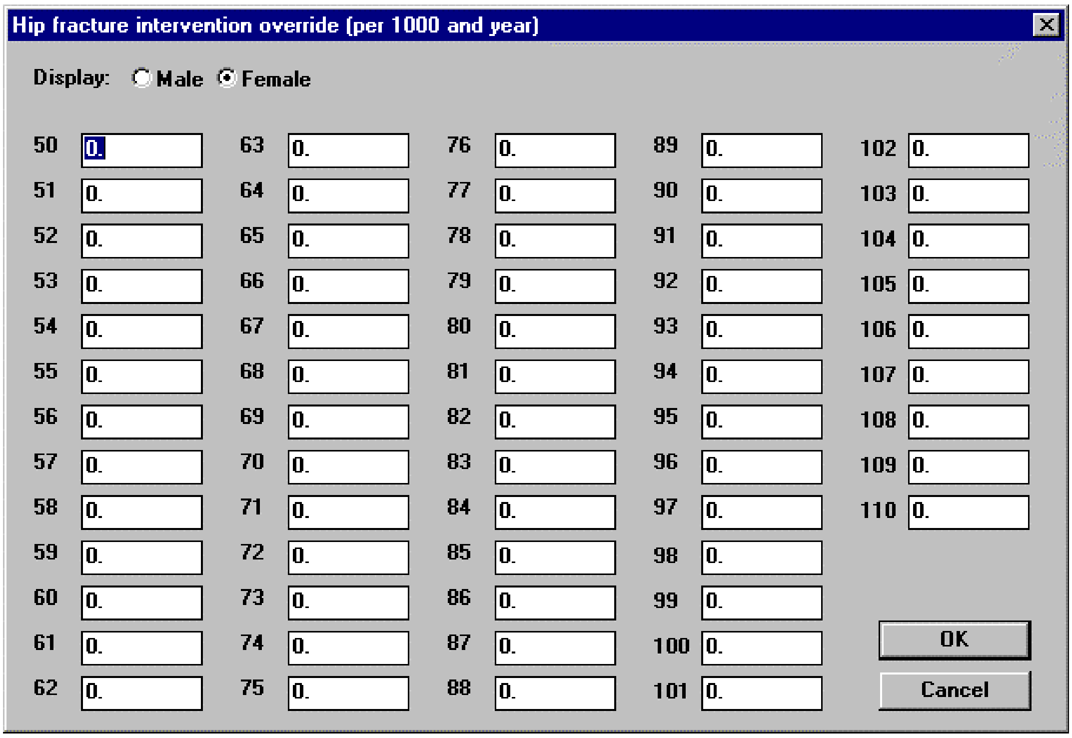
	CHD		Hip fracture		Spine fracture		Wrist fracture		Breast cancer	
	1st year	2nd year -	1st year	2nd year -	1st year	2nd year -	1st year	2nd year -	1st year	2nd year -
50-64	1	1	1	1	1	1	1	1	1	1
65-74	1	1	1	1	1	1	1	1	1	1
75-84	1	1	1	1	1	1	1	1	1	1
85-	1	1	1	1	1	1	1	1	1	1

OK Cancel

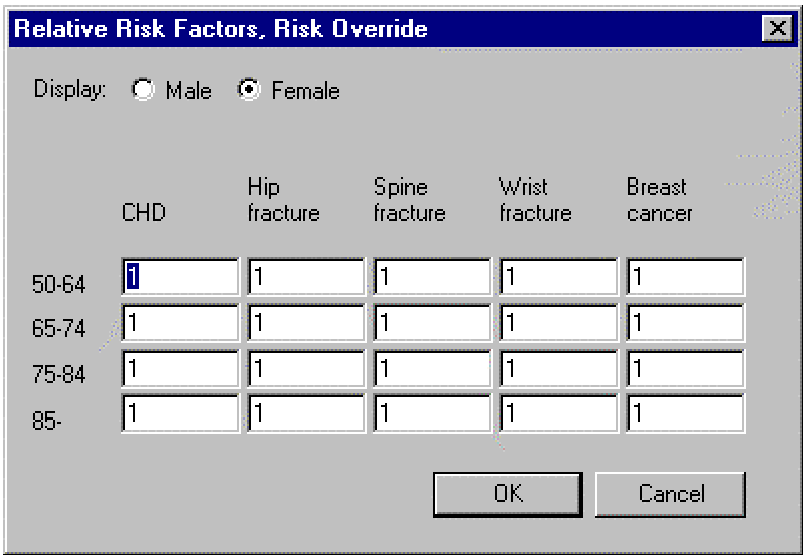
"**Mortality**" and "**Relative risk factors, mortality**". Using this menu it is possible to change the mortality rates for CHD, hip, spine, wrist fractures and breast cancer. E.g. if 1.5 is plugged into all the age-group fields of hip fracture this means that the mortality risk after hip fracture is increased by 50%. To activate the above menu the "Relative risks" have to be marked on the "Setup" and "Conditions" menu.



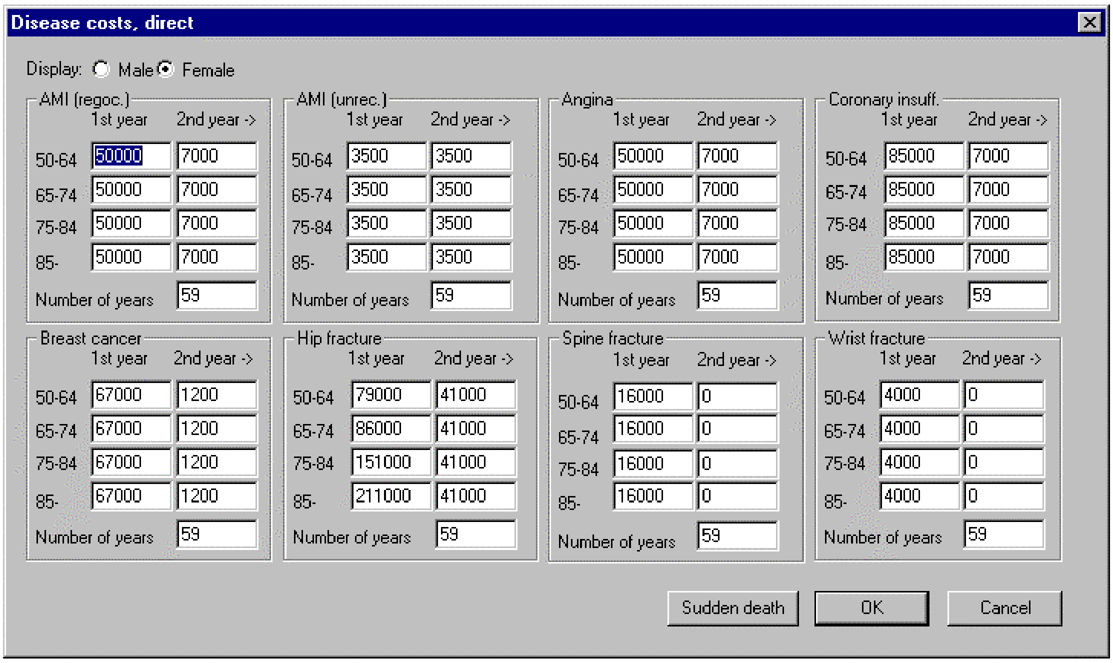
"**Override**" and "**Hip fracture risk override**". Specifies the base-case risk of hip fracture without treatment. When the value is set equal to 0 the risk is extracted from the risk equations instead of the table. The "risk override" is also available for spine and wrist fractures and for CHD and breast cancer. To activate the above menu the "Log fcn override" have to be marked on the "Setup" and "Conditions" menu.



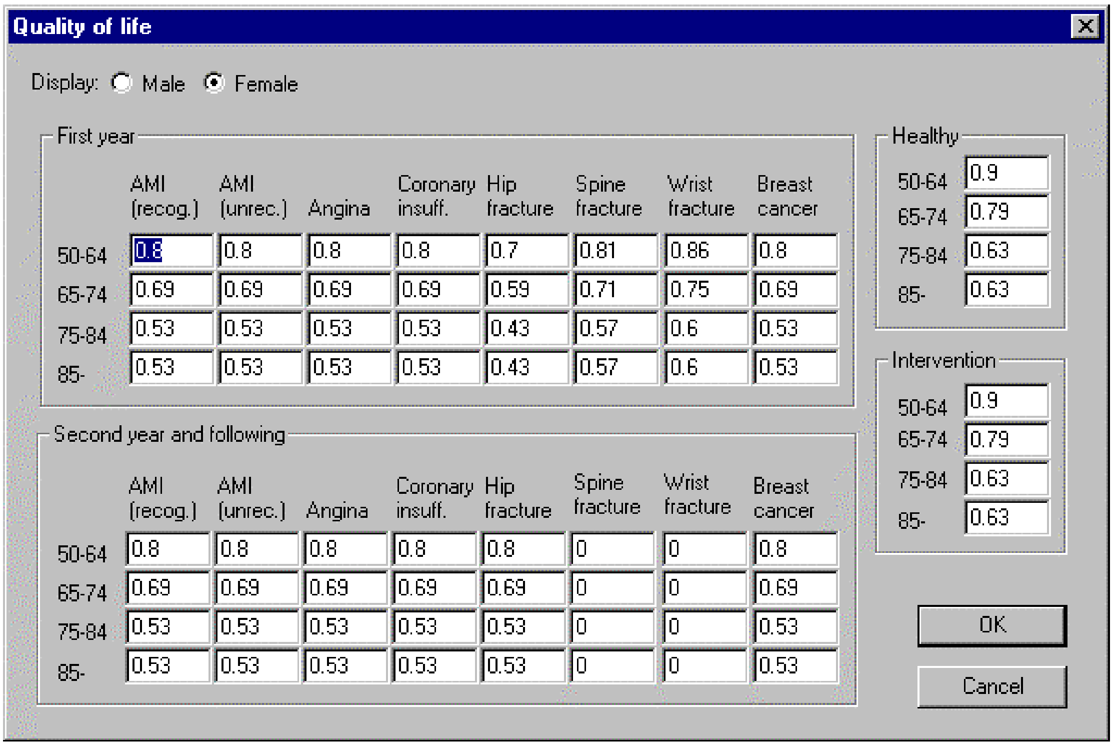
"**Override**" and "**Hip fracture intervention override**". Specifies the risk of hip fracture with intervention. When the value is set to 0 the risk with the intervention is calculated by combining the assumed risk reduction according to "Setup" and "Intervention" menu and the risk equations. The "intervention override" is also available for CHD, breast cancer, death other, spine and wrist fractures. To activate the above menu the "Risk and iv override" have to be marked on the "Setup" and "Conditions" menu.



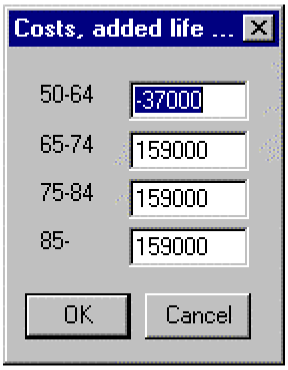
"**Override**" and "**Relative risk factors, risk override**". Enables changes in the base-case risk of CHD, hip, spine, wrist fractures and breast cancer when specified using the risk override tables. E.g. if 1.5 is plugged into all the age group fields of hip fracture this means that the base-case risk of hip fracture is increased by 50%. To activate this option mark the "Relative risks" square on the "Setup" and "Conditions" menu.



"**Disease costs**" and "**Direct**". Specifies the direct costs the first and second and following years after a disease event. A similar menu exists for indirect costs ("Disease costs" and " Indirect").



"**Quality of life**" menu. Shows a quality of life value between 0 and 1 the first and second and following years after the disease events and for healthy and for intervention. If values on the "Intervention" fields are lower than on the "Healthy" fields this means that the intervention is associated with side effects. To activate this menu mark the "quality of life" on the "Setup" and "Conditions" menu.



"**Costs added life years**". Specifies the costs referred to added life years due to the intervention defined as the difference between the annual consumption (private and public) and production. To activate this menu mark "cost in added life years" on the "Setup" and "Conditions" menu.

APPENDIX 2 - SUMMARY OF MODEL ASSUMPTIONS AND DEFAULT DATA

This appendix gives a summary of the model assumptions and data for the risks, mortality, costs and quality of life.

1. Risk functions:

The risk functions are specified as logistic distribution functions. The risk of hip fracture, spine fracture, wrist fracture and breast cancer are specified as logistic distribution functions and are represented by:

(A1)

where (A2)

For hip fracture the following risk function is specified:

X_0	1		-13.412
X_1	Age		0.11264

Source: The risk function is estimated from incidence data in the Stockholm County Council 1990. The following relationship is used (using the log of the odds ratio): *ln[p*$_i$*/1-p*$_i$*] =* . p_i is the probability of having a fracture for women of age , where *i=1,2...10*. The ages are: 52.5; 57.5; 62.5; 67.5; 72.5; 77.5; 82.5; 87.5; 92.5; 97.5.

Hip fracture risk per 1000, by age.

Age	Risk	Age	Risk	Age	Risk	Age	Risk	Age	Risk
50	0.42	63	1.80	76	7.76	89	32.70	102	127.56
51	0.47	64	2.02	77	8.67	90	36.46	103	140.63
52	0.52	65	2.26	78	9.70	91	40.63	104	154.80
53	0.59	66	2.53	79	10.84	92	45.26	105	170.12
54	0.66	67	2.83	80	12.12	93	50.38	106	186.61
55	0.73	68	3.16	81	13.54	94	56.05	107	204.32
56	0.82	69	3.54	82	15.13	95	62.32	108	223.24
57	0.92	70	3.96	83	16.91	96	69.23	109	243.38
58	1.03	71	4.43	84	18.89	97	76.85	110	264.72
59	1.15	72	4.96	85	21.09	98	85.23		
60	1.29	73	5.55	86	23.55	99	94.44		
61	1.44	74	6.20	87	26.28	100	104.52		
62	1.61	75	6.94	88	29.32	101	115.54		

For spine fracture the following risk function is specified:

X_0	1		-11.70069
X_1	Age		0.08347

Source: The risk function is estimated from incidence data in the Malmö County Council (Kanis et al. 1999). The following relationship is used (using the log of the odds ratio): *ln[p*$_i$*/1-p*$_i$*] =* . p_i is the probability of having a fracture for women of age .

Spine fracture risk per 1000, by age.

Age	Risk	Age	Risk	Age	Risk	Age	Risk	Age	Risk
50	0.54	63	1.59	76	4.69	89	13.76	102	39.67
51	0.58	64	1.73	77	5.10	90	14.94	103	42.97
52	0.64	65	1.88	78	5.54	91	16.22	104	46.54
53	0.69	66	2.04	79	6.02	92	17.61	105	50.39
54	0.75	67	2.22	80	6.54	93	19.12	106	54.53
55	0.82	68	2.41	81	7.11	94	20.74	107	59.00
56	0.89	69	2.62	82	7.72	95	22.51	108	63.81
57	0.96	70	2.85	83	8.39	96	24.42	109	68.98
58	1.05	71	3.10	84	9.11	97	26.49	110	74.54
59	1.14	72	3.37	85	9.90	98	28.73		
60	1.24	73	3.66	86	10.75	99	31.15		
61	1.35	74	3.97	87	11.67	100	33.77		
62	1.46	75	4.32	88	12.68	101	36.61		

For wrist fracture the following risk function is specified:

X_0	1		-8.799576
X_1	Age		0.04405

Source: The risk function is estimated from incidence data in the Malmö County Council (Kanis et al. 1999). The following relationship is used (using the log of the odds ratio): *ln[p_i/1-p_i] =* . p_i is the probability of having a fracture for women of age .

Wrist fracture risk per 1000, by age.

Age	Risk	Age	Risk	Age	Risk	Age	Risk	Age	Risk
50	1.36	63	2.41	76	4.27	89	7.55	102	13.30
51	1.42	64	2.52	77	4.46	90	7.88	103	13.89
52	1.49	65	2.63	78	4.66	91	8.24	104	14.51
53	1.55	66	2.75	79	4.87	92	8.60	105	15.15
54	1.62	67	2.88	80	5.09	93	8.99	106	15.82
55	1.70	68	3.01	81	5.32	94	9.39	107	16.52
56	1.77	69	3.14	82	5.56	95	9.81	108	17.26
57	1.85	70	3.28	83	5.80	96	10.24	109	18.02
58	1.94	71	3.43	84	6.06	97	10.70	110	18.82
59	2.02	72	3.58	85	6.33	98	11.18		
60	2.12	73	3.74	86	6.62	99	11.67		
61	2.21	74	3.91	87	6.91	100	12.19		
62	2.31	75	4.09	88	7.22	101	12.74		

For breast cancer the following risk function is specified:

X_0	1		-6.87
X_1	Age		0.0137

Source: The risk function is estimated from Swedish incidence data referring to 1993 extracted from the National Board of Health and Welfare (Socialstyrelsen), Sweden. The following relationship is used (using the log of the odds ratio): *ln[p_i/1-p_i] =* . p_i is the annual probability of having a breast cancer for women of age , where *i=1,2...8*. The ages are: 52.5; 57.5; 62.5; 67.5; 72.5; 77.5; 82.5; 87.5.

Breast cancer risk per 1000, by age.

Age	risk	Age	Risk	Age	risk	Age	Risk	Age	risk
50	2.06	63	2.46	76	2.93	89	3.50	102	4.18
51	2.08	64	2.49	77	2.97	90	3.55	103	4.24
52	2.11	65	2.52	78	3.01	91	3.60	104	4.30
53	2.14	66	2.56	79	3.06	92	3.65	105	4.36
54	2.17	67	2.59	80	3.10	93	3.70	106	4.42
55	2.20	68	2.63	81	3.14	94	3.75	107	4.48
56	2.23	69	2.67	82	3.18	95	3.80	108	4.54
57	2.26	70	2.70	83	3.23	96	3.85	109	4.60
58	2.29	71	2.74	84	3.27	97	3.91	110	4.66
59	2.33	72	2.78	85	3.32	98	3.96		
60	2.36	73	2.82	86	3.36	99	4.01		
61	2.39	74	2.85	87	3.41	100	4.07		
62	2.42	75	2.89	88	3.46	101	4.13		

For CHD the default risk data are specified in the override table. The risk of CHD (defined as acute myocardial infarction recognised (ICD=410), angina pectoris stable (ICD=413) and unstable (ICD=411A+B) is based on Swedish data extracted from the Centre for Epidemiology at the National Board of Health and Welfare. The data refer to the period 1990-1994 in Sweden. The annual age-specific risks are:

Age	Risk	Age	Risk	Age	Risk	Age	Risk	Age	Risk
50	1.68	63	6.68	76	18.37	89	24.81	102	21.52
51	1.91	64	7.37	77	19.64	90	23.87	103	21.52
52	2.13	65	8.05	78	20.77	91	22.93	104	21.52
53	2.41	66	8.73	79	21.75	92	21.99	105	21.52
54	2.73	67	9.42	80	22.74	93	21.52	106	21.52
55	3.06	68	10.18	81	23.72	94	21.52	107	21.52
56	3.39	69	11.01	82	24.71	95	21.52	108	21.52
57	3.71	70	11.84	83	25.30	96	21.52	109	21.52
58	4.12	71	12.67	84	25.51	97	21.52	110	21.52
59	4.62	72	13.50	85	25.71	98	21.52		
60	5.11	73	14.55	86	25.91	99	21.52		
61	5.60	74	15.82	87	26.11	100	21.52		
62	6.09	75	17.09	88	25.74	101	21.52		

The risk of a specific CHD event based on Swedish data is obtained by combining the above risk table with the CHD distribution table below showing the probability of different CHD states. The default values are shown below (%):

	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Sudden Death
50-64	44	0	46	10	0
65-74	56	0	36	8	0
75-84	64	0	30	6	0
85-	71	0	23	6	0

The risk of CHD can also be specified as a logistic regression function. The risk of CHD is specified as a risk function according to above as:

X_0	1		-15.2804537
X_1	Age		0.2440214
X_2	Age^2		-0.0012694
X_3	Cholesterol		0.0110831
X_4	Cholesterol□Age		-0.0001115
X_5	Blood pressure		0.0180007
X_6	Smoking status		0.0701393
X_7	Glucose intolerance		0.8444092
X_8	Left ventricular hypertrophy (LVH)		0.6745513

Source: The risk function is taken from Kannel et al, 1987.

The default values of the risk factors used in the empirical application were assumed to be: Diastolic blood pressure = 85. Serumcholesterol = 220.36. Share of smokers = 26%. Glucose intolerance = 0%. Left ventricular hypertrophy = 0%. Source: Folkhälsoinstitutet 1996; Johannesson, 1995.

The risk of CHD is expressed as a 8-year risk of CHD. To transform the eight-year risk to an annual risk the following transformation was made:

where □ denotes the annual risk at age *t*. The risk of CHD (defined as acute myocardial infarction recognised and unrecognised, angina stable and unstable, and sudden death) based on the US-data and the risk factors above is:

Age	Risk	Age	Risk	Age	Risk	Age	Risk	Age	Risk
50	2.55	63	7.63	76	14.75	89	15.72	102	15.72
51	2.82	64	8.16	77	15.24	90	15.72	103	15.72
52	3.11	65	8.69	78	15.72	91	15.72	104	15.72
53	3.42	66	9.23	79	15.72	92	15.72	105	15.72
54	3.75	67	9.79	80	15.72	93	15.72	106	15.72
55	4.10	68	10.35	81	15.72	94	15.72	107	15.72
56	4.47	69	10.91	82	15.72	95	15.72	108	15.72
57	4.86	70	11.48	83	15.72	96	15.72	109	15.72
58	5.28	71	12.04	84	15.72	97	15.72	110	15.72
59	5.71	72	12.60	85	15.72	98	15.72		
60	6.17	73	13.16	86	15.72	99	15.72		
61	6.64	74	13.70	87	15.72	100	15.72		
62	7.13	75	14.23	88	15.72	101	15.72		

The risk of a specific CHD event based on the Framingham data is obtained by combining the risk table with the CHD distribution table showing the probability of different CHD states. (Note that if the risk equation based on the Framingham study and related CHD distribution is used also the mortality tables used in the previous version of the model must be used (see below and in report by Zethraeus et al. 1998). The default values are shown below (%):

	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Sudden Death
50-64	15	10	60	10	5
65-74	25	15	40	10	10
75-84	25	15	40	10	10
85-	25	15	40	10	10

2. Risk-changes during HRT:

Coronary heart disease: 0, -20 and -50%.
Hip fractures: -40 and -50%.
Breast cancer: 0 and +35%.

Source: The assumed risk changes are based on SBU (1996), OTA (1995) and Hulley et al. (1998).

3. Mortality rates:

Normal mortality tables are used for spine (In a sensitivity analysis we assume a slight increase in the mortality after spine fracture, see Kado et al. (1999).) and wrist fracture the first year after and for hip fractures the second and following years after.

Normal mortality rates per 1000 for women.

Age	risk	Age	Risk	Age	risk	Age	Risk	Age	Risk
50	2.53	63	7.91	76	32.37	89	153.12	102	407.92
51	2.76	64	8.71	77	36.80	90	170.06	103	431.60
52	2.91	65	9.94	78	41.61	91	191.02	104	455.98
53	3.16	66	10.86	79	46.72	92	207.21	105	481.10
54	3.41	67	11.95	80	52.74	93	224.19	106	506.98
55	4.01	68	13.14	81	58.95	94	241.91	107	533.64
56	4.09	69	14.18	82	68.09	95	260.36	108	561.09
57	4.79	70	15.90	83	76.38	96	279.50	109	589.30
58	5.25	71	17.78	84	87.14	97	299.30	110	618.23
59	5.58	72	19.62	85	95.59	98	319.76		
60	6.24	73	22.61	86	107.30	99	340.84		
61	6.60	74	25.41	87	120.99	100	362.56		
62	7.43	75	27.75	88	135.14	101	384.91		

Source: Life tables for the period of 1989-1993. SCB, 1995.

Dead 1993 after underlying cause of death according to ICDs detail list, for women according to age. Number of cases.

	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-
All causes of death	718	976	1551	2650	4494	6719	9944	10092	8724
Malign tumour in the breast	111	123	120	165	203	194	182	150	72
Ischaemic Heart disease	52	109	234	506	1034	1743	2650	2643	2184
The share of women dying Of ischaemic heart disease or Malign tumour in the breast	0.227	0.238	0.228	0.253	0.275	0.288	0.285	0.277	0.259

Source: ICDs detail list of underlying causes of death, 1993.

Mortality rates per 1000 excluding CHD and breast cancer.

Death, other (per 1000)

Display: ○ Male ◉ Female

Age	Rate	Age	Rate	Age	Rate	Age	Rate	Age	Rate
50	1.96	63	6.1	76	23.04	89	110.74	102	302.43
51	2.13	64	6.72	77	26.19	90	126.08	103	319.99
52	2.25	65	7.42	78	29.61	91	141.62	104	338.06
53	2.44	66	8.11	79	33.25	92	153.63	105	356.69
54	2.64	67	8.92	80	37.72	93	166.22	106	375.88
55	3.06	68	9.81	81	42.16	94	179.35	107	395.64
56	3.12	69	10.59	82	48.7	95	193.03	108	415.99
57	3.65	70	11.52	83	54.63	96	207.22	109	436.91
58	4	71	12.89	84	62.32	97	221.9	110	458.36
59	4.25	72	14.22	85	69.14	98	237.07		
60	4.82	73	16.39	86	77.6	99	252.7		
61	5.09	74	18.42	87	87.51	100	268.8		OK
62	5.73	75	19.75	88	97.74	101	285.37		Cancel

Source: SCB, 1996. Mortality for death other is calculated as normal mortality multiplied by the share of all causes of death that is not explained by breast cancer and ischaemic disease in Sweden 1993.

Mortality rates per 1000 during 1 year after breast cancer.

Breast cancer mortality, first year (per 1000)

Age	Rate	Age	Rate	Age	Rate	Age	Rate	Age	Rate
50	29.46	63	42.63	76	104.94	89	216.64	102	452.33
51	29.69	64	43.41	77	109.04	90	232.31	103	474.23
52	29.83	65	44.59	78	113.49	91	251.69	104	496.78
53	30.07	66	45.48	79	118.22	92	266.67	105	520.02
54	30.32	67	46.53	80	123.78	93	282.38	106	543.96
55	38.87	68	47.68	81	129.53	94	298.77	107	568.62
56	38.95	69	48.68	82	137.98	95	315.83	108	594.01
57	39.62	70	50.34	83	145.65	96	333.54	109	620.1
58	40.07	71	52.16	84	155.6	97	351.85	110	646.86
59	40.38	72	53.93	85	163.42	98	370.78		
60	41.02	73	56.82	86	174.25	99	390.28		
61	41.37	74	59.52	87	186.92	100	410.37		OK
62	42.17	75	100.67	88	200	101	431.04		Cancel

Source: Breast cancer mortality (BCM) for a specific year is estimated using relative survival data (National Board of Health and Welfare, Epidemiological Centre). BCM = [1-NS*RS]*1000, where NS = Normal survival/1000, RS = CS/NS, where CS = Crude survival in breast cancer the year after breast cancer.

Mortality rates per 1000 second and following year after a breast cancer.

Breast cancer mortality, second year and following (per 1000)

Age	Rate	Age	Rate	Age	Rate	Age	Rate	Age	Rate
50	38	63	86	76	237	89	237	102	237
51	38	64	86	77	237	90	237	103	237
52	38	65	86	78	237	91	237	104	237
53	38	66	86	79	237	92	237	105	237
54	38	67	86	80	237	93	237	106	237
55	86	68	86	81	237	94	237	107	237
56	86	69	86	82	237	95	237	108	237
57	86	70	86	83	237	96	237	109	237
58	86	71	86	84	237	97	237	110	237
59	86	72	86	85	237	98	237		
60	86	73	86	86	237	99	237		
61	86	74	86	87	237	100	237		OK
62	86	75	237	88	237	101	237		Cancel

Source: National Board of Health and Welfare, Epidemiological centre.

Mortality rates per 1000 during one year after a hip fracture.

Hip fracture mortality, first year after fracture (per 1000)

Display: ○ Male ● Female

Age	Rate	Age	Rate	Age	Rate	Age	Rate	Age	Rate
50	17	63	48.1	76	128.7	89	301.5	102	557.8
51	18.4	64	52	77	138.2	90	319.1	103	578
52	20	65	56.2	78	148.3	91	337.3	104	598
53	21.7	66	60.8	79	159	92	356	105	617.7
54	23.5	67	65.7	80	170.4	93	375.1	106	636.9
55	25.4	68	70.9	81	182.4	94	394.6	107	655.8
56	27.6	69	76.5	82	195	95	414.5	108	674.2
57	29.9	70	82.6	83	208.3	96	434.7	109	692
58	32.4	71	89	84	222.2	97	455	110	709.3
59	35	72	96	85	236.8	98	475.5		
60	37.9	73	103.4	86	252	99	496.2		
61	41.1	74	111.3	87	267.9	100	516.8		OK
62	44.5	75	119.7	88	284.4	101	537.3		Cancel

Source: Estimated using all women having a hip fracture above the age of 49 in the city of Stockholm, 1992. The following logistic distribution function was estimated:

where where $X_0 = 1$ and $X_1 =$ age. = -8.1829 and = 0.0825

Mortality rates per 1000 second and following year after a hip fracture.

Hip fracture mortality, second year and following (per 1000)

Display: ○ Male ◉ Female

50	2.53	63	7.91	76	32.37	89	153.12	102	407.92
51	2.76	64	8.71	77	36.8	90	170.06	103	431.6
52	2.91	65	9.94	78	41.61	91	191.02	104	455.98
53	3.16	66	10.86	79	46.72	92	207.21	105	481.1
54	3.41	67	11.95	80	52.74	93	224.19	106	506.98
55	4.01	68	13.14	81	58.95	94	241.91	107	533.64
56	4.09	69	14.18	82	68.09	95	260.36	108	561.09
57	4.79	70	15.9	83	76.38	96	279.5	109	589.3
58	5.25	71	17.78	84	87.14	97	299.3	110	618.23
59	5.58	72	19.62	85	95.59	98	319.76		
60	6.24	73	22.61	86	107.3	99	340.84		
61	6.6	74	25.41	87	120.99	100	362.56		OK
62	7.43	75	27.75	88	135.14	101	384.91		Cancel

Source: Life tables for the period of 1989-1993. SCB, 1995.

<u>Mortality rates after CHD are shown both based on Swedish and US data:</u>

Mortality rates per 1000 during 1 year after AMI (recognised). Swedish data.

AMI (recog.) mortality, first year after disease (per 1000)

Display: ○ Male ◉ Female

50	97.88	63	181.09	76	351.49	89	594.63	102	1000
51	98.45	64	191.34	77	370.1	90	616.21	103	1000
52	99.02	65	201.59	78	389	91	637.79	104	1000
53	114.89	66	211.85	79	408.19	92	659.38	105	1000
54	119.55	67	222.1	80	427.38	93	692.16	106	1000
55	124.22	68	233.14	81	446.58	94	736.13	107	1000
56	128.88	69	244.97	82	465.77	95	780.11	108	1000
57	133.55	70	256.79	83	484.05	96	824.09	109	1000
58	139.89	71	268.62	84	501.43	97	868.07	110	1000
59	147.91	72	280.45	85	518.81	98	912.04		
60	155.92	73	295.67	86	536.19	99	956.02		OK
61	163.94	74	314.28	87	553.57	100	1000		
62	171.95	75	332.89	88	573.05	101	1000		Cancel

Source: The epidemiological centre at the National Board of Health and Welfare.

Mortality rates per 1000 second and following year after AMI (recognised). Swedish data.

AMI (recog.) mortality, second year and following (per 1000)

Display: ○ Male ◉ Female

50	17.65	63	37	76	98.38	89	244.23	102	684.73
51	19.02	64	39.26	77	104.9	90	263.12	103	724.14
52	20.38	65	41.51	78	114.49	91	282.01	104	763.55
53	21.72	66	43.77	79	127.15	92	300.9	105	802.96
54	23.04	67	46.03	80	139.82	93	330.05	106	842.36
55	24.36	68	50	81	152.48	94	369.46	107	881.77
56	25.68	69	55.68	82	165.14	95	408.87	108	921.18
57	27	70	61.36	83	175.91	96	448.28	109	960.59
58	28.31	71	67.04	84	184.8	97	487.68	110	1000
59	29.63	72	72.73	85	193.68	98	527.09		
60	30.95	73	78.83	86	202.57	99	566.5		
61	32.49	74	85.35	87	211.45	100	605.91	OK	
62	34.75	75	91.86	88	225.34	101	645.32	Cancel	

Source: The epidemiological centre at the National Board of Health and Welfare.

Mortality rates per 1000 during 1 year after Angina Pectoris and coronary insufficiency. Swedish data.

Angina mortality, first year after disease (per 1000)

Display: ○ Male ◉ Female

50	15.37	63	31.15	76	79.27	89	227.06	102	687.54
51	16.06	64	33.06	77	86.61	90	252.61	103	726.6
52	16.62	65	34.96	78	94.58	91	278.16	104	765.65
53	17.18	66	36.87	79	103.18	92	303.72	105	804.71
54	17.74	67	38.77	80	111.78	93	336.02	106	843.77
55	18.3	68	41.11	81	120.38	94	375.08	107	882.83
56	18.85	69	43.88	82	128.98	95	414.14	108	921.88
57	19.41	70	46.66	83	138.83	96	453.19	109	960.94
58	20.74	71	49.43	84	149.92	97	492.25	110	1000
59	22.84	72	52.2	85	161.01	98	531.31		
60	24.95	73	57.25	86	172.1	99	570.37		
61	27.05	74	64.59	87	183.19	100	609.42	OK	
62	29.15	75	71.93	88	201.51	101	648.48	Cancel	

Source: The epidemiological centre at the National Board of Health and Welfare.

Mortality rates per 1000 second and following year after Angina Pectoris and coronary insufficiency. Swedish data.

Angina mortality, second year and following (per 1000)

Display: ○ Male ◉ Female

50	9.67	63	17.08	76	58.9	89	193.9	102	663.6
51	10.02	64	18.84	77	64.83	90	213.96	103	705.65
52	10.36	65	20.61	78	71.54	91	234.03	104	747.7
53	10.71	66	22.38	79	79.02	92	254.1	105	789.75
54	11.06	67	24.14	80	86.51	93	285.16	106	831.8
55	11.4	68	26.34	81	93.99	94	327.2	107	873.85
56	11.75	69	28.96	82	101.48	95	369.25	108	915.9
57	12.1	70	31.58	83	111.08	96	411.3	109	957.95
58	12.66	71	34.21	84	122.8	97	453.35	110	1000
59	13.45	72	36.83	85	134.51	98	495.4		
60	14.23	73	41.11	86	146.23	99	537.45		
61	15.02	74	47.04	87	157.94	100	579.5		
62	15.8	75	52.97	88	173.83	101	621.55		

OK Cancel

Source: The epidemiological centre at the National Board of Health and Welfare.

Mortality rates per 1000 during 1 year after AMI (recognised). US data.

AMI (recog.) mortality, first year after disease (per 1000)

Display: ○ Male ◉ Female

50	100.	63	230.	76	433.33	89	933.03	102	1000.
51	110.	64	240.	77	450.	90	1000.	103	1000.
52	120.	65	250.	78	466.67	91	1000.	104	1000.
53	130.	66	266.67	79	483.33	92	1000.	105	1000.
54	140.	67	283.33	80	500.	93	1000.	106	1000.
55	150.	68	300.	81	535.89	94	1000.	107	1000.
56	160.	69	316.67	82	574.35	95	1000.	108	1000.
57	170.	70	333.33	83	615.57	96	1000.	109	1000.
58	180.	71	350.	84	659.75	97	1000.	110	1000.
59	190.	72	366.67	85	707.11	98	1000.		
60	200.	73	383.33	86	757.86	99	1000.		
61	210.	74	400.	87	812.25	100	1000.		
62	220.	75	416.67	88	870.55	101	1000.		

OK Cancel

Source: Kannel et al. (1988), Johannesson (1995).

Mortality rates per 1000 during 1 year after AMI (unrecognised) and Coronary Insufficiency and second and following year after AMI (recognised), AMI (unrecognised) and Coronary Insufficiency. US data.

AMI (unrec.) mortality, first year after disease (per 1000)

Display: ○ Male ◉ Female

50	10.	63	18.67	76	78.67	89	199.53	102	541.17
51	10.67	64	19.33	77	84.	90	215.44	103	584.34
52	11.33	65	20.	78	89.33	91	232.63	104	630.96
53	12.	66	25.33	79	94.67	92	251.19	105	681.29
54	12.67	67	30.67	80	100.	93	271.23	106	735.64
55	13.33	68	36.	81	107.98	94	292.86	107	794.33
56	14.	69	41.33	82	116.59	95	316.23	108	857.7
57	14.67	70	46.67	83	125.89	96	341.45	109	926.12
58	15.33	71	52.	84	135.94	97	368.69	110	1000.
59	16.	72	57.33	85	146.78	98	398.11		
60	16.67	73	62.67	86	158.49	99	429.87		
61	17.33	74	68.	87	171.13	100	464.16		OK
62	18.	75	73.33	88	184.78	101	501.19		Cancel

Source: Kannel et al. (1988), Johannesson (1995).

Mortality rates per 1000 during 1 year after Angina Pectoris and second and following year after Angina Pectoris. US data

Angina mortality, first year after disease (per 1000)

Display: ○ Male ◉ Female

50	7.5	63	14.	76	62.67	89	170.67	102	509.91
51	8.	64	14.5	77	67.	90	185.66	103	554.7
52	8.5	65	15.	78	71.33	91	201.97	104	603.42
53	9.	66	19.33	79	75.67	92	219.71	105	656.42
54	9.5	67	23.67	80	80.	93	239.01	106	714.08
55	10.	68	28.	81	87.03	94	260.	107	776.8
56	10.5	69	32.33	82	94.67	95	282.84	108	845.03
57	11.	70	36.67	83	102.99	96	307.69	109	919.26
58	11.5	71	41.	84	112.03	97	334.71	110	1000.
59	12.	72	45.33	85	121.87	98	364.11		
60	12.5	73	49.67	86	132.58	99	396.1		
61	13.	74	54.	87	144.22	100	430.89		OK
62	13.5	75	58.33	88	156.89	101	468.73		Cancel

Source: Kannel et al. (1988), Johannesson (1995).

4. Quality of life weights:

Quality of life weights at different disease events in different age groups the first and second and following year after a disease event. Quality of life weights for healthy women and for intervention in different age groups.

Quality of life

Display: ○ Male ● Female

First year

	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Hip fracture	Spine fracture	Wrist fracture	Breast cancer
50-64	0.8	0.8	0.8	0.8	0.7	0.81	0.86	0.8
65-74	0.69	0.69	0.69	0.69	0.59	0.71	0.75	0.69
75-84	0.53	0.53	0.53	0.53	0.43	0.57	0.6	0.53
85-	0.53	0.53	0.53	0.53	0.43	0.57	0.6	0.53

Second year and following

	AMI (recog.)	AMI (unrec.)	Angina	Coronary insuff.	Hip fracture	Spine fracture	Wrist fracture	Breast cancer
50-64	0.8	0.8	0.8	0.8	0.8	0	0	0.8
65-74	0.69	0.69	0.69	0.69	0.69	0	0	0.69
75-84	0.53	0.53	0.53	0.53	0.53	0	0	0.53
85-	0.53	0.53	0.53	0.53	0.53	0	0	0.53

Healthy

50-64	0.9
65-74	0.79
75-84	0.63
85-	0.63

Intervention

50-64	0.9
65-74	0.79
75-84	0.63
85-	0.63

OK

Cancel

Sources: Quality of life weights for hip fractures are taken from Jönsson et al. (1995) assuming a quality of life loss equal to 0.2 the first year after a fracture. The second year after a fracture 50% of surviving patients are assumed to be healthy, 90% near-normal functioning and 40% severely handicapped. The quality of life weights associated with these states are set to 1, 0.9 and 0.4. By multiplying the share of patients in the disease states with the quality of life weights and adding them together, the average quality of life weight the second year after fracture is obtained which is equal to 0.9. This implies a quality of life loss equal to 0.1. Quality of life weights for spine and wrist fractures are set to the values shown in the table. Quality of life weights for CHD are based on a study by Glasziou et al. (1994) indicating that the quality of life loss associated with CHD is 0.1. Quality of life weights for breast cancer is assumed to be equal to the quality of life weights for CHD. Quality of life weights healthy is taken from a study by Lundberg et al. (1999).

5. Costs:

Intervention costs

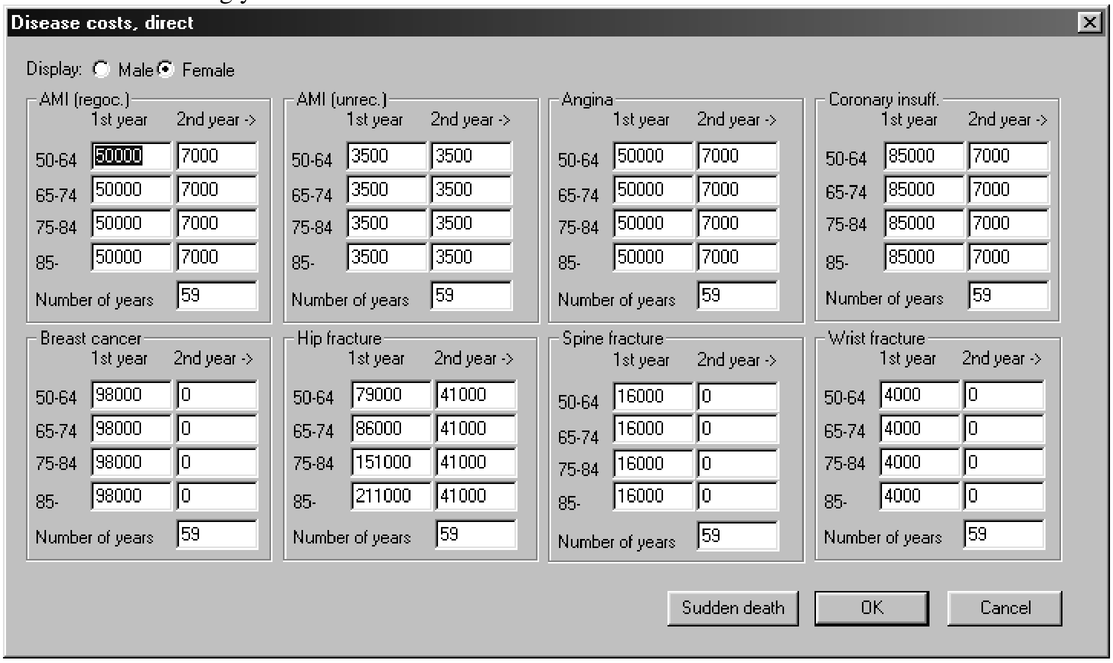
Oestrogen therapy: SEK 1,641 (Drugs, SEK 860; 1 physician visit each year, SEK 601, time and travelling SEK 180)

Oestrogen and Progestogen: SEK 2,226 (Drugs SEK 1 055; 1,5 physician visit each year SEK 901, time and travelling SEK 270)

Source: The cost data are taken from a study by Zethraeus (1998).

Morbidity costs

Direct disease costs (SEK thousand) for different disease events in different age groups the first and second and following years after a disease event.



Disease costs, direct

Display: Male Female

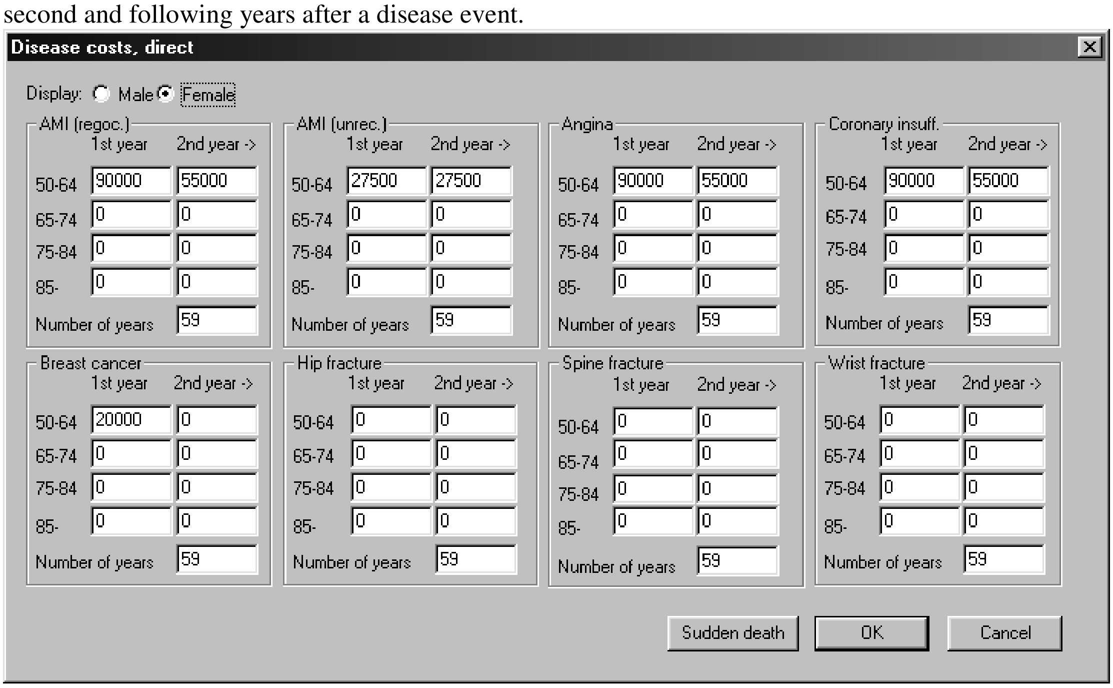
	AMI (regoc.) 1st year	AMI (regoc.) 2nd year ->	AMI (unrec.) 1st year	AMI (unrec.) 2nd year ->	Angina 1st year	Angina 2nd year ->	Coronary insuff. 1st year	Coronary insuff. 2nd year ->
50-64	50000	7000	3500	3500	50000	7000	85000	7000
65-74	50000	7000	3500	3500	50000	7000	85000	7000
75-84	50000	7000	3500	3500	50000	7000	85000	7000
85-	50000	7000	3500	3500	50000	7000	85000	7000
Number of years		59		59		59		59

	Breast cancer 1st year	Breast cancer 2nd year ->	Hip fracture 1st year	Hip fracture 2nd year ->	Spine fracture 1st year	Spine fracture 2nd year ->	Wrist fracture 1st year	Wrist fracture 2nd year ->
50-64	98000	0	79000	41000	16000	0	4000	0
65-74	98000	0	86000	41000	16000	0	4000	0
75-84	98000	0	151000	41000	16000	0	4000	0
85-	98000	0	211000	41000	16000	0	4000	0
Number of years		59		59		59		59

Sudden death OK Cancel

Sources: Hip fracture costs are collected from a study by Zethraeus et al. (1997). Hip fracture costs the second and following years after a hip fracture is based on the assumption that 10% of the patients is at a nursing home, at a cost of SEK 1,140 per day, for the rest of their lives. Breast cancer costs are collected from Liljegren (1995). CHD costs are based on Zethraeus et al. (1999) and Olsson et al. (1987). The costs of spine and wrist fracture are based on assumptions made by Jönsson et al. (1995).

Indirect disease costs (SEK thousand) for different disease events in different age groups the first and second and following years after a disease event.



Disease costs, direct

Display: Male Female

	AMI (regoc.) 1st year	AMI (regoc.) 2nd year ->	AMI (unrec.) 1st year	AMI (unrec.) 2nd year ->	Angina 1st year	Angina 2nd year ->	Coronary insuff. 1st year	Coronary insuff. 2nd year ->
50-64	90000	55000	27500	27500	90000	55000	90000	55000
65-74	0	0	0	0	0	0	0	0
75-84	0	0	0	0	0	0	0	0
85-	0	0	0	0	0	0	0	0
Number of years		59		59		59		59

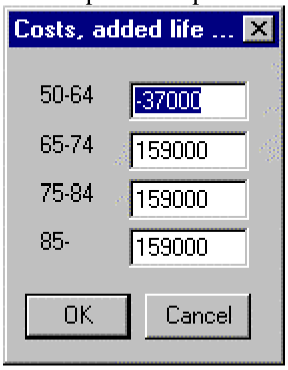
	Breast cancer 1st year	Breast cancer 2nd year ->	Hip fracture 1st year	Hip fracture 2nd year ->	Spine fracture 1st year	Spine fracture 2nd year ->	Wrist fracture 1st year	Wrist fracture 2nd year ->
50-64	20000	0	0	0	0	0	0	0
65-74	0	0	0	0	0	0	0	0
75-84	0	0	0	0	0	0	0	0
85-	0	0	0	0	0	0	0	0
Number of years		59		59		59		59

Sudden death OK Cancel

Sources: Indirect costs for CHD are based on Olsson et al. (1987) and Zethraeus et al. (1999). Indirect costs for breast cancer are based on Liljegren et al. (1995). The indirect costs of hip, spine and wrist fractures are assumed to be 0.

Costs in added life years

Costs in added life years (SEK) in different age groups based on the difference between annual consumption and production. Consumption includes private and public consumption.



Source: Johannesson et al. (1997).