A model for economic evaluations of smoking cessation interventions – technical report

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Content

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Tables

Introduction

This is a technical report on an updated version of a model, originally developed in year 2004 (Johansson, 2004), to enable systematic cost-effectiveness analyses of tobacco cessation interventions in Sweden. It aims to follow international and Swedish recommendations of cost-effectiveness analyses in health and medicine. The model holds a societal perspective, aiming to incorporate available disease-specific costs for all sectors of Swedish society. The updated model contains more recent data on societal costs, disease and death risks, and quality-of life-estimates, to enable estimates that reflects current Swedish conditions.

The model simulates the lifetime societal effects of quitting smoking on three diseases: lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular disease (CVD) including coronary heart disease (CHD) and stroke. The model incorporates the smoking-related disease risks, the remaining disease risks after tobacco quitting, the death risks in the diseases and unrelated diseases, as well as the societal effects of the diseases. The societal effects include medical treatment costs, costs for institutional care, drug costs, costs for informal care and other costs for patients and relatives, and morbidity productivity costs, as well as loss of life-years and quality-adjusted life-years (QALYs).

This technical report contains a description of the model structure, of all the data sources used and of the assumptions made. For validation purposes, it also reports model estimates for some selected age-groups and more detailed outcomes and sensitivity analyses for one age-group, men and women aged 50 years at the start of the simulations. To investigate model uncertainty, univariate and multivariate sensitivity analyses are reported, as well as a probabilistic analysis. The model validity is discussed in the final section of the report.

Method

The diseases

The model incorporates the three most smoking-related diseases: lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular disease (CVD) including coronary heart disease (CHD) and stroke, see table 1. The model is restricted to the effects on the individual smoker/quitter, thus not incorporating any side-effects on other people.

The model

The stochastic model simulates the societal effects of smoking cessation on three smoking-related diseases. It is constructed as a Markov-cycle tree model appropriate for microsimulations.

The Markov model is a health state-transition model (Sonnenberg & Beck, 1993; Briggs & Sculpher, 1998) using probabilities for transitions between health states. These probabilities are the age- and gender-specific disease risks, conditional on smoking status and years since quitting, and age-, gender- and disease-specific death risks. The states are mutually exclusive and collectively exhaustive, and transitions between disease states are not allowed. The only exits from disease states are death, in the disease in question or in unrelated diseases, except for 5-year survivors in lung cancer which are assumed to recover to complete health. All other disease states are assumed to last life-long. See figure 1 for the state-transition diagram.

The Markov stages are one year-long, with no half-cycle correction. The starting point is the state healthy. The model covers the ages 15 to 95 years. The Markov-cycle tree has been created in Treeage Pro (Treeage Inc., 2015).

Table 1. The model diseases, with ICD-10 codes.

Disease	ICD-10
Lung cancer	C34
COPD	J44
Stroke	I61 I63 I64
Coronary heart disease, CHD:	
Acute myocardial infarction, AMI	I21 I22 I23
Congestive health failure, CHF	I50.
Ischemic heart disease, IHD	I20 I24 I25
Sudden death	I46.1

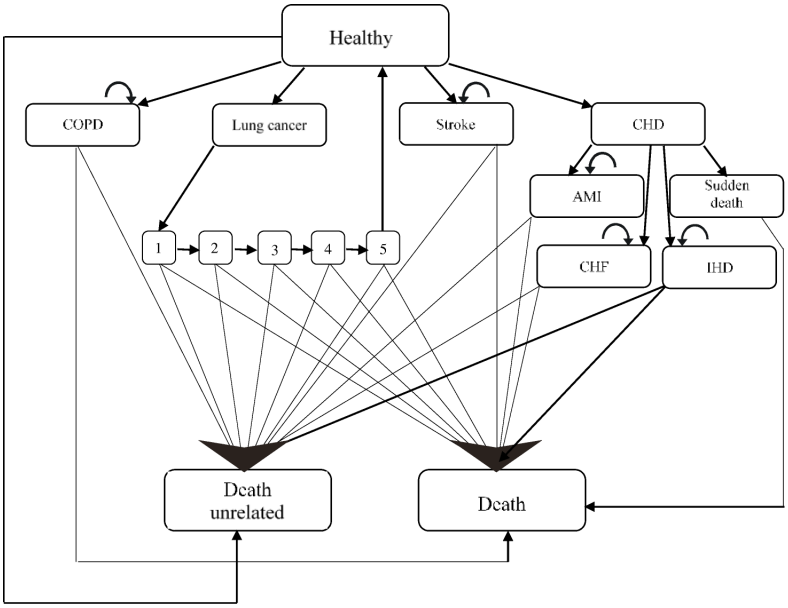

Figure 1. State-transition diagram

The model is set up with two reward sets; costs and effects. The incremental rewards are accumulated during time spent in the health states. The transitional rewards lost life years and some costs are recorded at transitions between healthy and disease state, and disease state and death.

The Markov-cycle tree is run as a microsimulation with 10 000 repetitions. The simulation ends at death or age 95 years. The model is run separately for age and gender groups. The result of each simulation is expected value, with accompanying distributions. The two simulations, the continuing smoker and the quitter, are compared outside the model. The results are presented as expected value per individual, specific for gender, age and smoking status.

Material

The model is based on principles for cost-effectiveness analysis in health and medicine (Gold et al, 1996; Drummond et al, 2005) and Swedish methodological recommendations (TLV, 2004). The model holds the societal perspective, aiming to incorporate disease-specific costs for all sectors of Swedish society.

The model uses Swedish register data and secondary data from previously published scientific articles. The secondary data was found through searches in the database MEDLINE and the reference lists of retrieved articles, choosing the data that is considered most relevant to present-day Swedish circumstances and the target group. No meta-analysis nor other synthesis of data was performed.

All costs are expressed in year 2014 SEK (USD 1=SEK 6.86; Euro 1=SEK 9.10), converted if necessary by the Swedish CPI (consumer price index). The annual discount rate is 3% for both costs and health effects.

The risks

Disease risks

All disease risks are annual age- and gender-specific excess incidence risk until the age of 95 years, see tables 2 to 5.

The COPD disease risk is taken from the Swedish population-based study Obstructive Lung Disease in Northern Sweden (OLIN), which was started in year 1985 (Lundbäck et al, 1991). The risk is the reported average excess seven-year incidence among smokers in three age groups, of which the youngest was 45 years at baseline, see table 2. COPD was defined according to the spirometer GOLD definition.

Table 2. Risks COPD.

	men & women	source
Disease risk		
Risk until age 45	0%	Lindberg et al, 2006
Excess annual risk for smokers, from age 46	1.6%	
Effect of quitting		
Risk fraction for quitters, years since quitting:		Inspired by Surgeon General, 1990
0-5	1	
6-15	0.5	
16-24	0.3	
>25	0.1	
Death risk		
Excess risk among diseased, as fraction of age-specific general death risk, by age:		Estimated from Lundbäck et al, 2009 Statistics Sweden, database
<58 years	1	
58-70 years	5	
>70 years	1	

Table 3. Risks lung cancer.

	men	women	source
Death risk			
Accumulated death risk until age 75			
Smokers	16.7%	10.4%	Peto et al, 2000
Non-smokers	0.4%	0.4%	
Risk for ages <40	0	0	Assumed, based on Peto et al, 2000
Smokers accumulated excess death risk until age 95	37.2%	23.1%	Interpolated, based on Peto et al, 2000
Age-adjusted conditional death risk	see table 8		
Disease risk			
Smokers accumulated excess disease risk until age 95	42.0%	26.3%	After interpolation, based on Peto et al, 2000 and Holm et al, 1995
Effect of quitting			
Risk fraction for quitters, years since quitting:			Peto et al, 2000
<10	0.66	0.69	
10-19	0.42	0.21	
20-29	0.18	0.05	
30-35	0.08	0	
>36	0	0	

The lung cancer disease risk is estimated from reports on lung cancer deaths until age 75 for smokers (15-24 cigarettes/day) and non-smokers, see table 3. The annual excess death risk is estimated by a quadratic function of the accumulated risk until age 75 years. The lung cancer death risk is assumed 0 until the age of 40 years, and assumed constant between ages 75 and 95. The disease risk is obtained by adjusting the annual death risk by the annual crude survival rate of lung cancer in Sweden for a similar time period as the Peto data, from Holm et al (1995).

Table 4. Risks CHD and stroke.

	men & women	source
Disease risk	Framingham, see tables 5-7	
Effect of quitting		
Risk fraction for quitters, years since quitting:		Surgeon General, 1990
on CHD:		
1	0.5	
>15	0	
on stroke:		
>10	0	
Death risk		
AMI, 1st year	see table 9	
Stroke, 1st year	see table 10	
CHF	see table 11	
Risks as fraction of age- and gender-specific general death risk:		Statistics Sweden
AMI, 2nd and following years, age 15-93 years	3	Henriksson et al, 2014
AMI, 2nd and following years, age >93 years	2	Assumed
Stroke, 2nd and following years, age 15-93 years	3	Henriksson et al, 2014
Stroke, 2nd and following years, age >93 years	2	Assumed
IHD, 1st year	2.5	Granström et al, 2012
IHD, 2nd and following years	2.15	Granström et al, 2012

Table 5. The annual risks of CHD.

μ_{chd} =5.5305+28.4441*Sex-1.479*Ln(Age)-14.4588*Ln(Age)*Sex+1.8515*(Ln(Age))^2*Sex-0.9119*Ln(SBP)-0.2767*Smok-0.7181*Ln(Chol/HDL)-0.1759*Diabetes-0.1999*Diabetes*Sex

P_{chd} =1-Exp(-Exp((- μ_{chd})/ Exp(0.9145-0.2784* μ_{chd})))

Source: Caro et al, 2007; Anderson et al, 1991

Table 6. The annual risks of stroke.

μ_{str} =26.5116+0.2019*Sex-2.3741*Ln(Age)-2.4643*Ln(SBP)-0.3914*Smok-0.0229*Ln(Chol/HDL)-0.3087*Diabetes-0.2627*Diabetes*Sex

P_{str} = 1-Exp(-Exp((- μ_{str})/ Exp(-0.04312* μ_{str})))

Source: Caro et al, 2007; Anderson et al, 1991

The CHD and stroke disease risk estimates are based on the Framingham CVD risk function, see table 4 and tables 5-6. As the Framingham CHD risk function only calculates CHD events, the division of these events into the particular diseases are based on recent Swedish register data, see table 7. To avoid over-estimation of risks, the risk factors for CHD and stroke are evaluated at minimal-risk levels; 120 mmHg for systolic blood pressure (SBP), HDL-cholesterol (HDL) at 1.5 and cholesterol (Chol) at 4. Diabetes is set at 0, while the variable smoking (smok) is set at 1 for the smokers.

Table 7. Distribution of diseases within CHD.

	Age < 65 years		Age >65 years	
	men	women	men	women
AMI	0.42	0.40	0.31	0.31
IHD	0.40	0.39	0.21	0.29
CHF	0.16	0.19	0.46	0.38
Sudden death	0.02	0.02	0.02	0.02

Source: Swedish National Board of Health and Welfare, Statistics database, Diagnoses in inpatient care from the Hospital Discharge Register, year 2013.

Table 8. Death risk lung cancer.

Age group	Years since diagnosis				
	1	2	3	4	5
0-54	0.550	0.172	0.034	0.034	0.034
55-74	0.610	0.168	0.030	0.030	0.030
75-95	0.743	0.120	0.021	0.021	0.021

Source Based on Talbäck et al, 2004

Death risks

All death risks are age-and gender disease-specific conditional risks; in some cases estimated as fractions of the general population age- and gender-specific mortality risk, see tables 2 to 4, and in some cases based on Swedish register data, see tables 8 to 11.

The COPD death risk is estimated from the study Obstructive Lung Disease in Northern Sweden (OLIN), which reported the 20-year mortality in three age groups. Comparison with the general age-specific mortality risks revealed no excess risk of death among those younger than 58 years and older than 70 years, but a considerable increased risk among those aged 58-70 years at follow-up. The excess risk was estimated at on average around 5 times the age- and gender-specific general population death risk, see table 2.

The lung cancer death risk is based on survival data from the Swedish National Cancer Registry, see table 8. The death risks for year 3 and 4 after diagnosis are estimated by linear interpolation between years 2 to 5. Lung cancer survivors at 5 years are assumed recovered, and returned to the health state healthy.

The death risks from CHD and stroke are taken from Swedish registers, see tables 9 to 11, or published scientific reports, see table 5. The death risks for AMI, stroke and IHD are divided into risks the first year after the first event and the second and following years after first event.

Table 9. Death risk AMI, 1st year.

Age group	men	women
20-49	0.077	0.077
50-64	0.137	0.101
65-69	0.159	0.149
70-74	0.172	0.141
75-79	0.206	0.191
80-84	0.255	0.224
>84	0.327	0.331

Source: Swedish National Board of Health and Welfare, The Swedish AMI Statistics, year 2013

Table 10. Death risk stroke, 1st year.

Age group	men	women
20-49	0.031	0.038
50-54	0.059	0.051
55-59	0.044	0.064
60-64	0.046	0.061
65-69	0.062	0.066
70-74	0.077	0.085
75-79	0.097	0.109
80-84	0.148	0.157
>84	0.216	0.257

Source: Swedish National Board of Health and Welfare. The Swedish Stroke Statistics, year 2013

Table 11. Death risk CHF.

Age group	men	women
15-49	0	0
50-69	0.057	0.015
70-84	0.245	0.162
>84	0.340	0.281

Source: Swedish National Heart Failure Register, year 2012

The model also incorporates the possibility of dying in unrelated diseases. The death risk in the health state Healthy is the average 5-year age group- and gender-specific risk adjusted for all model disease deaths, the last column in table 12. In disease health states, the risk of dying in unrelated disease is the average 5-year age group- and gender-specific

Table 12. Death risks, unrelated.

Age Group	Not COPD		Not Lung cancer		Not AMI		Not CHF		Not IHD		Not Sudden death		Not Stroke		Not model disease	
	m	w	m	w	m	w	m	w	m	w	m	w	m	w	m	w
<39	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.000
40-44	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
45-49	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001
50-54	0.003	0.002	0.003	0.002	0.003	0.002	0.003	0.002	0.003	0.002	0.003	0.002	0.003	0.002	0.003	0.002
55-59	0.005	0.003	0.004	0.003	0.004	0.003	0.005	0.003	0.004	0.003	0.005	0.003	0.005	0.003	0.005	0.003
60-64	0.008	0.005	0.007	0.005	0.007	0.005	0.008	0.005	0.007	0.005	0.008	0.005	0.008	0.005	0.008	0.005
65-69	0.013	0.008	0.012	0.008	0.012	0.009	0.013	0.009	0.012	0.009	0.013	0.009	0.013	0.009	0.013	0.008
70-74	0.021	0.013	0.020	0.013	0.019	0.014	0.021	0.014	0.020	0.013	0.021	0.014	0.020	0.014	0.021	0.013
75-79	0.037	0.023	0.036	0.023	0.035	0.024	0.037	0.024	0.035	0.023	0.038	0.024	0.036	0.023	0.037	0.023
>79	0.068	0.047	0.068	0.047	0.065	0.047	0.068	0.047	0.065	0.046	0.071	0.048	0.068	0.046	0.068	0.047

m=men, w=women

Source: Swedish National Board of Health and Welfare. The Swedish National Causes of Death Register, year 2014

risk adjusted for the deaths in each respective disease. For ages below 39 years the risk in the age group 35-39 years is used, and for ages 80-84 years the risk >79 years. For ages above 84 years, the general population age-and gender specific death risk is used for the unrelated death risk. As the lung cancer death risks are so high, the unrelated death risks for lung cancer among individuals aged above 84 years had to be adjusted, by deducting 0.05. For those aged below 85 years, the age- and gender-specific general population risk of death is only used for calculating some disease-specific death risks, see tables 2 and 4. The risk is taken from the Swedish national mortality statistics for the year 2014 (Statistics Sweden, 2015).

Changes in risk after quitting smoking

The excess disease risks for smokers are not eliminated immediately after quitting smoking. This "lead time" is 36 years for lung cancer, 16 years for CHD, and 11 years for stroke, while for COPD some excess risk remain life-long, see heading effect of quitting in tables 2 to 4. The disease risks after quitting are constructed by adjusting the smokers' risks by the remaining risk. The remaining risk is modelled as fractions of risk, given the number of years since quitting. The annual remaining risks are estimated by linear interpolation. The effects on the risk for CHD and stroke are modelled on the dummy variable smoking, adjusting the value of 1 by the remaining risk fraction.

The societal costs

The model is reflecting the societal perspective, including disease-related costs for all sectors of the Swedish society. The costs included are medical treatment costs, costs for institutional care and technical aids, pharmaceutical costs, informal care and other patient and relatives' costs, and morbidity productivity costs.

Most of the data on societal costs are taken from Swedish studies published during the 2010s. Data reported as distributions, i.e. with the Gamma parameters for costs, or bootstrapped 95 percent confidence interval were preferred and used in the model to

Table 13. Medical treatment costs. SEK 2014.

	mean	95% confidence interval	distribution	source	comment
Lung cancer	76 096	-	-	KPP register, SALAR 2015	Only inpatient care
COPD	10 120	6 120 - 14 920	-	Jansson et al, 2013	Moderate COPD
AMI year 1	171 660	-	Gamma 106;1622	Henriksson et al, 2014	
AMI year 2+	45 740	-	Gamma 17;2698	Henriksson et al, 2014	
CHF	33 850	-	-	Agvall et al, 2005	
IHD	51 610	-	-	Mourad et al, 2013	Angina pectoris
Stroke year 1	142 280	-	Gamma 114;1244	Henriksson et al, 2014	
Stroke year 2+	38 450	-	Gamma 48;800	Henriksson et al, 2014	

enable stochastic estimation. If data was reported as mean and standard deviation, the Gamma distribution was simulated employing the Treeage function. In one case, data was reported as fraction of patients consuming a specific resource, which was used for sampling within the model. Otherwise the reported point estimate, usually the average cost across the patient group, was used. If no Swedish data on a cost item was found, the cost was taken from studies reporting data from settings assumed similar to the Swedish.

All costs are reported in SEK year 2014 (USD 1=SEK 6.86; Euro 1=SEK 9.10), adjusted when necessary with the Swedish CPI. To adjust reported Gamma distributed parameters to the price level, only the second parameter, i.e. the scale parameter, was adjusted.

Medical treatment costs

Recent Swedish estimates on medical treatment costs were possible to obtain for all model diseases, see table 13. The costs are paid by the regional healthcare authorities.

Institutional care and technical aids costs

These costs include rehabilitation, terminal care, old age homes, support for individuals living at home, transportation and technical aids. In Sweden, institutional care and technical aids used by patients in their homes are the responsibility of the local authorities (municipalites, in Swedish: kommuner). The costs are not fully represented for any disease, see table 14. Estimates are not available for lung cancer and the only available costs for IHD are outdated, so the institutional care costs are probably underestimated.

Table 14. Costs for institutional care and technical aids. SEK 2014.

	mean	95% confidence interval	distribution	source	comment
Lung cancer	0	-	-		
COPD	0	-	-		Oxygen theraphy included in medical treatment costs
AMI year 1	16 680	-	Gamma 11;1502	Henriksson et al, 2014	Home care and nursing home
AMI year 2+	8 340	-	Gamma 11;751	Henriksson et al, 2014	Home care and nursing home
CHF	2 200	-	-	Agvall et al, 2005	Nursing home
IHD, age <65	3 140	-	-	Andersson & Kartman, 1995	Social services and aids, angina pectoris
IHD, age >64	8 260	-	-	Andersson & Kartman, 1995	Social services and aids, angina pectoris
Stroke year 1	82 130	-	Gamma 11;7184	Henriksson et al, 2014	Home care and nursing home
Stroke year 2+	41 070	-	Gamma 11;3593	Henriksson et al, 2014	Home care and nursing home

Table 15. Pharmaceutical costs. SEK 2014.

	mean	95% confidence interval	distribution	source	comment
Lung cancer	0	-	-		
COPD	0	-	-		included in medical treatment costs
AMI year 1	11 960	-	-	Mourad et al, 2013	
AMI year 2+	9 250	-	-	Mourad et al, 2013	
CHF	8 420	-	-	Agvall et al, 2005	
IHD	12 690	-	-	Mourad et al, 2013	Angina pectoris
Stroke year 1	2 120	-	-	Ghatnekar et al, 2013	
Stroke year 2+	2 820	-	-	Ghatnekar et al, 2013	

Pharmaceutical costs

Costs for pharmaceuticals in Sweden ought to be divided between the county councils and the patients, as patients pay a considerable share in co-payment. This is however not possible, given the data available. Table 15 therefore presents the drug costs to the regional healthcare authorities. The costs of pharmaceuticals dispensed during hospital stays are included in the medical treatment costs.

Informal care and other patient and relatives' costs

These costs include the value of care given to patients by relatives and other costs for patients or relatives, such as time, co-payments paid for health care and drugs as well as costs for transportation, modifications at home etc. Complete estimates could not be obtained for any disease, see table 16, except IHD which however might be outdated. Informal care in present-day Sweden probably constitute a sizeable part of total societal costs.

Table 16. Informal care and other patient and relatives' costs. SEK 2014.

	Mean	95% confidence interval	distribution	source	comment
Lung cancer	140 810	-	-	Gridelli et al, 2007	Informal care, estimated from 3 months home care
COPD	0	-	-		
AMI year 1	2 090	-	Gamma 44;48	Henriksson et al, 2014	Informal care
AMI year 2+	1 050	-	Gamma 44;24	Henriksson et al, 2014	Informal care
CHF	0	-	-		
IHD, age <65	5 180	-	-	Andersson & Kartman, 1995	Travel and time costs for healthcare contacts, angina pectoris
IHD, age 65+	2 500	-	-	Andersson & Kartman, 1995	Travel and time costs for healthcare contacts, angina pectoris
IHD	680	-	-	Andersson & Kartman, 1995	Informal care, angina pectoris
Stroke year 1	28 260	-	Gamma 44;636	Henriksson et al, 2014	Informal care
Stroke year 2+	14 130	-	Gamma 44;308	Henriksson et al, 2014	Informal care

Table 17. Productivity costs, morbidity. SEK 2014.

	mean	95% confidence interval	sd	distribution	source	comment
Lung cancer	0	-	-	-	Ford et al, 1999	Simulated in model: 9% of pat. 100% disability 20% of pat. 80% disability 40% of pat. 50% disability 31% of pat. 20% disability
					Statistics Sweden	Age- and gender-specific mean wages year 2014
COPD	21 800	6 011 - 42 583	-	-	Jansson et al, 2013	Moderate COPD
AMI year 1	38 180	-	-	Gamma 9;4242	Henriksson et al, 2014	
AMI year 2+	19 090	-	-	Gamma 9;2121	Henriksson et al, 2014	
CHF	29 880	-	49 210	-	Zethraeus et al, 1999	Difference year before and after disease onset
IHD	121 020	-	99 880	-	Mourad et al, 2013	Angina pectoris
Stroke year 1	194 100	-	-	Gamma 9;21567	Henriksson et al, 2014	
Stroke year 2+	97 050	-	-	Gamma 9;10783	Henriksson et al, 2014	

Productivity costs

The productivity costs only value the lost production because of morbidity before the age of 66 years, not mortality. The productivity costs for lung cancer is simulated within the model, via sampling from the fraction of patients on sick leave and combined with age- and gender-specific average monthly wages, including 40% employer taxes. Remaining data is taken from the literature, see table 17, and most estimates are recent. The costs are valued by the human capital method, and thus only include losses in salaried work before the official age of retirement.

The health effects

Life years lost

The number of life years lost (YLS) are calculated until the age of 95 years, and only for individuals dead in the modelled diseases. Life years lost are presented both discounted 3% and undiscounted.

QALYs

The number of quality-adjusted life years (QALYs) are calculated during healthy years and years spent diseased, until death or the age of 95 years.

The QoL weights used during healthy years are mean age group- and gender-specific population weights, see table 18. The data is somewhat dated, but it is the only general population QoL weights available in Sweden. The QoL of the age group 20-29 years is used

Table 18. Average Swedish population QoL weights.

Age group	men	women
20-29	0.91	0.88
30-39	0.90	0.86
40-49	0.86	0.85
50-59	0.84	0.82
60-69	0.83	0.78
70-79	0.81	0.78
80-88	0.74	0.74

Source: Burström et al, 2001

also for younger ages, and the QoL of the age group 80-88 years is used for those aged 89-95 years. This last assumption is probably an overestimate.

The disease-specific QoL used in the health states are all, except one, modelled as decrements from the average population age-group and gender-specific QoL, see table 19. For lung cancer no data was available on the marginal effect of the disease on the population average QoL, so a fixed value over the ages and genders had to be used.

Sensitivity analyses

Several univariate and multivariate sensitivity analyses have been performed. Analyses on some methodological issues, as well as a probabilistic sensitivity analysis, have also been performed. The analyses are reported for men and women aged 50 years.

To give another measure of the uncertainty surrounding the cost-effectiveness ratio, the 95% confidence interval for the difference between smokers and quitters is reported, calculated from the standard deviation of outcomes.

Table 19. QoL weights and QoL decrements due to disease.

	QoL	source
Health state weight		
Lung cancer	0.653	Nafees et al, 2008
Decrement from average QoL		
COPD	0.0142	Sullivan et al, 2005
AMI	0.0627	Henriksson et al, 2014
CHF	0.0700	Granström et al, 2012
IHD	0.0900	Granström et al, 2012
Stroke	0.1384	Henriksson et al, 2014

Univariate analyses

Univariate analyses have been performed on all model parameters:

A. disease risks: +100%, -50%

B. death risks: +-10%. (As the unrelated death risks for those aged over 84 years are so high they had to be adjusted by deducting 0.05 for the diseases stroke, IHD and AMI, and omitted for lung cancer, to enable the simulation.)

C. risk fractions of disease after quitting: +-0.1

D. all disease costs: +-25%

E. QoL weights: QoL weight 1 during healthy years

Multivariate analyses

Two sets of multivariate analyses have been performed:

F. high risk – low risk: death risks +100%, disease risks +10% and risk fractions +0.1 *vs* death risks -50%, disease risks –10% and risk fraction –0.1

G. high risk, high costs – low risk, low costs: death risks +100%, disease risks +10%, risk fraction +0.1 and all costs +25% *vs* death risks -50%, disease risks –10%, risk fractions –0.1 and all costs –25%

Analyses on methodological issues

Three analyses have been performed on methodological issues:

H. discount rate: 5%, 0%

I. perspective: healthcare and personal social services perspective (UK NICE perspective); excludes informal care and other patient and relatives' costs and productivity costs

J. recent Swedish data: only includes data from a Swedish context from year 2005 onwards. Excludes the data from Andersson & Kartman (1995) on institutional care and patient and relatives' costs for IHD, from Gridelli et al (2007) on lung cancer patient and relatives' care, from Ford et al (1999) for lung cancer productivity costs and from Zethraeus et al (1999) on CHF productivity costs

Probabilistic analysis

A bootstrap sampling was performed using the smoker and quitter Monte Carlo simulations of 10 000 runs. A sample of 1 000 from each simulation was drawn, with replacement, performed in Microsoft Excel. The mean of the difference in costs and QALYs between smokers and quitters was then calculated. This was replicated 1 000 times. The bootstrap is represented as a scatterplot in the cost-effectiveness plane.

Results

In this chapter, the model estimates of QALYs, YLS and societal costs are presented for men and women in some selected ages, mainly for validation purposes. More detailed simulation outcomes as well as the results of the sensitivity analyses are presented for men and women at age 50 years. Model estimates can be obtained for men and women for all ages between 15 and 95 years.

The model estimates

In table 20 the simulation results for QALYs (quality-adjusted life-years) experienced until the age of 95 years are presented, for the selected ages 15, 30, 50 and 70 years at the start of the simulations. As can be expected, the number of QALYs are highest in the younger age groups, and somewhat higher for women in most age groups. In the selected age groups, the differences between smokers and quitters are at a maximum at age 30; 0.68 for females and 0.81 for males. The confidence intervals, calculated via the mean and standard deviation (sd) from the 10 000 model runs, indicate that there are differences in QALYs between smokers and quitters.

The YLS (life-years saved) lost before the age of 95 years are presented in tables 21 and 22, discounted 3% and undiscounted. The differences in discounted YLS between smokers and quitters are somewhat higher than the differences in QALYs. The undiscounted YLS in table 22 show the number of years that smokers and quitters are expected to lose before the age of 95 years. For the ages 15, 30, and 50 the number of lost life-years is estimated at around 6 years for women smokers and 9 years for men, implying that the female smokers are estimated to live until age 89 and the male until age 86. In the oldest age group presented here, age 70, the number of lost life-years are only 1-2 years. The quitters are estimated to lose considerably fewer life-years; 1-4 years for the women and 3-5 years for

Table 20. QALYs, until age 95 years, discounted 3%.

age	smoker		quitter		difference			
	mean	sd	mean	sd	mean	95% CI		
women								
15	23.20	2.26	23.70	2.28	0.50	0.44	-	0.57
30	20.02	2.85	20.71	2.82	0.68	0.60	-	0.76
50	14.15	4.19	14.76	4.15	0.61	0.49	-	0.73
70	8.24	3.75	8.50	3.82	0.26	0.16	-	0.37
men								
15	23.21	2.84	23.83	2.70	0.63	0.55	-	0.70
30	19.65	3.20	20.46	3.19	0.81	0.72	-	0.90
50	13.18	4.34	13.95	4.47	0.77	0.65	-	0.89
70	6.78	3.61	7.15	3.76	0.37	0.27	-	0.48

Feldman I, *et al. BMJ Open* 2019; 9:e030934. doi: 10.1136/bmjopen-2019-030934

Table 21. Life years lost (YLS), before age 95 years. Discounted 3%.

age	smoker		quitter		difference			
	mean	sd	mean	sd	mean	95% CI		
women								
15	0.97	1.90	0.23	0.87	0.74	0.70	-	0.78
30	1.55	3.02	0.51	1.83	1.04	0.97	-	1.11
50	2.35	4.82	1.49	4.09	0.86	0.74	-	0.99
70	1.22	3.31	0.92	2.98	0.30	0.22	-	0.39
men								
15	1.42	2.25	0.43	1.21	0.99	0.94	-	1.04
30	2.18	3.44	0.79	2.15	1.40	1.32	-	1.48
50	3.51	5.57	2.09	4.69	1.41	1.27	-	1.56
70	2.22	4.30	1.68	3.94	0.53	0.42	-	0.65

the men. As expected, the difference between smokers and quitters diminish with age, with a maximum at around 5 years for the females and around 6 years for the males at age 15.

The societal costs estimated for the smokers and quitters for the selected age groups are presented in table 23. The highest costs are found for age 50; 200 000 SEK and 250 000 SEK for the smokers and 130 000 and 170 000 for the quitters, in both cases higher among the men. The highest difference between smokers and quitters is however found at age 30, with a difference of 100 000 among the females and 120 000 among the males. The difference among the eldest, at age 70, is around 20 000 SEK. These cost differences reflect the amount that tobacco cessation interventions could spend on achieving one quitter and still be cost-saving.

Table 22. Life years lost (YLS), before age 95 years. Undiscounted.

age	smoker		quitter		difference			
	mean	sd	mean	sd	mean	95% CI		
women								
15	6.46	11.80	1.68	5.86	4.78	4.52	-	5.04
30	6.58	11.93	2.22	7.25	4.37	4.09	-	4.64
50	5.67	10.94	3.55	9.19	2.12	1.84	-	2.40
70	1.97	5.18	1.47	4.64	0.50	0.37	-	0.64
men							-	
15	9.25	13.51	3.05	7.89	6.20	5.89	-	6.50
30	9.21	13.39	3.51	8.68	5.70	5.39	-	6.02
50	8.42	12.57	5.01	10.53	3.40	3.08	-	3.73
70	3.56	6.70	2.68	6.11	0.87	0.70	-	1.05

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Table 23. Societal costs. In SEK 2014 and discounted 3%.

age	smoker		quitter		difference		
	mean	sd	mean	sd	mean	95% CI	
women							
15	113 097	278 446	40 761	207 879	72 337	65 526	- 79 147
30	170 047	386 905	71 569	293 477	98 478	88 960	- 107 996
50	201 760	415 452	133 902	366 313	67 858	57 002	- 78 714
70	85 818	189 827	63 824	171 358	21 994	16 981	- 27 006
men							
15	145 233	320 143	54 148	227 222	91 085	83 390	- 98 779
30	216 626	453 147	92 782	349 085	123 844	112 632	- 135 055
50	254 279	484 787	168 598	434 603	85 681	72 920	- 98 442
70	101 358	188 991	80 927	184 794	20 431	15 250	- 25 611

Selected model outcomes

The underlying estimated disease outcome is presented in figures 2 and 3, for the age 50 years. For both women and men, there is a marked decrease for quitters in the number of diseased and dead in the model diseases, which is somewhat offset by an increase in the number of deaths in unrelated diseases. The number of diseased and deaths are higher for

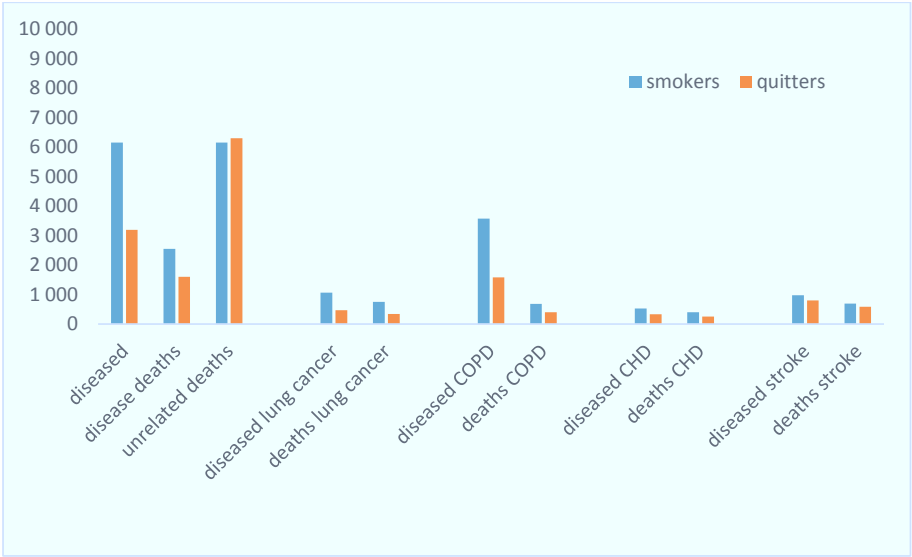

Figure 2. The disease outcome, number of diseased and dead per 10 000 for smokers and quitters, women aged 50 years.

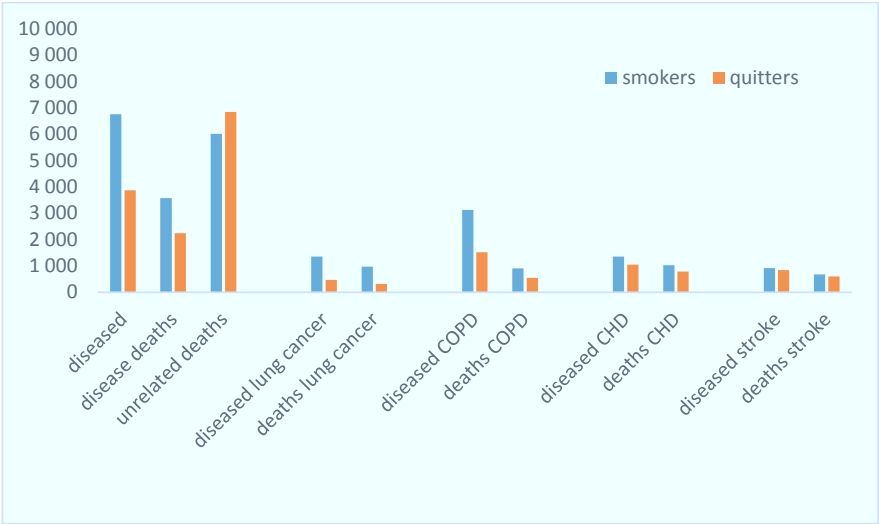

Figure 3. The disease outcome, number of diseased and dead per 10 000 for smokers and quitters, men aged 50 years.

men, mainly originating from CHD. The model disease with the highest smoking-related incidence is COPD, for both genders. The increase in unrelated deaths for the quitters is an example of competing risks, which decreases the difference in life-years and QALYs between smokers and quitters.

Table 24 and 25 shows the full model simulation results of the societal cost savings because of tobacco quitting at age 50 years. For women, the highest estimated savings are found in lung cancer, COPD and stroke at around 15-20 000 SEK per quitter. For men the cost savings because of lung cancer are considerable higher, at around 35 000, due to the higher incidence among the men. The cost item with the largest cost savings are medical treatment costs for both genders, at around 30 000 SEK. Most of the difference in savings between men and women originate from the productivity costs, possibly reflecting disease onset at younger ages among men. Note that a cost saving of zero means that no cost is being modelled, as cost data was lacking.

Table 24. Societal cost savings, in SEK 2014. Women aged 50 years.

	Lung cancer	COPD	AMI	CHF	IHD	Stroke	Sum
Medical treatment	5 171	13 573	2 337	439	3 410	5 500	30 430
Institutional care and technical aids	0	0	365	29	408	4 880	5 681
Pharmaceuticals	0	0	361	109	838	306	1 615
Informal care and other patient and relatives' costs	9 569	0	44	12	282	1 673	11 580
Productivity costs	3 971	6 456	192	243	3 228	4 462	18 552
Sum	18 711	20 029	3 300	832	8 166	16 821	67 858

Table 25. Societal cost savings, in SEK 2014. Men aged 50 years.

	Lung cancer	COPD	AMI	CHF	IHD	Stroke	Sum
Medical treatment	8 477	11 478	3 203	596	4 738	3 907	32 399
Institutional care and technical aids	0	0	456	39	596	3 379	4 470
Pharmaceuticals	0	0	473	148	1 165	214	2 000
Informal care and other patient and relatives' costs	15 685	0	59	16	377	1 164	17 301
Productivity costs	13 002	8 357	319	400	3 785	3 649	29 511
Sum	37 164	19 835	4 510	1 199	10 661	12 312	85 681

Sensitivity analyses

The results of the sensitivity analyses are presented on women and men at starting age 50 years. Figure 4 shows the results for women and figure 5 for men.

All analyses show a similar pattern between men and women, and also similar ranges. The univariate sensitivity analyses on the model parameters, analyses A to E, result in small changes in costs and QALYs. Also the multivariate analyses F and G, which are constructed as scenarios that allow the risk parameters to vary consistently upwards or downwards, and along with the costs in analysis G, show moderate changes from the base case estimates. The methodological choices have a more pronounced effect, as the largest difference in QALYs is achieved by varying the discount rate (analysis H) between 0 and 5%, which also affects the costs substantially. The two analyses that reflect the choices of which costs to include in the estimates, analysis I that reflects the UK NICE health care and social services perspective and analysis J that only include Swedish data published since the year 2005, both decrease the cost differences between smokers and quitters.

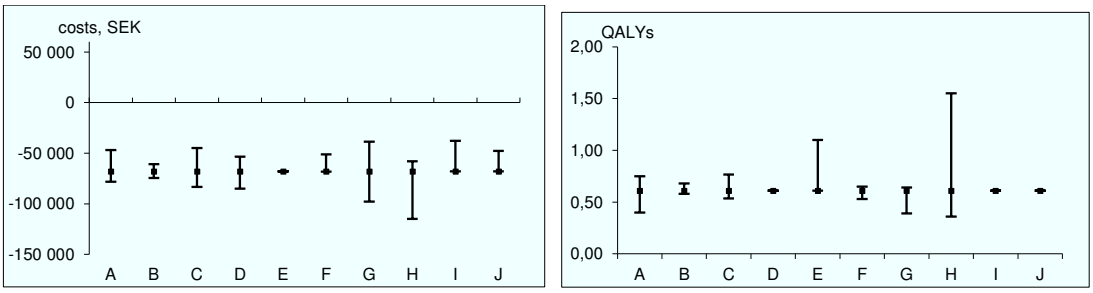

Figure 4. Sensitivity analyses on societal cost and QALY differences between smokers and quitters, women aged 50 years.

Notes: **A**. disease risks. **B**. death risks. **C**. risk fractions of disease after quitting. **D.** all costs. **E**. QoL weights. **F**. high risk – low risk. **G**. high risk, high costs – low risk, low costs. **H**. discount rate. **I**. perspective. **J.** recent Swedish data.

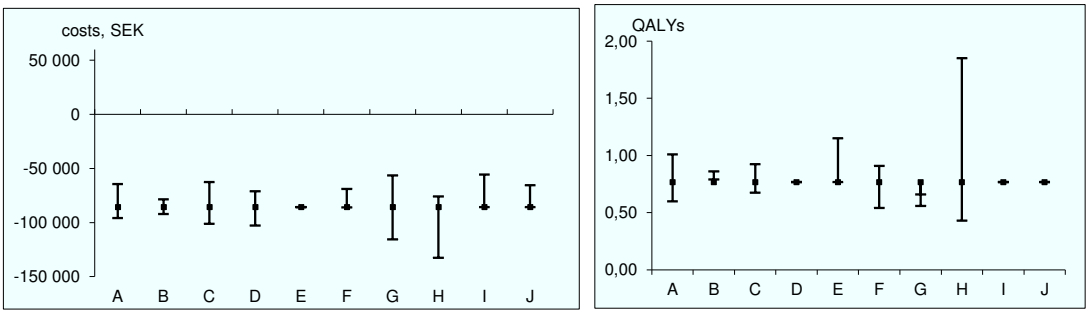

Figure 5. Sensitivity analyses on societal cost and QALY differences between smokers and quitters, men aged 50 years.

Notes: **A**. disease risks. **B**. death risks. **C**. risk fractions of disease after quitting. **D.** all costs. **E**. QoL weights. **F**. high risk – low risk. **G**. high risk, high costs – low risk, low costs. **H**. discount rate. **I**. perspective. **J.** recent Swedish data.

The scatter plot of the bootstrap analysis based on the microsimulation results for women and men aged 50 are shown in figures 6 and 7. The uncertainty is higher for the men, as the plots are more scattered. All plots are however situated in the cost decrease and QALY increase quadrant, with costs below -20 000 SEK and QALYs over 0.2.

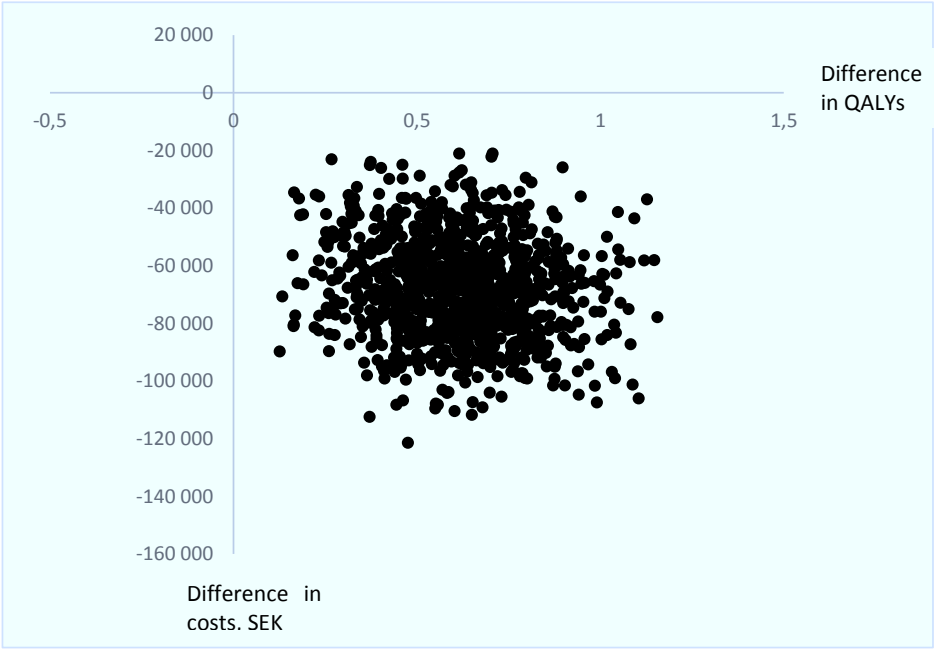

Figure 6. The cost-effectiveness plane with resultat från bootstrap, women aged 50 years.

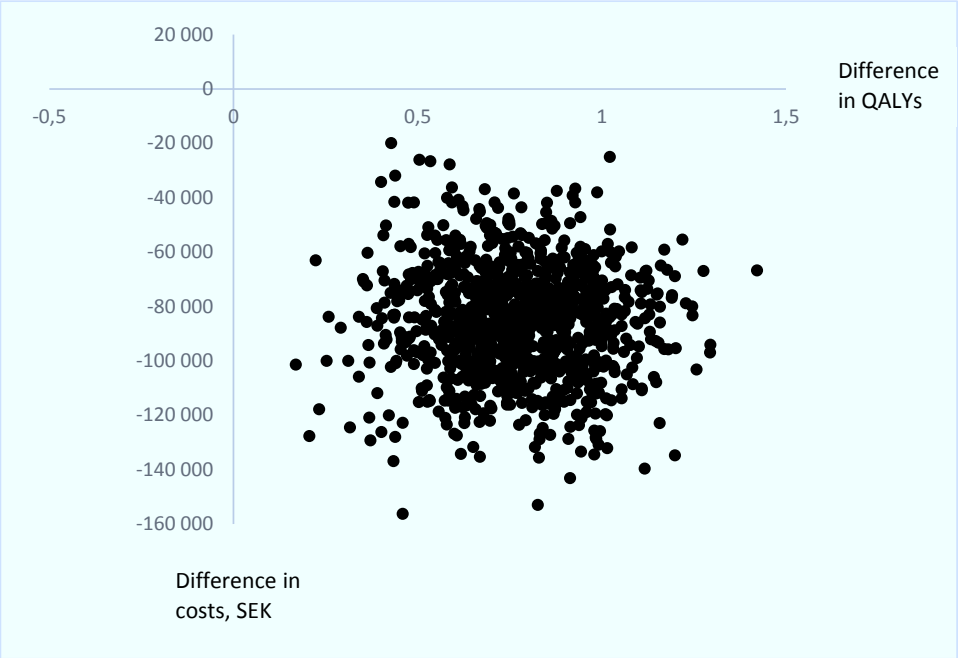

Figure 7. The cost-effectiveness plane with resultat from bootstrap, men aged 50 years.

Discussion: Model validity

The discussion of the model validity is structured around four aspects as proposed by McCabe & Dixon (2000): the structure of the model, the inputs to the model, the results of the model and the value of the model to the decision-maker.

The structure of the model

The structure of the model is a Markov model constructed for microsimulations, on the three most smoking-related disease groups; lung cancer, COPD, and CVD including stroke and CHD. The present updated version of the model includes one less CHD disease compared to the first version of the model, as unrecognized acute myocardial infarction now is included in the IHD disease, mainly because the disease definition is rarely used nowadays. Choosing only three disease groups is a clear simplification as smoking is known to cause hundreds of different diseases. The effects from smoking, and thus quitting, are furthermore confined to the individuals themselves; no side-effects on other individuals such as environmental tobacco smoke or smoking uptake are included. These two features leads to an underestimate of the true effects of tobacco quitting.

The same disease-specific approach has been taken by most other tobacco cessation models (Bolin, 2012), even though some of them include more diseases, such as asthma. Another approach would be to use the overall differences in mortality between current, former, and never-smokers taken from large US studies, as some early tobacco cessation models did (Secker-Walker et al, 1997; Tengs et al, 2001). In order not to overestimate the effects of quitting tobacco, we chose to model the smoking-related risk for certain diseases instead, as it is improbable that all differences in mortality and morbidity between smokers and former smokers are due to the smoking habit (Doll et al, 1994).

The model aims to reflect disease onset related to smoking tobacco. As disease in all the three disease groups included in model may be caused by other factors than smoking only the excess risks for smokers are modelled. For the diseases lung cancer and COPD this implies that the risk for smokers found in epidemiological studies is adjusted by the risk found for non-smokers. For the disease group CHD and stroke, where a large fraction of disease onset is caused by other factors than smoking, this adjustment for smokers´ excess risk was performed by setting the other risk factors in the risk function at minimal risk levels. This is an underestimate, as the risk factor levels among smokers can be expected to be at least as elevated as among the general population. The underestimate is aggravated by the fact that the functional form of the risk function results in a multiplier effect of the risk factors.

The present version of the model includes seven health states: lung cancer, COPD, stroke, and CHD divided into four diseases. This is a clear simplification, as the costs and QoL can be expected to vary considerable between patients with different severity levels within the diseases. This is particularly true for COPD which is a chronic progressive disease, i.e. the

diseased get more severely ill over time. However, a model with 7 health states with accompanying disease-specific death risks, costs and QoL weights is fairly complex as well as data-demanding. For the purposes of this study´s model, the division of diseases into severity levels was not deemed necessary.

An obvious problem with the model, inherent in all Markov models, are the mutually exclusive health states; any individual can only contract one disease, and once diseased the individual never recovers (apart from the very rare 5 year survivors in lung cancer). This feature implies both an overestimate and an underestimate of the true effects. The underestimate stems from the fact that co-morbidity is very common, especially among the individuals with the chronic diseases COPD, CHD, and stroke. The overestimate of costs and effects arise as individuals stay in the health states until death. If the costs and outcomes associated with the health states are taken from severely ill individuals, then these become grossly overestimated. This overestimate is partly offset by the use of separate costs for the first and subsequent years, for all societal costs due to AMI and stroke. In order not to overestimate the numbers of years spent in disease states, the possibility of dying in unrelated diseases is present in all health states. This feature is also included in the CHD Policy Model (Weinstein et al, 1987).

Most tobacco cessation models are built for cohort estimation (Bolin, 2012), but this model is constructed for individual-level estimation using the microsimulation methodology. As the data available admitted a microsimulation structure, e.g. the risk functions, the methodology was chosen as the advantages to model and to obtain a richer data set with results that reflect the heterogeneity of outcomes between individuals was deemed to offset the disadvantages of calculation burden. The use of the software Treeage also facilitates the use of microsimulation. Age- and gender-specific estimates can thus be obtained from the model, between ages 15 and 95 years.

The model stages are one-year long, which seems accurate given the risk estimates and the long time horizon of the model. The reason for the model maximum age of 95 years is the lack of risk estimates for older ages. Some extrapolations of risk estimates to the age of 95 years indeed resulted problematic, as some disease-specific death risks expressed as multipliers of the average age-specific death risk resulted in risks above 1. Further extrapolations beyond the age of 95 years were deemed unnecessary, as most of the relevant differences between smokers and quitters would have arisen by that age.

The inputs of the model

The second aspect of model validity is the inputs of the model. The model contains a large number of data taken from different sources. This is of course a threat to the internal validity of the model, shared with most models. However, the data have been chosen to reflect current Swedish circumstances. The current updated version of the model has exchanged almost all cost data, if more recent estimates were available, and all death risks to recent Swedish register data. As the number of studies on any particular data items are few, no meta-analysis or any other synthesis of data was carried out.

The disease risks are of course are pivotal for the result. The lung cancer disease risks are probably the best that can be obtained, from a large epidemiological study (Peto et al, 2000). The risk equation used for CHD and stroke is taken from the Framingham studies, and even though there are more recent risk scores developed from the study (D'Agostini et al, 2008), the Anderson et al (1991) risk functions are still frequently employed. The disease COPD has been the subject of a large long term epidemiological study in Sweden, The Obstructive Lung Disease in Northern Sweden (OLIN) (Lundbäck et al, 1991), which is thus the most relevant data source for the model.

In the model, there is an increased risk for a smoking-related disease remaining for some years after the tobacco cessation, in accordance with epidemiological evidence (Surgeon General, 1990; Omenn et al, 1990). The feature is also considered a marker of high quality tobacco cessation models (Bolin et al, 2012).

The majority of the cost data are taken from Swedish studies published during the 2010s. To take fully advantage of the microsimulation structure and to obtain stochastic estimates, the preferred data sources were the ones reported as distributions, i.e. as Gamma parameters or bootstrapped 95 percent confidence intervals. If no Swedish data was found, an international estimate was instead used in order to seek to represent the full societal costs. However, apart from certain cost items and for some of the diseases, the lack of data results in considerable underestimates of the true societal costs. This is particularly true in the cases of the costs for care, both institutional and informal. The institutional care could amount to considerable costs, exemplified by the costs for stroke and AMI patients, see table 14. In particular for lung cancer the lack of data results in considerable underestimates of the true disease-related costs. This is why the possible overestimate of the informal care for the disease, obtained from an Italian study, probably does not bias the overall result. To investigate the issue, one sensitivity analysis only included recent Swedish data. The analysis lead to decreases in cost savings for quitters aged 50 years of around 30%.

The QoL estimates are constructed as disease-specific decrements from the average age- and gender-specific QoL, except for lung cancer for which no QoL decrement could be found (De Geer et al, 2013). The average population age- and gender-specific QoL weights, which are certainly not 1, are also used during healthy years for the base case estimates. This means that the model assumes that an individual that avoids the smoking-related diseases is not having perfect health, but the health of an average Swede at the same age, as recommended (Gold et al, 1996).

The stated purpose of the model is to reflect the societal perspective, which for Sweden includes the morbidity productivity costs, but not the productivity costs resulting from mortality. All the model data on productivity costs value them according to the human capital approach for individuals under the age of 65, the customary Swedish age of retirement.

A full societal perspective might also include other aspects, considering that this is a model on individuals that are participating in an intervention that aims to change their lifestyle. The previous version of the tobacco cessation model, version 1 (Johansson, 2004), reported

sensitivity analyses that modelled some effects on the tobacco quitters, by including savings from cigarette purchases and a decreased QoL because of withdrawal effects during the first year. When that analysis was applied to an intervention, a decreased QoL during the first year was also deducted for the smokers that failed to quit, as the failure to achieve a personal goal might to lead to a decrease in QoL.

The results of the model

The third aspect of model validity is the results of the model, e.g. a comparison with reality or with other study results. A direct comparison with reality is not possible, since the model covers the ages 15-95 years, with a follow-up time of 80 years for the youngest age group.

The model estimates that around 60% of the women and 70% of the men aged 50 at the start of the simulations will contract one of the modelled diseases, and that around 50% of those will die in the diseases before the age of 95 years. The disease risks for the quitters at age 50 are not eliminated; 30-40% of them will still contract the smoking-related diseases because of remaining disease risks after quitting. As expected, the unrelated deaths increase among the quitters, in sum leading to an increase in YLS (undiscounted) of 2-3 years for those quitting at age 50, compared with continuing smokers. The increases in QALYs (discounted 3%) are smaller because of less-than-perfect health among those aged 50 years and above; 0.61 for women and 0.77 for men. The disease outcomes are fairly similar to the estimates from the previous versions of the model, but because of decreased death risks, the outcomes in terms of YLS and QALYs are considerably higher. The 2004 version of the model estimated an increased YLS of 0.93 and of 1.66 for women and men aged 50-54 years, and QALY gains of 0.36 and 0.71, respectively. The differences are due to the longer time perspective of the present version, 95 years versus 85 years, and the somewhat decreased case-fatality risk (i.e. the mortality risk among those with disease) because of improvements in medical technologies during the past decade.

Apart from increases in health, the societal cost savings because of quitting smoking are considerable. For men, the cost savings amount to around 100 000 SEK for quitters aged between 15 and 50 years, and around 70-90 000 SEK for women. Even in the age group 70 years there are estimated cost savings of around 20 000 SEK per individual quitter. This implies that substantial funds could be invested in smoking cessation interventions, and the interventions would still be cost-effective, or even cost-saving. The cost savings in the present model are considerably higher than those of the previous model, in part due to changes in price year.

Comparisons of model estimates with other models' are difficult to perform, as the time horizon, costs included, jurisdiction, and the diseases included differ. Among the recently reported model estimates (Bolin, 2012), there are two Australian models. The model developed within ACE (Bertram et al, 2007) report estimates of life-years saved that are considerable higher than the present model's; 5.7 years for men and 6.6 years for women in age group 50-54 years. That model time horizon is however 100 year, but it is unlikely

that the feature fully explains the difference between the model estimates. The estimates of average health care cost saved per quitter (inferred from table 3) however seems to be very similar to the present model's; around 33 000 SEK. The other Australian model, the Quit Benefits Model (Hurley & Mathews, 2007), reports considerably lower estimates of both life-years and health care costs saved, e.g. 0.1 – 0.2 YLS and QALYs saved for men and women quitters. The lower estimates, in comparison with both the present model and the ACE model, are probably partly explained by the time horizon of only ten years.

There have been two, to my knowledge, reports of tobacco cessation model estimates for Sweden, one using the Benesco model (Bolin et al, 2007) and one using an extended version of the HECOS model (Bolin et al, 2006). Comparison with those model estimates are unfortunately not possible, due to lack of reporting detail. However, estimates from the previous version of this model were fairly consistent with the HECOS model estimates (Orme et al, 2001) for Sweden, available at the time (Johansson, 2004).

The value of the model to the decision-maker

The fourth aspect of validity is the value of the model to the decision-maker. There are several models on tobacco cessation that conforms to international recommendations on how to perform cost-effectiveness analyses (Bolin, 2012). This model however reflect Swedish circumstances, with Swedish cost and QoL data, why the model might be useful for Swedish decision-makers.

We hope that the model will be used to perform economic evaluations of a range of tobacco cessation interventions. For tobacco prevention interventions, i.e. prevention of initiation of smoking, another model version, version 2, has been constructed and is available for analyses. The use of these models will in time enable incremental and marginal calculations of the cost-effectiveness of different tobacco interventions and their components and suitable target groups. The basis for decisions on which tobacco cessation and prevention interventions to implement will then be more comprehensive.

Another frequent use of models is to forecast future events. This model is not suitable for estimating what the costs of smoking will be in the future. The reason is that the model does not incorporate any adjustments of possible future developments. The risk of smoking is based on studies with follow-up periods of sometimes 30 years, which means that the risks are reflecting the smoking behaviour among smokers 30 years ago. The changes in cigarette content and in the frequency of smoking might lead to changes in disease risk in the future. Also the costs for the smoking-related diseases might change in the future, because of changes in health care technology. Another example would be the value of the morbidity productivity costs, as well as informal care, as wages and productivity often are expected to increase in the future.

Nevertheless, the model actually forecasts what the costs for smokers and quitters will be in 80 years' time, for the youngest age group. That implies that we know that the model forecasts will be wrong, but it is of minor significance as the model is constructed to be used for comparisons between two groups, smokers and quitters, thus eliminating some

of the biases. Furthermore, the model is constructed to be used now, for present-day decisions, which have to be based on present-day information.

The uncertainty

Another aspect of model validity is the uncertainty surrounding the model estimates.

The univariate sensitivity analyses on the model parameters (analyses A-F in figures 4 and 5 for men and women aged 50) show minor deviations from the base case result, while the multivariate analysis on costs and risks combined (analysis G) affects in particular the cost estimates. The methodological choices affect the results to a greater extent, with the discount rate (H) heavily influencing the QALYs and the more restricted perspective (I) decreasing the cost-savings. The multivariate analysis that only include higher-quality data (J) also imply decreases in the cost differences between smokers and quitters, but the difference remains substantial; around 50 000 SEK for females aged 50 years and 60 000 SEK for men, respectively. The overall conclusion from the parameter sensitivity analyses is that the QALY gains are at least 0.35 and 0.40 and the cost savings at least SEK 35 000, for female and male quitters aged 50, respectively.

The probabilistic analysis shows no uncertainty whether quitting tobacco leads to cost-savings and increases in QALYs, as all bootstraps are placed in the southeast quadrant of the cost-effectiveness plane. The bootstrap results exhibit a mixture of first and second order uncertainty, as it reflects both the probabilistic structure of the Markov model and the simulation of some parameter values (Briggs, 2000).

Another measure of uncertainty is the confidence intervals around the estimated mean differences, reported in tables 20-23. However, that measure is not fully appropriate as the large sample sizes of the Monte Carlo simulation (10 000 runs) diminishes the standard error of the mean (Briggs, 2000).

The structural uncertainty of the model, i.e. whether the results would be different if the model would have been constructed in another way, have not been studied. Alternatives to the chosen model structure could have been deterministic or discreet event simulations, more or less health states, other functional forms of risk functions, and other subgroups than men and women and five-year age-groups model results. The flaw is however shared with most tobacco quitting models (Bolin, 2012).

Checking for technical errors

The model contains a large number of trackers, i.e. variables that count events, to enable checking for technical errors. Tentative runs were executed after the introduction of every new variable, with cost items undiscounted, and the simulation results examined manually. Thus, the model has been thoroughly checked for technical errors.

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Conclusions

The aim of this study is to develop a model predicting health and economic consequences of smoking cessation, to be used for cost-effectiveness analyses of smoking cessation interventions. The updated model strives to incorporate data that is recent, accurate and appropriate for Sweden in year 2015. The model also adhere to Swedish recommendations on how to perform cost-effectiveness analyses within the health care sector. Data is however lacking to completely fulfil these requirements. Many model parameters are based on very few studies. Some information just does not exist, at least not accessible to us.

These are issues shared with most model, however. The purpose of modelling is to assemble the most accurate information at a point of time, to enable decision-making at that particular point of time. This is in accordance with one of the fundamentals of economics: decision-making under uncertainty, which implies that decisions have to be made even if there is no full information. We hope that the model will be applied to a range of different tobacco cessation interventions, which in time will enable a more comprehensive basis for decision-making.

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