Public Health Research Consortium

Project Report

Economic model of adult smoking related costs and consequences for England

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Preface: What this study adds to knowledge

This project has two objectives:

a) To present a literature review of the existing economic models of smoking-related conditions;
b) To present methodology and results from a *de novo* economic model that is developed for this project to evaluate the costs and consequences of smoking related conditions among adults in England.

Our literature review identified a wide range of studies making point estimates of the annual costs in a static framework. In 2005, the direct annual cost to the NHS in England due to smoking related conditions was estimated to be £4.4 billion, which was equal to 6.5% of the total health care budget for England (Allender et al, 2009). Few attempts have been made to model the costs of longer term smoking related diseases. Moreover, our review identified the need for an economic model for England that is based on population-specific epidemiological data. Hence, the model developed for this project uses a dynamic framework using population-specific baseline risk to estimate lifetime costs and health gains as a result of smoking cessation. The model uses a cohort of smokers from the general population and takes account of the change in risk as a function of age and years since smoking cessation to estimate lifetime costs to the health services. The model is flexible enough to accommodate future epidemiological evidence and changes in baseline risk.

We present the design, methodology and results of our economic model for adult smokers. The model evaluates four smoking-related conditions, i.e. myocardial infarction, stroke, chronic obstructive pulmonary disease and lung cancer. These conditions are known to have the highest economic and health related consequences associated with smoking. The economic model also takes account of higher risk of mortality from other diseases among smokers and ex-smokers compared to non-smokers. Lifetime costs and consequences were modelled for three population groups, i.e. never smokers, current smokers and ex-smokers. The probability of events in the latter two groups was modelled using relative risk estimates from the published literature. The model shows that the cost of health resource use reduces as a function of the number of years since quitting. Moreover, smoking cessation results in significant gain in life years due to reduced morbidity and mortality. These lifetime benefits in health consequences are also project for the current prevalent population of England to demonstrate significant cost savings for the NHS from smoking cessation and prevention.

The model can be used to estimate the impact of public health interventions aimed at improving smoking cessation rates in the population.

Executive summary

Background

Smoking is a major avoidable cause of morbidity and mortality in the United Kingdom. A recent study suggested that smoking was responsible was 109,164 deaths in the UK during the year 2005-06 (Allender et al 2009). The direct cost to the NHS in the UK due to smoking related conditions was estimated to be £5.2 billion per annum in 2005. The costs were highest in England (£4398.9m, equal to 6.5% of the total health care budget for England), followed by Scotland (£409.4m), Wales (£234.2m) and Northern Ireland (£127.9m).

Doll et al (2004) in their analysis of 50 year observations on British male doctors found that the age standardised mortality rate (ASMR) per 1,000 men per year for smokers was almost twice that of never-smokers (35.40 versus 19.38). The higher mortality was attributable to higher probability of ischaemic heart diseases, cerebrovascular diseases, chronic obstructive pulmonary disease (COPD), lung cancer and other vascular diseases.

Aims

The aims of the study are:

a) To conduct a literature review of the cost models of adult smoking, and

b) To develop an economic model of adult smoking for England.

This report presents the findings of a literature review of cost models, and the design, methodology and results of the economic model of smoking cessation.

Literature review

A literature review identified studies estimating the health care costs of smoking related disease. A wide range of studies were identified making point estimates of the annual cost in a static framework. In 2005, the direct annual cost to the NHS in England due to smoking related conditions was estimated to be £4.4 billion, which was equal to 6.5% of the total health care budget for England(Allender et al, 2009). These static models making point estimates are limited in their usefulness, and cannot be used to project potential longer term savings from interventions reducing the prevalence of smoking and consequently smoking related disease.

Few attempts have been made to model the costs of longer term smoking related disease in a dynamic framework. Dynamic cost models may be less prolific because these projections are particularly data intensive, requiring extensive demographic,

smoking prevalence, disease and cost information. Much of this data is not routinely available and has itself to be modelled to generate data in the form that can be used to estimate these long term costs of smoking. In addition to disease and cost data limitations, uncertainty over the timeframe over which to project these costs and the wide range of diseases which may be included make these models difficult to specify.

Design and Methods

The design and methodology of our economic model for adult smokers in England are discussed in detail in the report. The model evaluates four smoking-related conditions, i.e. myocardial infarction, stroke, chronic obstructive pulmonary disease and lung cancer. These conditions are known to have the highest economic and health related consequences associated with smoking. The economic model also takes account of higher risk of mortality from other diseases among smokers and ex-smokers compared to non-smokers. Lifetime costs and consequences were modelled for three population groups, i.e. never smokers, current smokers and ex-smokers. The probability of events in the latter two groups was modelled using relative risk estimates from the published literature. Risk reduction in ex-smokers was modelled as a function of time since quitting smoking. The event probabilities for myocardial infarction pathway are presented in detail.

Results

The model was evaluated using cohorts of 1,000 non-smokers, smokers and quitters by allowing for varying cessation rates from 0 – 100% with intervals of five percentage points. The model runs separately for men and women and estimates costs for each smoking-related group and the cost savings and life years gained associated with smoking cessation at varying cessation rates. The results estimate that the lifetime health care costs for a cohort of 1,000 non-smokers are £20.7 million (not discounted) or £5.2 million (discounted at 3.5%); the costs for a comparable cohort of current smokers are £29.3 million (not discounted) or £9.3 million (discounted) and for quitters are £24.3 million (not discounted) or £6.7 million (discounted). The figures for women are following: non-smokers (not discounted: £17.5 million; discounted £3.9 million), current smokers (not discounted: £25.4 million; discounted £7.0 million) and quitters (not discounted: £20.5 million; discounted £4.9 million).

We investigated the impact of varying smoking cessation rates on lifetime health care cost savings. The results are presented here: 5% cessation rate in a cohort of 1,000 smokers (men: £246,320; women: £241,365), 10% cessation (men: £492,640; women: £482,730), 20% (men: £985,280; women: £965,459), 30% (men: £1,477,919; women: £1,448,189), 40% (men: £1,970,559; women: £1,930,919) and 50% (men: £2,463,199; women: £2,413,649). Similarly, the difference in the life years lived by the smoker and quitter cohort was estimated as life years gained as a result of smoking cessation. These estimates are summarised here for a cohort of 1,000

smokers: 5% cessation rate in a cohort of 1,000 individuals (men: 213.1 years; women: 226.7 years), 10% (men: 426.2; women: 453.4), 20% (men: 852.5; women: 906.8), 30% (men: 1278.7; women: 1360.2), 40% (men: 1705.0; women: 1813.6) and 50% (men: 2131.2; women: 2267.0). It should be noted that the model may underestimate the costs associated with smoking because it does not explicitly incorporate concurrent risk of multiple conditions. However, the results clearly demonstrate the benefits of smoking cessation in terms of cost savings and life years gained.

The cost of smoking-related diseases and potential cost savings from smoking cessation were further evaluated for the current prevalent population of England. We estimate that the total lifetime cost of smoking for the prevalent population of England (≥35 years of age) is £44.8 billion (or £26.5 billion after discounting at 3.5%). We also estimate that the maximum cost savings as a result of smoking cessation in this population is £23.3 billion (or £14.7 billion after discounting at 3.5%).

Contribution:

The model enables the user to estimate the costs and life years saved as a result of adult smoking in England. Using these estimated costs and life year gains, we demonstrate that changes in smoking rates can have an impact upon the cost of treating smoking related diseases in the population. This model addresses the need for a lifetime economic model of smoking-related costs and consequences that is based on population-specific epidemiological data. We present cost and life year gains as a result of quitting for a cohort of 1,000 individuals in the English population, and also evaluate cost savings for the prevalent population of England.

The model provides a useful 'bolt-on' for evaluators, as the cessation rates from smoking cessation interventions can be inserted into the model to estimate the potential longer term cost savings following a successful quit. This permits the evaluator to project health care cost savings using a longer timeframe than the 12 month follow up traditionally employed in the majority of economic evaluations to date. Therefore a ranking of different interventions driven by effectiveness, health care cost savings and programme costs, can be constructed in order to demonstrate potential value for money afforded by different strategies.

1. BACKGROUND

Smoking is a major avoidable cause of morbidity and mortality in the United Kingdom. A recent study suggested that smoking was responsible was 109,164 deaths in the UK during the year 2005-06 (Allender et al 2009). This is equal to 18.6% of all deaths in that year. The percentage was significantly higher among men (27.2% of all deaths, equal to 77,154 deaths) compared with women (10.5% of all deaths, equal to 32,010 deaths). The proportion of smoking attributable deaths ranged from 19.7% in Scotland to 12.2% in Northern Ireland, with England at 18.7% and Wales at 19.2% of total deaths.

The prevalence rate of smoking in Britain is 21% in the adult population, with 22% among men and 21% among women (General Lifestyle Survey 2008). This is equal to approximately 13 million adult smokers at any one time point. Prevalence is highest in Scotland (24%), followed by 21% in England and Wales. In Northern Ireland, the prevalence was 24% in 2008/09 (Continuous Household Survey Bulletin 2008/09). The intensity of cigarette smoking in the UK varies by age, region and gender. In 2008, an average male smoker smoked 14 cigarettes a day compared with 13 cigarettes smoked by female smokers (General Lifestyle Survey 2008). Age also plays an important role in determining smoking behaviour, with 31% of those between the ages 20-24 currently smoking compared with 12% aged 60 and over. Historically, the difference between age groups has been smaller; however, it has increased as a result of higher smoking cessation rates amongst older people (Office of National Statistics 2010).

The burden of illness of smoking can primarily be attributed to increased risk of cardiovascular illnesses including myocardial infarction (MI), cerebrovascular conditions including stroke, chronic obstructive pulmonary diseases (COPD), and cancers of lung and other parts of the body. The data from the World Health Organisation on the developed European countries suggest that the total disability-adjusted life years (DALYs) lost due to smoking-related conditions were predominantly attributable to cardiovascular diseases (5.9%), respiratory tract and lung cancers (4.1%) and COPD (2.6%) (Allender et al 2009). This was further supported by Doll et al (2004) in their analysis of 50 year observations on British male doctors. They found that the age standardised mortality rate (ASMR) per 1,000 men per year for smokers was almost twice that of never-smokers (35.40 versus 19.38). The higher mortality was attributable to higher probability of ischaemic heart diseases [difference in ASMR between smokers and non-smokers = 3.91], cerebrovascular diseases [difference in

ASMR = 1.57), COPD (difference in ASMR = 1.45), lung cancer (difference in ASMR = 2.32) and other vascular diseases (difference in ASMR = 1.87).

The increased risk of illness is associated with increased costs of treating smoking-related conditions. The direct cost to the NHS in the UK due to smoking related conditions was estimated to be £5.2 billion per annum in 2005. The costs were highest in England (£4398.9m, equal to 6.5% of the total health care budget for England), followed by Scotland (£409.4m), Wales (£234.2m) and Northern Ireland (£127.9m) [figures not adjusted for population size]. The additional cost of treating smoking-related cardiovascular conditions was £2508.0m, smoking-related COPD was £1396.3m and for lung cancer was £276.7m (Allender et al 2009). These conditions are the major contributors to the smoking-related costs in the UK.

On the positive side, several cross-sectional surveys have suggested that most smokers, at least in the developed countries, want to stop smoking at some point (Hyland et al 2006). Recent UK statistics suggest that 66% of current smokers want to give up smoking for one or other reason (Office of National Statistics 2010). Most of these individuals smoke less than 20 cigarettes per day. The most common reason for wanting to quit smoking is health concerns (86%), followed by concerns over the cost of buying cigarettes (27%), family pressure (20%) and the effect on children (15%). Most smokers make several attempts every year, and almost half expect that they will not be smoking in a year's time. However, most smokers fail to quit, with only 2-3% becoming successful every year (Taylor et al 2006). Most unassisted quit attempts fail because of nicotine dependence (Hughes et al 2004). Despite this, the overall prevalence rate of smoking in Britain has declined in recent years, although the rate has increased among younger age groups.

Smoking cessation is known to have positive impact on the risk of smoking-related diseases. In a prospective observational study of British male doctors, Doll et al (2004) found that smoking cessation at ages 60, 50, 40, or 30 years resulted in gain in life expectancy of about 3, 6, 9, or 10 years respectively. Smoking cessation at age 50 almost halved the hazard of smoking-related mortality, and cessation at age 30 avoided almost all of it. In another survey that recruited 1.3 million women in the UK in 1996-2001, it was found that smoking cessation reduced the risk of smoking-related mortality with every passing decade, such that women who stopped for 30 years or more had almost the same level of risk as never smokers (Pirie et al 2009).

The UK government makes a sizeable investment in smoking cessation interventions. These include, amongst others, provision of pharmacotherapies including nicotine replacement therapy, varenicline and bupropion, and interventions to provide behavioural support and counselling. The recent annual statistical bulletin on NHS Stop Smoking Services (NHS SSS) (April 2008 – September 2008), estimates that, in England alone, the total government expenditure on NHS SSS was £33 million (The NHS information Centre 2009). This has increased significantly from £26 million in the same period in 2007. The cost per quitter in 2008 was £244 compared with £148 in the same period in 2007/08 and £181 in 2006/07. However, the bad news is that quit rates have fallen in the last few years, despite an increase in NHS spending. The above mentioned report notes that, between April and September 2008, a total of 273,164 people set a quit date through the NHS Stop Smoking Services, a decrease of 22 per cent from 350,494 over the same period in 2007/08. At 4 week follow-up, 49 per cent of those setting a quit date had successfully quit (based on self-report), in comparison to 73% successful quitters in the same period in 2007/08. The reason for such low success rates need to be investigated.

2. PURPOSE OF THE PROJECT

The purpose of this project is to develop a decision analytic model to estimate long-term health and economic consequences of smoking, and benefits of smoking cessation. The specific objectives of this project are:

a) To conduct and present a literature review of cost models of adult smoking, and

b) To develop a cohort model for economic and health consequences of continued smoking and smoking cessation for adult in England

c) To estimate lifetime health care costs and number of life years for predefined cohorts of non-smokers, smokers and ex-smokers in England

d) To estimate population-level lifetime health care cost of continued smoking and lifetime cost savings due to cessation for the prevalent adult population of England

For the latter parts, the report details the modelling framework, the decision analytic structure and the process of parameter estimation. The report then presents summaries of the benefits of quitting on health care costs and life years saved.

3. LITERATURE REVIEW: MODELLING THE COSTS OF ADULT SMOKING

A literature search was undertaken to identify studies using economic models to estimate the cost of adult smoking within specific populations. The search strategy is shown in the Appendix (see appendix 1). Papers identified by the search were categorised into *annual* and *lifetime* cost studies following the criteria used by Max (2001) in her review. The literature was searched to identify cost models. Hence papers using only health outcomes without applying costs were omitted from the review.

3.1. Models estimating annual cost of smoking

A wide range of studies were identified that made annual point estimates of smoking related costs by applying smoking attributable fractions to annual health care costs. Studies in this category estimated the costs of smoking in a number of different countries and localities, such as England (Parrott et al 1997), Canada (Xie et al 1999; Single et al, 1998; Baliunas, 2007), Germany (Ruff et al, 2000), California (Max et al, 2004), Hong Kong (McGhee et al 2006), Vietnam (Ross et al, 2007), Thailand (Leartsakulpanitch, 2007), Sweden (Bolin & Lindgren, 2007) and Japan (Shimada, 2007). These studies took a range of different perspectives and used various data sources, including public and private health care insurance data and primary and secondary risk data to attribute disease cases as a result of smoking.

However, these papers, presenting point estimates of smoking related disease costs, were excluded from further consideration, since they use different modelling techniques and methodologies compared to the dynamic approach which is of interest in the current review. Instead, by simply applying smoking attributable fractions to annual costs within a static framework, these models to not encompass a dynamic approach.

Studies omitted from further consideration also included the widely referenced SAMMEC model (Shultz et al 1991) as projections of future health care costs in a dynamic setting are not incorporated, and the model cannot be used to project the future impact on health care costs following changes in smoking rates as a consequence of cessation programmes.

Also excluded were studies which used regression techniques to undertake retrospective analyses of cohort data to estimate differences between smokers, ex-smokers and never-smokers in the preceding period (Miller et al, 1999; Fishman et al, 2003; Kuriyama et al, 2004). These studies take a different methodological perspective to the current study, attempting to use historic data to quantify differences in health care costs, as opposed to projecting costs into the future using disease rates, population and smoking prevalence data.

3.2. Models estimating lifetime cost of smoking

A total of seven studies were included in the review (Hodgson 1992; Lightwood & Glantz 1997; Barendgredt et al 1997; Orme et al 2001; van Genugten et al 2003; Rasmussen et al 2005; Chung et al 2007; Hurley and Mathews 2007). These studies show considerable variation in methodology, disease states included, cost data and discount rates as explained in the following section. A summary of the key methodological features and results of previous economic models of adult smoking are presented in appendix 2.

Hodgson (1992)

Hodgson (1992) estimated the lifetime medical care expenditures for males and females in the United States who never smoked and for moderate and heavy smokers, including both current and former smokers. Moderate smokers were defined as those individuals smoking less than 25 cigarettes a day and heavy smokers were those smoking 25+ per day. The analysis compared lifetime expenditures of smokers and never-smokers, hence permiting a comparison of becoming a smoker versus not becoming a smoker, but not the impact of stopping smoking.

The estimates determined the excess medical expenditures required by smokers and the aggregate future excess expenditures of the current population of smokers. Future costs were discounted at 3% for costs from age 17 to death. Data were sourced from the National Health Interview Survey for use of hospital and physician services; the National Nursing

Home Survey and the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study for nursing-home care; the American Cancer Society's Cancer Prevention Study II for mortality; and the National Medical Care Utilization and Expenditure Survey and Medicare data files for charges for medical care.

Expected health care expenditures (E_t) during age interval t are given by:

$$E_t = E_{at} \times P_{at} + E_{dt} \times P_{dt}$$

where

E_{at} = expenditures during age interval t if the individual survives through t
E_{dt} = expenditures during age interval t if the individual dies in t
P_{at} = probability of surviving through age interval t
P_{dt} = probability of dying during age interval t

Lifetime expenditures from age 17 are given by the sum of expected expenditures, E, during each of the age intervals for ages 17-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85 and over.

Medical care expenditures included are for short-term inpatient hospital care, physicians' services (to hospital inpatients and ambulatory patients in doctors' offices, hospital clinics and emergency rooms, patients' homes, and by telephone), and nursing- home care. Variation of medical care use with age is easily accounted for by employing age-specific data.

Results showed that the cumulative impact of excess medical care required by smokers at all ages while alive outweighed the shorter life expectancy, and smokers incur higher expenditures for medical care over their lifetimes than never-smokers. The study estimated that in the first five years from baseline the population of smokers aged 25 and over incurred excess medical expenditures of $187 billion or $2,324 per smoker. The population of cigarette smokers in 1985 who are age 25 and older were expected to incur excess medical expenditures of $501 billion, or $6,239 per smoker, over their remaining lifetime.

The author concluded that smoking raised medical care expenditures over the smoker's lifetime. Reductions in the number of persons who smoke would benefit all payers of medical care, decreasing the financial obligations of both public and private sources of funding. However, the model does not assess the impact of quitting smoking. Former smokers consist

of two groups, those who quit while in good health and those who quit in an attempt to prevent or reduce further exacerbation of an existing smoking-related health problem. Health care use and mortality of the former group would likely decline over a period of time from at or below the levels of all current smokers, to approach levels experienced by those who have never smoked. The impact of quitting on an individual smoker's lifetime medical expenditures will depend on whether the smoker quits when in good or failing health, number of years of smoking, and age at quitting. The key factor may be age at quitting and number of years smoked. Quitting at earlier ages increases the number of years of reduced medical expenditures and may result in lower annual expenditures and further increases in life expectancy.

Barendgredt et al (1997)

Barendgredt et al (1997) estimated the health care costs for smokers and non-smokers and estimated the economic consequences of smoking cessation using life tables to examine the effect of smoking on health care costs. Simulations were run for a mixed population of smokers and non-smokers, a population of smokers, and a population of non-smokers. Dynamic methods were utilised to estimate the effects of smoking cessation on health care costs over time.

This model looked at the impact of smoking in a population of smokers and non-smokers, using the incidence, prevalence, and mortality associated with heart disease, stroke, lung cancer, other cancers, and chronic obstructive pulmonary disease (COPD). Disease data and all other cause mortality were used in a multistate life table, that also included an 'alive, healthy' and 'alive, with heart disease' state.

Rate ratios were used to estimate the difference in disease states between smokers and non-smokers, smoking prevalence and the age- and sex-specific incidence of the smoking-related diseases in the mixed population of smokers and non-smokers. The life tables were used to estimate the difference in mortality and morbidity between smokers and non-smokers, and to drive the model results, with data constructed from Statistics Netherlands and rate ratios from a literature review. Medical costs were based on research that allocated the total costs for health care in the Netherlands to categories of age, sex, and disease. Demographic data were used based on the Dutch population with estimated health care costs representing an estimated cost of health care based on a zero smoking rate.

Epidemiologic changes and the changes in the population over time were based on a dynamic model of linked life tables, one for each point in time, with the population at a given age (*a*) and time (*t*) depending on the population at age *a-1* and time *t-1,* and on the incidence of disease and the associated mortality between *t-1* and *t.* The model parameters were estimated using Prevent Plus software.

This dynamic model projected future health care costs and the economic impact of an intervention was compared with the scenario in which no intervention is undertaken. Discount rates of zero, 3, 5 and 10 percent were used in the projections.

The results from the dynamic model showed that annual health care costs for smokers at a given age were almost 40% higher than those for non-smokers. Using a non-smoking population total costs were approximately 7% and 4% higher amongst men and women respectively as compared to the mixed population, due to the increased longevity of non-smokers and their accumulation of health care costs in later life as a result of other diseases. If all smokers quit, health care costs would initially drop but after a period of about 15 years costs would increase beyond current levels. Long term costs would increase in a scenario of complete smoking cessation. The authors concluded that smoking cessation would save short term health care costs, but costs would escalate in the longer term.

As is common with all dynamic smoking models, the model used in the Barendgredt study was heavily reliant on rate ratios from epidemiologic studies to estimate the differences between smokers and non-smokers. These parameters drive all of the calculations that estimate the different scenarios with and without smoking cessation interventions. In addition, limitations are exposed by the robustness of the cost data. For example, female smokers had much lower lung cancer costs than male smokers which the authors found difficult to explain physiologically. Further issues raised were the selection of which diseases to include, the duration of the cost projections and the discounting of these lifetime costs.

Lightwood & Glantz (1997) Lightwood & Glantz (1997) use a very limited group of diseases to simulate potential health care cost savings. The authors estimate the fall in risk of acute myocardial infarction (AMI) and stroke after smoking cessation and simulate the model impact of a 1% absolute reduction in smoking prevalence on the number of and short-term direct medical costs associated with the prevented AMIs and strokes. The model attempts to project the one year savings resulting from a reduction in the number of heart attacks and

strokes amongst 35 to 64 year-old adults due to a 1% absolute reduction in smoking prevalence (three to 4% of smokers quitting) and the effect of a seven year annual 1% absolute reduction in prevalence in cumulative terms. The analysis is restricted only to direct health care costs, with indirect costs and productivity costs excluded.

The model applied strict criteria to a literature search to derive estimates of the relative risk of AMI and stroke after cessation, as a function of time. Meta-analytic pooling methods were not possible for the estimation of a continuous decline curve because there were seldom two statistics from different studies that estimated relative risk across the same time interval. Instead, the model combined all of the reported relative risks and estimated a function for the decline in relative risk from the combined data as a function of time. Data for the fall in risk of stroke after smoking cessation for both male and female were pooled due to lack of significant differences between male and female relative risks. AMI hospitalization rates needed to convert estimated relative risks into absolute incidences among current and ex-smokers were estimated using never-smoker hospitalization rates from published data on smoking prevalence, relative risks, and observed AMI hospitalizations for the entire population (including both smokers and non-smokers). Equations were then estimated to specify relative risks as a function of time from quitting. In terms of survival, smokers and ex-smokers who have never had an event were assumed to have an annual survival probability equal to that of the average current smoker aged between 35 and 64 years.

The model used costs based on the average hospital room and service charges, physician and other health professionals' fees, and ancillary charges. Cost estimates were taken from the studies used to estimate risk. These cost estimates were based on very large numbers of patients, so the uncertainty of estimated mean costs was very low, and the authors treat them as constants. Typical costs included charge data adjusted for Medicare Cost Report cost-to-charge ratios, Medicare allowable charge ratios, and actual average patient and third-party reimbursements for services.

Minitab software was used to run simulations estimating the distribution of the reduction of AMI events in the cohort of 35- to 64-year-old quitters as opposed to an identical cohort that continued to smoke. The simulations ran 5,000 individual trials for each of male AMI, female AMI, and stroke.

The authors estimated that in the first year following cessation there would be 924 fewer hospitalizations for AMI and 538 for stroke. The cost saving of this reduction in cases would be an estimated $44 million. Projecting the results forward, a seven year program reducing prevalence by an annual 1% would result in a total of 63 840 fewer hospitalizations for AMI and 34,261 fewer for stroke. The estimated saving would be $3.20 billion. The programme would also prevent in the region of 13,100 deaths resulting from AMI that occur before people reach the hospital.

On an individual level, for each individual who stops smoking the estimated saving in medical costs associated with AMI and stroke would be $47 in the first year and $853 during the next 7 years. A discount rate of 2.5% was used in the analysis.

However, it should be noted that this study is limited in its coverage of disease areas. The model assumes that the relative risk of further events remains constant after the first event for smokers and ex-smokers. The studies used to derive the relative risk estimates were also subject to limitations. In particular, the three retrospective case-control studies in the review reported greater reductions in events than other study designs.

The analysis is also truncated at age 64, so no account is made for those who age beyond 64 after the first year of the programme. This is due to the lack of evidence on the time course of relative risk following smoking cessation amongst the elderly. The studies that were identified do not present sufficient data to permit the quantification of the effects in this age group.

Orme et al (2001)

The HECOS (Health and Economic Consequences of Smoking) model (Orme et al 2001) estimates the health and financial consequences of smoking, and also the potential benefits from a range of smoking cessation interventions.

An overview of the development of the model equations and user interface were provided in a 2001 Tobacco Control paper, which demonstrated the model using data for the UK.

The results illustrated a typical smoking cessation strategy that cost approximately £1,200 per life year gained and £22,000 per death averted. The model successfully captured the

complexity required to model smoking behaviour and associated mortality, morbidity, and health care costs. Furthermore, the interface provided the simple results in a tabulated manner that was accessible to policy makers and evaluators. However, the model is no longer available in an on-line format.

HECOS is based on the relationship between smoking and smoking related disease, the estimated associations being crucial to the workings of the model. The HECOS model is based on a review of the literature to estimate these parameters. The model is based in discrete population steps, where growth is a function of the preceding time period as the basis of a simple Markov model without memory. This excludes the probability of quitting as being a function of previous quit attempts.

The HECOS model is based on three smoking states; current smoker, recent quitter and long term quitter (quit over a year ago). The model assumes that smoking cessation aids are targeted at recent quitters and withdrawal symptoms gradually diminish over time. Smoking cessation interventions increase the likelihood of a successful quit attempt and long term quitters should have a lower relapse rate compared to recent quitters. Smoking cessation programmes are modelled by increasing the rate at which smokers quit for the first year of the model.

Smokers may die prematurely as a result from smoking related disease. In addition, ex-smokers may acquire a smoking related disease, but the associated risk is lower than for current smokers. Once an individual has acquired a smoking related disease they cannot move back to a 'no disease' state. The smoking related diseases covered by HECOS were chronic obstructive pulmonary disease, asthma, chronic heart disease, stroke, lung cancer, and low birth weight pregnancies.

The model is based upon changes in health statuses and smoking over successive one year time frames based on an individual being a current smoker, a recent quitter (less than one year quit) or a long term quitter (at least one year since quit). Health statuses are no disease, disease and dead making a total of seven possible states. The transition from one state to another is determined by changes in smoking behaviour and disease and mortality rates. However, the model excludes any death from non-smoking related disease, which the authors

state is due to absence of data. Costs in the model are estimated by multiplying the time in smoking related disease states by an annual unit cost of disease, over a 20 year timeframe, and costs are discounted over this period.

The population is divided into subpopulations aged 0–34, 35–69, and 70+ for males and females. The effects of smoking cessation are estimated by running the model twice, once with and once without the change in the smoking rate, and then calculating the difference in costs. In year one, a simple calculation reallocates smokers from the recent quitters state to the long term quitters state, based upon the effectiveness rates applied to the smoking cessation programme. At the same time, the model runs without this change and the differences between the two runs are calculated in order to estimate the net change and this is repeated for the following years. The number of life years saved through a particular intervention is the difference in the total years survived with an intervention, compared to the total life years survived without an intervention. The HECOS model was not available for critical appraisal and is not in current use. Hence, it was not possible to provide detailed analysis of the modelling framework, assumptions, parameterisation and general validity of the methodology of the HECOS model. The model developed for this project is independent of the HECOS model and does not bear any direct relationship with it.

Van Genugten et al (2003)

Van Genugten et al (2003) used a dynamic framework to estimate the future health gain of health education campaigns aimed at keeping (young) people from starting to smoke, campaigns aimed at persuading smokers to quit, and tax measures to reduce smoking prevalence. Policy scenarios based on evaluations of several health promotion campaigns were devised and implemented into a dynamic multistate model to simulate smoking prevalence, loss of life-years, and costs for several future decades.

Four smoking-related diseases were included in the model: lung cancer, coronary heart disease, stroke, and COPD. The Dutch population is divided into birth cohorts and followed from 1994. Each individual may in the following year start smoking and may have one or more diseases based on transition probabilities. Incidence of smoking-related diseases depends on age, gender, and smoking behaviour, and was projected to the year 2050. The model used Dutch population data from Statistics Netherlands, incidence rates, 1994 prevalence rates, and disease-specific mortality rates. Incidence and prevalence estimates of

smoking-related diseases were obtained from general practitioner registrations. The mortality rates for smoking-related diseases were estimated as the difference between mortality in the general population and mortality amongst patients and the 1994 gender-and age-specific incidence and mortality rates were used for the period 1994 to 2050. As is commonplace with these dynamic disease models, it was assumed that once in a smoking-related disease state it was not possible to return to a disease-free state.

Gender- and age-specific start and quit rates for smoking were estimated for 1987 to 1994 using age-period-cohort analysis. Incidence rates for smokers were calculated from the observed gender- and age-specific incidence rates in the population and the relative risks or risk ratios of smokers and former smokers for incidence of smoking-related diseases.

The model uses several scenarios specifically aimed at teenagers to illustrate the results. Based on evaluations of these interventions the authors assumed a reduction of 20% in the number of individuals who started smoking.

A health education campaign encouraging smokers to quit resulted in a 14% decrease in smoking prevalence in the first year which was used for a second scenario. The effectiveness of tax measures were based on UK data. The evaluations are based on the scenarios presented in Table 1.

Table 1: Scenarios used in Van Genugten et al (2003)

1.	*Reference scenario:* Future smoking prevalence based on trend extrapolation	
2.	*Don't start scenario:* Continuous health promotion aimed at keeping (young) people from smoking; over a 3-year period (1998–2000)	Number of starters is reduced by 20%.
3.	*Quit scenario:* Continuous health promotion urges smokers to quit; in the first year (1998)	4% reduction of the smoking prevalence
4.	*Tax scenario:* Tax measures increase tobacco prices with 50%.	Consequently in the first year starting rates are 60% lower than the reference value, while quitting rates among male and female smokers are 4% and 11.5% respectively.

The results from van Genugten et al's model showed the short-run health gain in the quit scenario is substantial but after reaching a maximum of about 40,000 years in 2025 for males and a maximum of about 50,000 in 2035 for females, the annual number of life-years saved is declining again. Costs to be avoided will be almost €80 million for males and €100 million for females.

However, eventually the health gain and avoided costs of the 'don't start' scenario will go beyond the yield of the quitting scenario. The tax scenario behaves very similar to the scenario in which individuals do not start smoking but works through faster, reaches a higher health gain and will eventually catch up with the quitting scenario.

Van Genugten's model is one of a small number of papers identified to project long term health care costs and savings. However, the paper does not include details of how the model is formulated and how these projections are made, so it is difficult to draw conclusions as to the reliability of the findings or the validity of the model used to make the projections.

Rasmussen et al (2005)

Rasmussen et al (2005) presented a dynamic (life cycle) model of the lifetime costs of smoking taking into account differences in life expectancy. The main outcome measures were direct and indirect lifetime health costs for smokers and never-smokers, and cost ratios measure by the ratio of those who had ever smoked to never-smokers. The estimates used in the model specification were based on annual disease rates of use of healthcare resources, smoking related risks, smoking prevalence and unit costs of health care.

Health care costs in the Rasmussen et al model included all costs related to smoking between the ages of 35 and 89 based on the assumption that amongst individuals falling outside this age interval the effects of smoking on disease rates, and therefore health costs, are negligible. Total health care costs were defined as the sum of direct costs and indirect costs based on four major disease groups; cancer (ICD–10: C00–C99), vascular disease (ICD–10: I00–I99), respiratory disease (ICD–10: J00–J99), and all other diseases.

Direct costs included frequencies and costs of discharges by cost weights according to diagnosis-related groups and outpatient costs based on Danish Ministry of Health speciality specific prices. Market prices were used for drug costs; a cross-sectional study based in

Holland was used to determine the frequency of GP visits. Absence from work was based on diagnostic groups of diseases available from The Danish Working Environment Authority. Mortality rates were based on the National Register of Causes of Deaths. Survival probability for 1998-99, private income (1997), frequencies of occupation, and employment (1999) were taken from Statistics Denmark.

In order to estimate total lifetime health costs, cost-of-illness and life expectancy data were combined for a given smoking status using ever-smokers and never-smokers as the two main groups. Direct costs were estimated by the economic resources used in the health care sector (diagnostics, nursing and treatment of disease).

Also included in the analysis were 'indirect costs' which were estimated using the human capital method to measure the value of lost production as a result of smoking related short-period and long-period disease and premature death. Population attributable risk percentages were used as indicators for parts of output as well as parts of costs attributable to smoking.

The costs attributable to smoking were estimated using Danish smoking proportions and Danish estimates of relative mortality risks. To estimate costs per person-year by smoking status, age, gender, and disease category, the direct and indirect costs were multiplied by population attributable risk percentages and then calibrated and divided by the number of persons in each category.

The assumption was made that the remaining direct and indirect costs were independent of smoking status, and these costs were assigned according to age and gender. Total costs per person-year were estimated by smoking status, age, and gender by adding direct and indirect smoking-related costs to the direct and indirect remaining costs.

Statistics Denmark (1998–99) publish life tables which were used to estimate the survival probabilities by smoking status and gender, based upon the probability of being alive at given ages (35, 40,……, 75), up to 89 years. Multiplying cost per person-year by the survival probabilities and discounting by 5% per year, total, direct, and indirect lifetime health costs were obtained for men and women by smoking status and age (35–89, 40–89, up to 75–89 years). A discount rate of 5% was used to convert lifetime costs to present values.

Different relative risk rates and discount rates were used to test the sensitivity of the results. The risk rate variations used the upper and lower bounds of the RR estimates, whilst the discount rate was varied between zero and 8% per annum.

Rasmussen's results showed that both direct and indirect costs for those who had ever smoked were higher than for those who had never smoked, a result which held across all age groups of both men and women. Direct and indirect cost ratios were highest at age 45 for women, and respectively at ages 35 and 40 for men. When life expectancy differences were included in the analysis both direct and indirect lifetime health care costs for men aged 35, (when discounted at 5% per year) were 66% and 83% higher amongst those that had smoked cigarettes when compared to those who had never smoked. The estimates for women were 74% and 79%. A range of scenarios were presented, with results showing insensitivity to changes in the discount rate, and even no discounting, together with variations in risk estimates.

However, as is common with previous lifetime cost models, the findings are limited by uncertainty of the RR-estimates, and they may overestimate the effect of smoking due to positive confounding by other factors. There is also a degree of uncertainty with respect to the smoking proportions, which were based on a self-report survey. Furthermore, survival probabilities may influence the validity although the authors note that the estimates tend to be supported by a Danish empirical study of never-smokers and smokers with different smoking habits.

Uncertainty is also evident around the discount rate, as is noted above, with no universal agreement over which rate should be employed in such analyses. As expected, lower discount rates would increase the total lifetime health care cost estimate and reduce the percentage difference between ever-smokers and never-smokers. Rasmussen et al's analysis does show that with no discounting the total lifetime health costs of being a never-smoker were less than those of ever-smokers within the same age and gender groups.

The results estimated by Rasmussen et al are similar to the earlier findings of Hodgson (1992) but are at odds with Barendregt et al's findings. The reasons put forward were that Barendregt et al's lifetime costs due to limited lifetime costs for heart disease, lung cancer, stroke, other cancers, and chronic obstructive pulmonary, and the assumption that costs for all

other diagnoses were independent of smoking status. In addition, the five smoking-related diseases included in their model accounted for less than 20% of the total lifetime costs. These assumptions were disputed by Rasmussen et al who point out that smoking has been shown to be associated with chronic bronchitis, peripheral artery occlusive diseases, and aortic aneurysm.

Chung et al (2007)

Chung et al (2007) estimated the lifetime financial burden on the national health insurance system in Taiwan system, which is a compulsory national insurance programme implemented in 1995, and now covering over 97% of the country's population. The analysis also estimated life years lost as a result of smoking related diseases.

The authors used ten smoking related diseases (cancers of the lips, oral cavity and pharynx, cancer of the oesophagus, stomach cancer, cancer of the rectum, liver/gallbladder cancer, lung cancer, cancer of the cervix/uterus, stroke, acute myocardial infarction (AMI) and chronic obstructive pulmonary disease (COPD)). Linked cohorts from the National Death Registry and the National Cancer Registry (NCR) database were used to generate survival data together with patient data from the National Taiwan University Hospital (NTUH). Cohort data were recorded between 1991 and 2000, which were verified to be about 80.7% comprehensive for all cancer cases. The incidence of stroke, AMI or COPD in 2001 were computed by using cases where a patient was being treated for these diseases with a confirmed primary diagnosis during 2001 but had not been treated for the same disease during the preceding five years. This process permits the estimation of the total number of incident cases of stroke, AMI and COPD for the sample of 200,000 individuals identified within the NHI database. The incidence of stroke, AMI and COPD during 2001 for the population aged 35 and over was calculated by using adjusting national age and gender data to adjust the rates.

Smoking attributable fractions were derived by combining the relative risks of smokers compared to non-smokers, together with smoking prevalence data for Taiwan. Taiwan has a very unequal smoking prevalence between genders, with a national health interview survey by the Bureau of Health Promotion estimating rates for those aged over 35 years of 48.0% for males and 4.7% for females. Life years lost as a result of smoking were calculated for the study diseases by combining the survival analysis results, the smoking attributable fractions and the annual disease incidences for each of the ten selected disease areas. Lifetime

medical expenditures for the study diseases were estimated by integrating the survival curve for each disease area, with disease costs being derived from NHI reimbursement records.

The ten diseases selected for the analysis yielded 241,280 incidents during 2001. The model suggested that approximately 53,648 of these cases (22.2%) could be attributed to smoking. Overall an estimated 191,313 life years were lost at a mean 3.6 years lost per case.

Based on each case, mean survival time was approximately 10.2 years. A sensitivity analysis was undertaken by varying the discount rate between 1% and 3%, which was justified by the authors due to Taiwan's long term interest rate of about 2%. Using a 3% discount rate the total lifetime financial burden was estimated at between $291 million (approximately £147 million). Using a 1% discount rate the burden was approximately $336 million (approximately £665 million) based on a price year of 2001. This was about 24.6% of the total estimated lifetime medical expenditure for all recorded cases of the 10 study diseases.

The authors also acknowledge the omitted financial burdens to the victims' families, and also that each patient will suffer physically, emotionally and socially before death. They also argue for the future incorporation of quality of life data into such models.

The estimates in the Chung et al analysis are argued by the authors to be an under-estimate. Firstly, the effects of passive smoking are not included in the analysis. Secondly, smoking during pregnancy is not taken into account. However, these impacts may be relatively small given the very low smoking prevalence rates amongst Taiwanese females.

Thirdly, only statistically significant relative risks were taken from the cohort in the study when making smoking attributable fraction calculations. Females in the study cohort were much younger than in the general population, and given the low prevalence of smoking among women (approximately 1.4%), there were few or zero cases of observed deaths. Therefore Chung et al did not report health effects attributable to smoking for four of the cancer diseases and COPD among females. The authors also point to the limitation of using only 10 diseases, which would certainly lead to underestimation of the impacts on health in general as a direct result of smoking. The paper also excluded the impact of smoking on general health and the quality of life during the lifespan of an individual. Life expectancy was also based on the life expectancy in the general Taiwanese population. This population

also includes smokers, so life expectancy will be underestimated. Finally, productivity costs are excluded. Coding issues with cause of death are also evident from the Taiwanese data, whereby people with COPD may not be certified as dying of this disease since mortality data in Taiwan were generally coded with only one underlying cause of death that is less likely to be COPD if a person also had a major cancer. Therefore, the estimation of the smoking attributable fraction of COPD might be affected and the total incidence might be underestimated.

Hurley and Mathews (2007)

Hurley and Mathews (2007) developed the Quit Benefits Model (QBM) to assess the effect of smoking cessation on an individual smoker. The approach used was to develop a Markov cycle tree model using the TreeAge Pro software to be used as a tool to evaluate tobacco control programmes where estimates of the number of quitters are available. The model was developed primarily for the Australian population using Australian demographic and epidemiological data. Quitting outcomes were assessed for males and females in 14 five year age-groups from 15–19 to 80–84 years.

The model focused on four clinical conditions that accounted for over 80% of the morbidity and mortality attributable to smoking in Australia. These included acute myocardial infarction (AMI), stroke, lung cancer and COPD. The model evaluated consequences of quitting in terms of cases avoided of the four specified diseases, life-years (LYs) and QALYs gained and health care costs saved. These were estimated by subtracting the expected outcomes and costs for smokers from the expected outcome and costs for quitters. The model takes account of age and sex when estimating risk of developing the conditions. The QBM assumes that quitters do not commence smoking again.

All individuals in the model start off in disease-free state, i.e. 'well' state, and then develop one of the four conditions based on the underlying transition probabilities that are function of age, sex and smoking status. The estimates of relative risk in smokers were obtained from the literature while those for ex-smokers were estimated by fitting exponential models to the data from large case-control and cohort studies to allow for decline in risk over time after quitting. Once diseased, individuals in the model were expected to follow specific pathways for the relevant disease conditions. As required, 'tunnel states' were introduced in the model to account for the fact that individuals have higher risk of death following events such as AMI

and stroke. The model runs separately for smokers and ex-smokers to estimate the health and cost benefits of smoking cessation. Individuals in the model were followed until the age of 85 or death, whichever occurred first.

The QBM study reported the benefits of smoking cessation in terms of life-years, QALYs and costs followed up for ten years after quitting smoking. The outcomes were estimated with discount rates of 0%, 3% and 5% per annum. The results are reported for a simulated group of 1,000 quitters and compared against the same sized group of smokers from the Australian population aged between 15 and 74. The modelling exercise estimated that for every 1,000 males chosen at random from the reference population who quit smoking, the average savings in health care costs associated with AMI, COPD, lung cancer and stroke in the first ten years following quitting will be A$408,000. The corresponding savings in 1,000 female quitters was equal to A$328,000; hence, the average savings per 1,000 random quitters is estimated to be A$373,000. In terms of disease diagnosis, overall 40 of these quitters will be spared a diagnosis of AMI, COPD, lung cancer and stroke in the first ten years following quitting, resulting in an estimated 47 life-years saved and 75 QALYs.

Hurley and Matthews model is analytically more advanced and developed compared to most previous models. However, the model has some limitations, most of which have been explicitly discussed by the authors. The model focuses primarily on the four major conditions associated with smoking that account for 80% of the smoking related morbidity and mortality in Australia. The authors acknowledge that this would underestimate the benefits of smoking cessation. Furthermore, individuals following a particular disease pathway were not allowed to have concurrent conditions, i.e. an individual following the stroke pathway was not allowed to interact with the MI pathway to develop concurrent conditions. Again, this assumption is likely to result in underestimation of the impact of smoking cessation. Another limitation not explicitly discussed by the authors is the fact that the clinical pathway in the model does not explicitly allow for recurrence of events. Hence, once an individual develops the first AMI, they can either die from the condition or survive and move to tunnel states based on time since the event. However, the case fatality rates following the first AMI and stroke were adjusted to account for second and subsequent events. However, costs incurred and QALYs lost due to non-fatal recurrent MI were not explicitly taken into account in the model. This is likely to be a limitation of the choice of cycle tree modelling framework used which limits the number of health states over time. As a result, further underestimation of the

costs and life year savings is expected. Also, the model does not explicitly incorporate excess risk of smoking for other conditions. Finally, the model uses a limited time horizon of 10 years that is not long enough to capture lifetime benefits of smoking cessation.

3.3. Summary of the literature review

Few attempts have been made to model the lifetime costs of smoking using a dynamic modelling framework. Despite the numerous static models which apply smoking attributable fractions to annual costs to derive point estimates, longer term health care costs have been neglected. Indeed, much debate surrounds the specification of the more simple short term point estimates, as described by Warner et al (1999) who highlights numerous methodological flaws and differences in the annual cost estimates across a range of papers.

The dearth of long term cost models may be due to a range of factors, such as disease and cost data limitations, uncertainty over the timeframe over which to project these costs, and disagreements over which diseases to include in the modelling exercises. These models are particularly data intensive, requiring demographic, smoking prevalence, disease and cost information. Much of this data is not routinely available and has itself to be modelled to generate data in the form that can be used to estimate these long term costs of smoking.

The projection of health care costs over the remaining lifetime of individuals also has the potential to magnify any errors in the attribution of diseases to smoking faced with uncertainties in the parameter estimates used to drive the model. Further complexities arise with other causal factors linked with smoking making it difficult to attribute the causal factor entirely and exclusively to smoking. There is also disagreement over the discount rate to apply to longer term costs, with rates of between zero and 10% evident in the literature. Whilst UK guidance recommends a 3.5% rate (NICE, 2008), this is not universally accepted, hence making the presentation of results difficult to generalise and interpret without extensive sensitivity analysis.

In summary, our literature review highlights the need for a long-term economic model to estimate lifetime costs and consequences associated with smoking and the benefits of smoking cessation. The model should take account of the dynamic attributes, including age and years of smoking cessation, that are directly related to clinical events. Moreover, the

literature review identified the need for a model that is specific for the context of England and is based on population-specific epidemiological data. Hence, this project has developed a population-based cohort model that uses a Markov framework to project lifetime impact of smoking cessation. The modelling structure is flexible enough to accommodate future epidemiological evidence and any changes in baseline risk. The framework can also incorporate evidence from other countries to estimate costs and health gains for different population groups.

4. THE ECONOMIC MODEL: DESIGN AND METHODS

This section will discuss in detail the modelling approach used in this study. This includes the framework used for modelling, the Markov structure of the model, event probabilities for all groups of interest and the estimation of costs.

4.1. Modelling framework

Decision analytic models are commonly employed to evaluate the long-term health and economic consequences of medical and public health interventions. These models use comprehensive modelling frameworks to represent the complexity of clinical pathways and their consequences in terms of quantity and quality of life and the associated costs. They represent a reasonable compromise between descriptive realism and computational simplicity that allows transparency and flexibility for the purpose of evidence-based policy making. The models use a systematic approach to decision making under uncertainty (Raiffa 1968).

The most commonly employed form of decision analytic models in the health economics literature is the Markov model. These are cohort simulation models that are most useful when the decision analysis involves random processes or risks that evolve over time (Sonnenberg and Beck 1993). This is particularly relevant to long term conditions that have time dependent risks. For instance, in the case of smoking cessation, the health benefits in terms of reduced risk of developing cardiovascular conditions depend on the number of years since quitting. Similarly, for individuals with a history of myocardial infarction, the risk of a subsequent infarction depends on the time since the initial cardiovascular event. Markov models allow for incorporation of these time dependent transitions within a comprehensive

decision analytic framework. This framework aids transparency and understanding of the modelling approach, and allows flexibility to capture key aspects of the disease process (Briggs et al 2007).

Markov models use distinct health states and clinical events; patients are assumed to be in one health state at any one time. Depending on the underlying risk, individuals can move between health states over a discrete time period, known as a Markov cycle. Patients who do not move to another health state during a Markov cycle either stay in the same health state or die. Transitions to other states are dictated by the underlying state transition probabilities that, in the case of smoking cessation model, are a function of age, gender and smoking status. Markov models assume that transition probabilities depend only on the current health state and not on the history of how each patient arrived in the current health state – this is known as the 'Markovian' assumption or the assumption of memorylessness. However, if the evidence suggests that the clinical history may play a significant role in certain state transitions, then additional health states can be defined to 'tunnel' the patient through time to capture the evolving risk.

In order to capture costs and consequences of smoking cessation strategies, each health state has its associated resource use (or costs) and health outcome consequences. The model is then run over a large number of cycles, often over the lifetime horizon of the cohort, to estimate the long-term costs and consequences associated with health behaviours and health care interventions (Briggs and Sculpher 1998).

4.2. General structure of the smoking cessation model

Models are simplifications of reality; hence, it is not possible to model all possible costs and consequences of smoking and all possible benefits of smoking cessation. The decision analytic model developed in this study focuses on four important clinical conditions that are known to have significant health and economic consequences for smokers. These include myocardial infarction, stroke, chronic obstructive pulmonary disease (COPD) and lung cancer. The primary reason for focusing on these four conditions is that these diseases contribute most to the smoking-related costs and morbidity/mortality (Allender *et al* 2009; Doll *et al* 2004). Also, the Markov framework used in the current model benefits from explicit specification of disease pathways that can be evaluated for relative risk associated with continued smoking and quitting. If more disease conditions were explicitly defined in

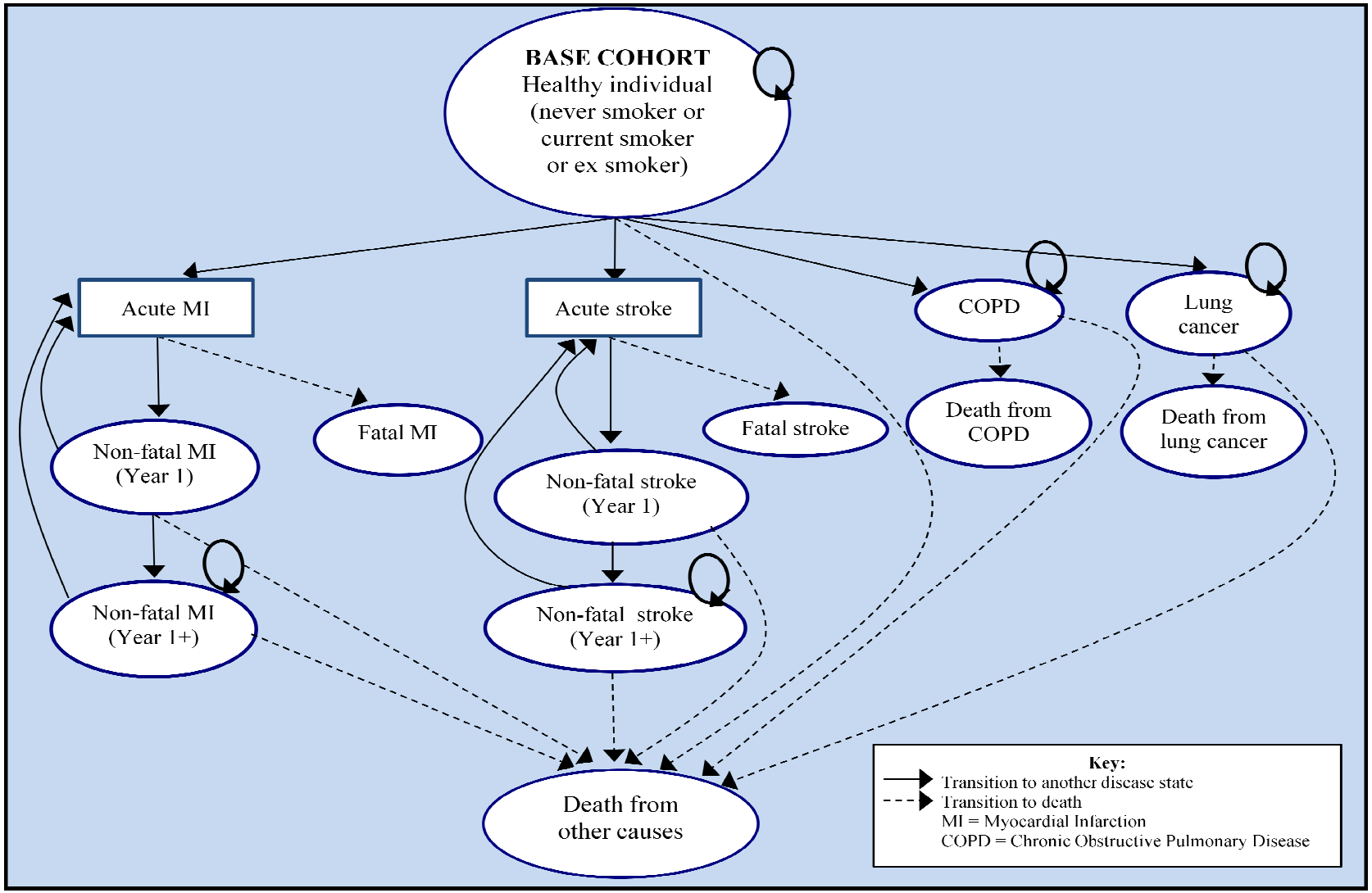
the modelling framework, it would result in unmanageably large number of disease states. Moreover, epidemiological data on age, sex and smoking status-specific relative risk estimates is not insufficiently available for many other conditions. However, to overcome this limitation, we have explicitly allowed for higher risk of death and cost incurrence from 'other disease conditions' for smokers and ex-smokers compared to non-smokers; this is intended to capture higher relative risk of conditions other than the four diseases explicitly modelled.

The model is evaluated for three smoking related groups: never smokers, current smokers and quitters. Outcomes are assessed separately for male and female cohorts in the adult population. Where data is available, the model accounts for the changing risk of clinical events as a function of the number of years since quitting; however, the risk for current smokers has not been modelled as a function of pack years, primarily due to data limitations. The model evaluates only the direct impact of smoking and quitting on smokers; hence, the impact on other people due to environmental exposure to smoke (passive smoking or second hand smoke) is ignored. However, the model has the flexibility to include this risk at a later stage. The model has been developed in Microsoft Excel (version 2007) which will allow easy accessibility and transparency for the purpose of validation.

Because many of the published studies used to parameterise the current model report baseline risk in adults $\geq$ 35 years of age, the default start age of the cohorts in the model is set to 35 years; however a later start age can be defined. When further age-specific data becomes available, the model can be adapted to capture risk at earlier ages. The model runs until individuals die or reach the age of 100 years. Hence, the lifetime risk of the four smoking-related conditions is captured in the model. The model can also run for other start ages that can enter in the model as a user-defined interactive parameter. The model cycle length is set to 1 year.

The state transition diagram for the Markov model is presented in figure 1. In order to facilitate clear understanding of the model structure, the four pathways in the model (related to the four clinical conditions highlighted above) are also presented separately in figures 2 – 5. The oval shapes in the diagrams represent health states and the arrows represent transitions between health states. Transition to death is represented with a discontinuous arrow to distinguish it from transitions to 'alive' health states. The rectangular boxes represent predicted events. These are not modelled as health states, i.e. patients experiencing an event immediately move to fatal or non-fatal (year 1) health states. This approach allows us to

Figure 1: State transition diagram for the Markov model for smoking and quitting



capture the costs and health consequences of acute events that last much shorter than the length of the Markov cycle in the model. The model has currently been set up as deterministic; however, the current framework can be extended to make the model probabilistic at a later date.

4.1. The base model and disease pathways

Three base cohorts of 1,000 individuals are created, one each for non-smokers, current smokers and quitters (or ex-smokers). Individuals in the base cohort start as healthy adults, i.e. they do not have any of the four clinical conditions explicitly modelled here. The base models (developed separately for never, current and ex-smokers) allow individuals in each respective base cohort to move from the healthy state to enter one of the four disease pathways or die of other causes (see figure 1). The transition probabilities of entering disease pathways depend on the underlying age and sex-specific probabilities of the first event of each smoking-related condition. Individuals who do not develop one of the four diseases or die of other causes remain in the base cohort to become available for transitions in the following Markov cycle. Once patients develop a disease condition, they follow the respective pathway until they die from the disease or other causes. The model uses one-yearly Markov cycles. Death is modelled as an absorbing state – a state which, once entered, cannot be left. The model makes a distinction between fatality due to one of the four diseases and death from other causes. This allows us to use relevant costs associated with death.

The base model takes a competing risk approach which in effect implies that individuals in the base cohort may enter either of the four disease pathways depending on the probability of each pathway. It also implies that if risk of one of the fatal conditions is reduced during early years of life due to smoking cessation, it may result in an increase in the incidence of the same or different condition during later years of life. For example, a quitter may avoid developing an acute fatal MI during early years of life but may end up developing the same condition or a chronic and/or more expensive condition in later years. Similarly, in a competing risk model, if women have lower risk of myocardial infarction compared to men, then they stay longer in the base (healthy) model and in turn may become more likely to follow other pathways explicitly modelled within the Markov framework. The beneficial effect of smoking cessation will be reflected in the life years gained and cost savings over the

lifetime. Hence, in competing risk models, event rates for specific conditions may not be evaluated in isolation.

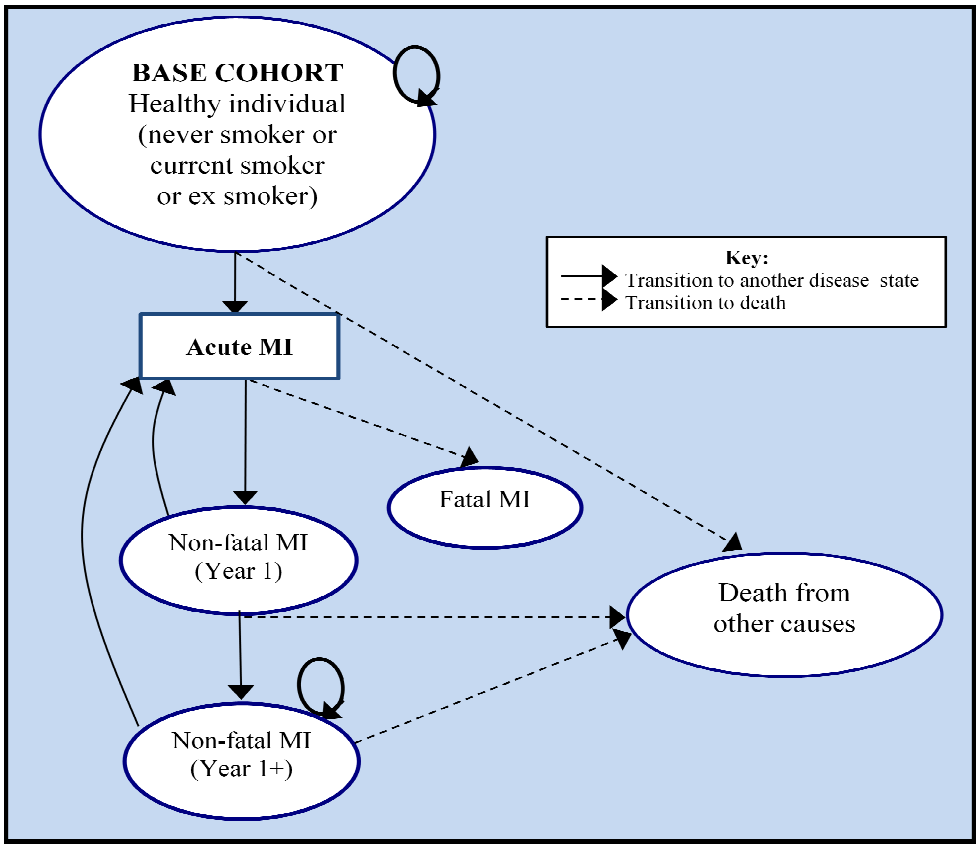
Below we discuss the Markov diagram for each clinical pathway. These are components of figure 1 that are discussed separately.

I. **Myocardial infarction (Figure 2):** During a Markov cycle, healthy individuals in the base cohort may develop first-ever acute MI event. The transition probability of this event is estimated for non-smokers, current smokers and ex-smokers from the published literature. MI may either be fatal, in which case individuals will move to the absorbing state 'fatal MI', or non-fatal, in which case they move to the state of 'non-fatal MI (year 1)'. Once in the 'non-fatal MI (year 1)' state, individuals may die due to other causes, have another acute MI event or move to non-fatal MI (year 1+) state. Beyond year 1 post-MI, the individual may remain in the same health state, or have another acute MI or die from other causes. Individuals who have a second acute MI will follow the same pathway as the first acute MI. Based on the evidence in the literature, the model assumes that the risk of recurrent MI during year 1 is greater than the risk in subsequent years. The model structure also allows the users to assign higher relative risk of stroke-related death in individuals with a history of MI. However, for the purpose of this project, the model assumed no excessive risk after MI.

   The model makes four implicit assumptions; firstly, the risk of death after acute MI is assumed to be independent of the previous history of MI or the smoking status. In other words, we assume that previous history of MI or smoking does not directly influence the outcome of MI. This assumption is likely to produce conservative estimates of the impact of smoking cessation since smokers tend to have more primary MI events compared with quitters. Secondly, the risk of recurrent MI is assumed to become stable after the first year post-MI. The risk in year 1 onwards is assumed to be lower than the risk in year 1 but higher than the risk of MI in healthy patients with no history of MI (Briggs *et al* 2007). Finally, the health care costs for MI (and other conditions modelled here) were assumed to be the same in never, current and ex smokers. This is a reasonable assumption since the primary management of care for MI patients is understood to be independent of the smoking history. While some of these assumptions may seem

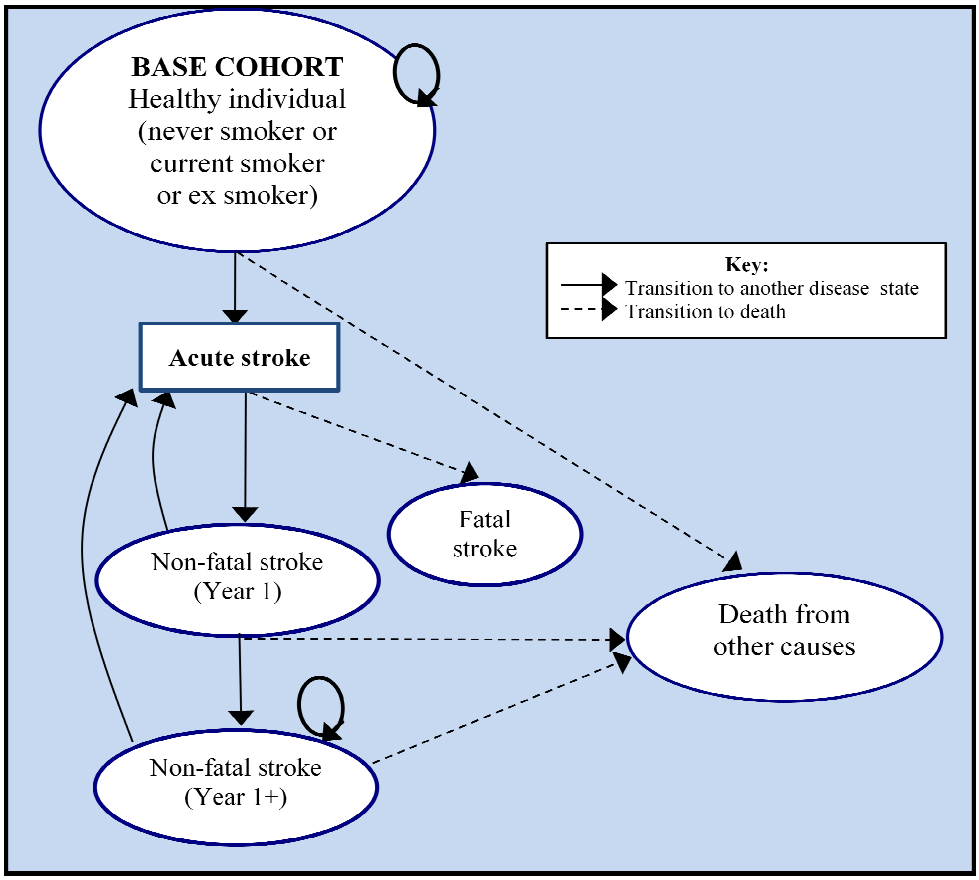
restrictive, we believe that the trade-off between model simplicity and realism adequately address the decision problem.

Figure 2: State transition diagram for the Markov model of myocardial infarction



II. **Stroke (Figure 3):** The stroke pathway is similar to the myocardial infarction pathway. Healthy individuals (never smoker or current smoker or ex-smoker) may suffer an acute stroke event which may either be fatal (health state: 'fatal stroke') or non-fatal (health state: 'non-fatal stroke (year 1)'). Like the 'non-fatal MI' patients, those with 'non-fatal stroke (year 1)' move either to 'death due to other causes' or have another acute stroke event or move to 'non-fatal stroke (year 1+)' health state. Beyond year 1, individuals either remain in the same health state, or have another acute stroke or die from other causes. The implied assumptions for the stroke pathway are the same as the MI pathway.

Figure 3: State transition diagram for the Markov model of stroke



III. **Chronic obstructive pulmonary disease (COPD) (Figure 4):** The COPD pathway has a chronic course with individuals staying with the condition until they die from COPD or due to other causes. The model accumulates costs of consumption of health care resources for all the years lived with COPD. The model allows for greater risk of death from lung cancer in COPD patients. The higher relative risk is based on the published literature.

Figure 4: State transition diagram for the Markov model of COPD

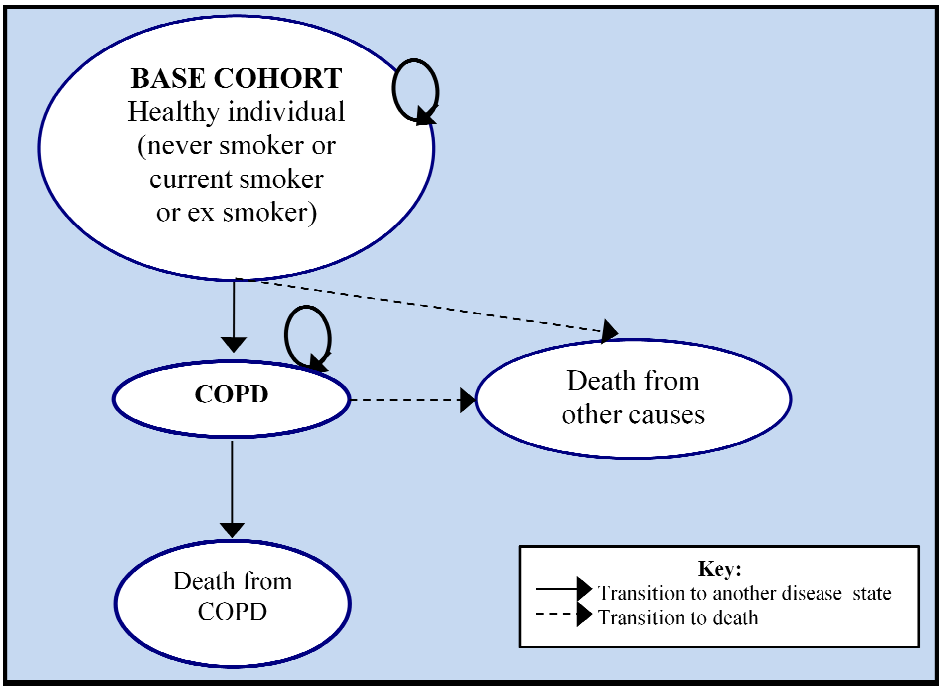
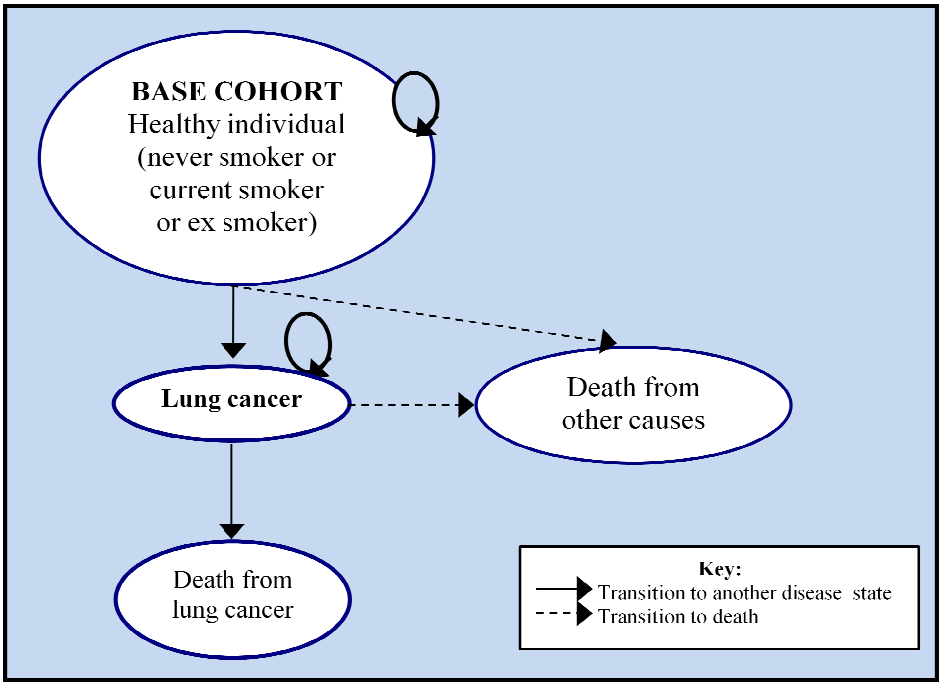


Figure 5: State transition diagram for the Markov model of lung cancer



IV. Lung cancer (Figure 5): The lung cancer pathway is similar to the COPD pathway. Once patients have developed lung cancer, they stay with the condition until death from lung cancer or other causes. During this period they incur costs associated with diagnosis and early management of lung cancer, followed by average annual cost of lung cancer

management and finally the cost of terminal care before death. The model assumes that once a patient develops lung cancer, their probability of death is independent of their smoking status.

The model runs for cohorts of never smokers, current smokers and ex smokers to estimate costs and outcomes for each pathway, for males and females. Future costs and life years are then discounted to represent societal and personal preference for the present over future.

4.2. Model parameters

Decision analytical models are driven by state transition probabilities. The model makes use of epidemiological data from published studies based on the population of England (and when not available, the UK population and beyond) to estimate age and sex-specific incidence rates and probabilities for the three smoking-related population groups, i.e. never smokers, current smokers and ex smokers. These probabilities are estimated for each transition pathway for the four clinical conditions discussed above and the transition to death. Below, we discuss the methods and the data sources used to estimate the transition probabilities. The general approach used for parameter estimation is similar in all four pathways. Data for model parameters was based on International Classification of Disease 10th Revision (ICD-10) codes outlined in table 2.

Table 2: ICD-10 codes for the smoking-related conditions evaluated in the model

Disease condition	ICD codes	Description
Myocardial Infarction	ICD 10 code: I21	Acute Myocardial Infarction
Stroke	ICD 10 code: I61	Intracerebral hemorrhage
	ICD 10 code: I62	Other non-traumatic intracranial hem.
	ICD 10 code: I63	Cerebral infarction
	ICD 10 code: I64	Stroke, not specified as inf. or hem.
Lung Cancer	ICD code: C33	Malignant neoplasm of trachea
	ICD code: C34	Malignant neoplasm of bronchus and lung
COPD	ICD 10 codes: J40 - J44	Bronchitis, emphysema and other COPD
	ICD 10 codes: J47	Bronchiectasis

I. State transition probabilities for the Myocardial Infarction and Stroke pathways

In this section, the report will discuss how the state transition probabilities for the MI and stroke pathway were estimated.

[a] **Annual probability of first ever MI or stroke in the general population:** Hardoon et al (2008) provide the incidence rate per 1,000 person years for first-ever acute MI in the British male population. These estimates were available by age groups, and included both fatal and non-fatal MIs based on 25 year follow-up of 7,735 men in the British Regional Heart Study. Age-specific rates for the longest duration of follow-up were used in the model. We estimated the one-year probability ($\text{Probability}_{1-\text{year}}$) of first ever acute MI in men using the following equation:

$$\text{Probability}_{1-\text{year}} = 1 - \exp\left(-\text{IncidenceRate}_{1-\text{year}} * 1\right) \qquad (1)$$

The annual incidence rates and probabilities for women were estimated separately by multiplying the risk ratio of acute MI in women versus men as observed in Goldacre et al (2001) by the rate reported in men in Hardoon et al (2008). Hence, the raw figures from the Goldacre et al (2001) were adjusted to more recent estimates. Appendix 3 summarises the incidence rates and the one-year probability (expressed as percentage chance) of first ever acute MI for men and women in the general population for ages 35-85+ years.

To estimate transition probability for the first ever stroke in the general population, the incidence rates reported in the Oxford Vascular Study (2002- 2004) as reported in Rothwell et al (2004) were used (see Appendix 3). The study reports incidence rates for men and women by age groups which were converted to one-year transition probabilities using equation (1).

[b] **Annual probability of first ever MI or stroke in never-smokers:** The estimates of first ever MI/stroke discussed above [a] represent the transition probabilities in the general population that includes all three smoking related groups, i.e. never, current and ex-smokers. We calculated the transition probabilities specifically for the non-smoker group by adjusting the general population estimates using the following equation from Hurley and Matthews (2007):

$$D_{ns} = D_p/((1 - p_{ex} - p_s) + p_{ex} * RR_{ex} + p_s * RR_s \qquad (2)$$

Here D_{ns} and D_p represent disease probabilities in never smokers and general population respectively, p_s and p_{ex} represent prevalence of current and ex-smokers respectively, and RR_s and RR_{ex} represent the relative risk in current and ex-smokers respectively. The prevalence of smoking was obtained from the Health Survey of England (2008) (see table 3 below). Data on relative risk for smokers (RR_s) and ex-smokers (RR_{ex}) was obtained from the INTERHEART study (Yusuf et al 2004 and Teo et al 2006) which investigated the risk factors (including smoking) associated with first-ever acute MI using data from 52 countries, including the UK. Using relative risk estimates from this study, we used equation (2) to calculate annual probability of first ever acute MI in never smokers (Appendix 4). The same approach was followed for the other three clinical pathways in the model. The relative risk estimates used in the model are summarised in table 4.

Table 3: Prevalence of smokers and ex-smokers by age groups and sex‡

Cigarette smoking status	Age groups	Men (%)	Women (%)
Current cigarette smoker	16-24	28	25
	25-34	34	25
	35-44	30	25
	45-54	22	20
	55-64	18	16
	65-74	13	13
	75 and over	6	8
	ALL	24	20
Ex-smoker	16-24	5	8
	25-34	15	17
	35-44	19	19
	45-54	27	22
	55-64	42	31
	65-74	52	32
	75 and over	59	32
	ALL	27	22

‡ Source: Health Survey of England (2008)

To estimate the relevant transition probabilities for stroke, we used the same approach as above, using relative risk estimates from Chiuve et al (2008) who studied a cohort of 71,243 men and 43,685 women to estimate the risk factors associated with primary stroke. The study reports the relative risk estimate for current smokers (RR: men = 2.01 [95% CI: 1.43 – 2.81]; women = 2.59 [95% CI: 2.16 – 3.11]) and ex-smokers (RR: 1.12 [95% CI: 1.00–1.25]).

Table 4: Estimates of odds ratio or relative risk used in the model of first event

		Smokers		Ex-smokers (time since quitting)	
		Relative Risk/Odds Ratio*	**Source**	**Relative Risk/Odds Ratio***	**Source**
First ever MI	Men	3.33 [Age: 35 - 54] 2.52 [Age: 55 and beyond]	Yusuf et al (2004)	Overall risk for ex-smokers [compared with non-smokers]: 2.0 [age: 35-39], 1.63 [age: 40 - 49], 1.67 [age: 50 - 59] and 1.51 [age: 60+] Risk based on time since quit: [compared with non-smokers] 1.88 [time since quit >1 - 3 yrs]; 1.65 [>3 - 10 yrs]; 1.61 [>10 – 15 yrs]; 1.44 [>15 yrs]	Yusuf et al (2004)
	Women	4.49 [Age: 35 - 64] 2.14 [Age: 65 and beyond]			
First ever Stroke	Men	2.01	Chiuve et al (2008)	Overall risk for ex-smokers [compared with non-smokers]: 1.12 Risk based on time since quit: [compared with current smokers]: 0.73 [time since quit 0 - <2]; 0.59 [2 - 4 yrs]; 0.59 [≥5 yrs]‡	Chiuve et al (2008); Kawachi et al (1993)
	Women	2.59			
Lung Cancer	Men	9.87	Gandini et al (2008)	Overall risk for ex-smokers [compared with non-smokers]: □ Men: 3.79; Women: 3.03 Risk based on time since quit: [compared with non-smokers]: □ Men: 6.16 [0 - <5 yrs]; 3.88 [5 - <10 yrs]; 1.33 [≥10 yrs] Women: 6.67 [0 - <5 yrs]; 3.07 [5 - <10 yrs]; 1.35 [≥10 yrs]	Freedman et al (2008); Gandini et al (2008)
	Women	7.58			
COPD	Men Women	6.15	Rodriguez et al (2009)	3.45	Rodriguez et al (2009)
Other diseases	Men Women	1.70	Jha et al (2008)	1.17 ∫	Kenfield et al (2008); Jha et al (2008)

*Note: Any inconsistent estimates were assumed to be equal to the risk in the last period

† RR for ex-smokers from Freedman et al (2008) was adjusted using Gandini et al (2008)

‡ Risk beyond 5 years was assumed to be equal to the earlier period to avoid inconsistent estimates for time since quitting

□ Risk in Freedman et al (2008) was adjusted using Gandini et al (2008)

∫ Risk in Kenfield et al (2008) was adjusted using Jha et al (2008)

[c] **Annual probability of first ever MI or stroke in current and ex-smokers:** Estimates for current and ex-smokers were obtained using the following equations respectively:

$$D_s = D_{ns} * RR_s \qquad (3)$$

$$D_{ex} = D_{ns} * RR_{ex} \qquad (4)$$

Here D_{ns} was the same as reported in Appendix 3 while the relative risk for smokers (RR_s) and ex-smokers (RR_{ex}) was estimated from the INTERHEART study (Yusuf et al 2004, Teo et al 2006) for MI and from Chiuve et al (2008) for stroke. The age and sex-specific probabilities are summarised in Appendix 4 and 5.

[d] **Annual probability of first ever MI or stroke as a function of time since quitting in ex-smokers:** The model takes account of the decreasing risk of developing first ever MI or stroke as a function of time since quitting. We used odds ratios (ORs) from Teo et al (2006) to estimate diminishing risk of acute MI in ex-smokers compared with never smokers. The ORs were used to calculate age and sex-specific relative risk, using the following equation from Zhang and Yu (1998).

$$RR_{ex(1-3yrs)} = \frac{OR_{ex(1-3yrs)}}{(1 - D_{ns})\left(D_{ns} * OR_{ex(1-3yrs)}\right)} \qquad (5)$$

Here $RR_{ex(1-3yrs)}$ and $OR_{ex(1-3yrs)}$ represent relative risk and odds ratio respectively in ex-smokers who have quit for 1-3 years. Using age and sex-specific D_{ns} in equation (5), we estimated RR for the following categories of years since quit: >1 – 3 years, >3 – 5 years, >5 – 10 years, >10 – 15 years, >15 – 20 years and >20 years. Following on from this, relative risk estimates were used to calculate age and sex-specific probabilities as a function of years since quitting:

$$D_{ex(1-3yrs)} = D_{ns} * RR_{ex(1-3yrs)} \qquad (6)$$

For the stroke pathway, the risk in ex-smokers was calculated using relative risk estimates from Kawachi et al (1993) that evaluated a prospective cohort of 117,006

women for 12 years to assess the impact of smoking cessation on first ever stroke. The RR estimates were available with reference to current smokers. Any inconsistencies in the reported estimates were adjusted by assuming the relative risk to be equal to the immediately preceding period. Hence, the model assumed that the risk of stroke in ex-smokers becomes stable 2 – 4 years after quitting. Since comparable estimates for men were not available, the model assumed the same RR for men. However, when estimating age and sex-specific probabilities, equation (6) multiplied the RR in quitters with sex and age specific D_{ns}.

These parameter estimates are presented in Appendix 4 and 5.

[e] **Probability of fatal MI or fatal stroke (following first and subsequent events):** The probability of MI being fatal is estimated from a recent study (Brophy et al 2010) that evaluated mortality rate in 157,142 MI patients in England (Hospital Episodes Statistics) and Wales (Patient Episode Database) between 2003 and 2006. The study reports 90-day mortality by age and sex for diabetic and non-diabetic patients. We calculated a weighted average of diabetic and non-diabetic study populations to estimate the mortality rate following MI. However, since we were interested in early mortality following MI, the 90-day mortality rate was adjusted to estimate acute phase (30-day mortality). This was done by multiplying the 90-day mortality in Brophy et al by the ratio of 30-day to 90-day mortality calculated from a US study by Fihn et al (2009) [ratio = 0.67].

Similarly, the risk of death following acute stroke was estimated from Lewsey et al (2009) that reported 30-day case-fatality rate following stroke in a 20 year study based on the entire Scottish population. The probability of non-fatal stroke was equal to 1 minus the probability of fatal stroke (the same is the case with non-fatal MI).

[f] **Probability of recurrent MI or stroke:** Patients who survive acute MI or stroke may have a second MI or stroke, respectively. For MI patients, the risk of recurrence in the 1st year is estimated from a recent European trial (EUROPA) that randomised 12,218 patients with stable coronary heart disease to ACE inhibitor Perindropil or placebo (Briggs et al 2007). During this trial, probability of 0.161 was estimated for recurrent cardiovascular event in the 1st year. This was taken as the probability of recurrence in

the general population and was used to estimate the risk of recurrence among non-smokers using equation (2). The risk of recurrence among smokers and ex-smokers was then estimated using a relative risk of 1.51 for smokers and 1.48 for quitters of >1-3 years and 1.02 for quitters beyond 3 years of cessation (Rea *et al* 2002). The same approach was used for recurrence beyond year 1 of the incident MI. For stroke patients, the probability of recurrence in year 1 was 0.093 based on follow-up of stroke patients in the EXPRESS study which was nested within the population-based Oxford Vascular Study (Rothwell et al 2007). This was taken as the probability of recurrence in the general population. Risk in non-smokers, smokers and ex-smokers was subsequently calculated using RR estimates available for the incident stroke, using the same approach as above. Beyond Year 1, the probability of acute stroke was taken to be equal to 5% (Lip and Kalra 2009). We assumed the same rate of subsequent MI for year 1+ following MI.

II. State transition probabilities for the Lung Cancer and COPD pathways

[a] **Annual probability of developing lung cancer:** Age and sex-specific incidence rates of developing lung cancer in the general population were based on the estimates from Cancer Research UK (2007) [see Appendix 3]. The risk in non-smokers was estimated using equation (2) above. The relative risk in current smokers was taken from a meta-analysis of observational studies published between 1961 and 2003 that evaluated the association between tobacco smoking and each type of cancer, including lung cancer (Gandini et al 2008). For ex-smokers, the relative risk was estimated from a recent study (Freedman et al 2008) that followed 279,214 men and 184,623 women between the ages 50 to 71 from 1995/6 to 2003. The risk observed in Freedman et al (2008) for ex-smokers was much higher than the risk in current smokers reported in the meta-analysis (Gandini et al 2008). Hence, we adjusted the risk for quitters in Freedman et al (2008) by using equation 7.

$$RR_{(ex:1-<5yrs)} = RR_{f(ex:1-<5yrs)} * \frac{RR_{g(smokers)}}{RR_{f(smokers)}} \qquad (7)$$

Here $RR_{(ex:1-<5yrs)}$ is the estimated relative risk in ex-smokers (compared to non-smokers) for 1-<5 years since quitting, $RR_{f(ex:1-<5yrs)}$ is the risk reported in Freedman et al (2008), $RR_{f(smokers)}$ is the relative risk in smokers (Freedman et al 2008) and

$RR_{g(smokers)}$ is the relative risk in smokers as reported in the meta-analysis (Gandini et al 2008). The relative risk estimates are summarised in table 4.

[b] **Probability of death from lung cancer:** In the model, lung cancer patients can either stay alive with lung cancer, die from lung cancer or die of other causes. The probability of death from lung cancer was estimated based on data from Cancer Research UK that provides estimates of 5-year probability of survival from lung cancer. These estimates were used to calculate 5-year mortality rate (= 1 – Survival rate) and then 1-year mortality rate for lung cancer using the following equation:

$$\text{IncRate}_{1-\text{year}} = \frac{\left[\ln\left(1 - \text{IncRate}_{5-\text{year}}\right)\right]}{5} \qquad (8)$$

Subsequently, annual rate was converted to annual probability by using equation (1).

We noticed in the literature that not all deaths in lung cancer patients are due to lung cancer itself. Tammemagi et al (2003) note that several studies have found that approximately 25% - 40% of non-small cell lung cancer patients died due to competing causes with no evidence of disease progression or recurrence; hence, the assumption that all lung cancer patients die from their disease may be inappropriate. Therefore, we assumed that 30% of the mortality in lung cancer patients was due to causes other than the disease itself; hence the probability of death from lung cancer was rescaled to reflect the adjusted mortality. This approach was taken to avoid double counting deaths due to other causes that are already captured as death due to other causes.

[c] **Annual probability of developing COPD:** Age and sex-specific incidence rates for COPD were obtained from Rodriguez et al (2009) that report COPD incidence in individuals aged between 40-89 years with no previous diagnosis of COPD, asthma or cancer. The cohort was identified from the UK General Practice database of primary care records. The study provides incidence rates for non-smokers, current smokers and ex-smokers.

[d] **Probability of death from COPD:** COPD is a chronic condition and the risk of death from the disease is smaller than acute conditions associated with smoking. Case fatality rate from COPD was obtained from Rodriguez et al (2010). This was then

converted to annual probability rate using equation (1). We further noted in the literature that only a small proportion of deaths in COPD patients happen due to the disease itself. Hence, in order to avoid double counting, the probability of death from COPD was adjusted using Keistinen et al (1998) that showed that 21.4% of deaths in male COPD patients and 27.1% of deaths in female COPD patients occurred due to the disease itself. This adjusted rate was then used to derive annual probability of death due to COPD.

III. Probability of death due to other causes

The probability of death due to other causes (other than myocardial infarction, stroke, lung cancer and COPD) was estimated using the population life tables for England and Wales (Office for National Statistics 2008). Since life tables include the deaths caused by the four diseases modelled here, these deaths were taken out from the tables using specific ICD codes (table 2) for each of these disease conditions. Hence, the rate of 'death from other causes' in the base model was estimated by eliminating deaths from all four conditions, while the rate for each disease pathway was estimated by taking away respective disease specific deaths from the life tables. These were taken as the underlying rates in the general population. We then used equation (2) to estimate the rate among non-smokers. Since smoking increases the risk of mortality due to other causes, the risk of death from other causes was adjusted for smokers by multiplying the risk in the general population by 1.7 (Jha et al 2008). The relative risk in ex-smokers was estimated by multiplying the relative risk in smokers in Jha et al (2008) by the risk ratio of death from other causes in ex-smokers and current smokers as reported in Kenfield et al (2008). Based on this approach, the risk in ex-smokers was estimated to be 1.17 times the risk in non-smokers. These relative risk estimates were then explicitly incorporated in the estimation of costs and life years in the base (healthy state) model as well as each disease-specific pathway to allow patients to die from other causes and also incur costs associated with mortality due to other causes. This approach allows capturing of additional risk of mortality and costs associated with continued smoking and smoking cessation, over and above the increased risk due to MI, stroke, lung cancer and COPD.

4.3. Health care costs for smoking-related diseases

The health care costs for the four smoking related conditions modelled in this study are summarised in table 5. Only the direct costs were estimated for each health state. Costs are measured in British Pounds. Cost estimates were obtained from a focused review of literature to identify economic papers or cost of illness studies that reported condition-specific costs. When multiple cost studies were available, the most recent and relevant costs were adopted by mutual agreement between researchers. Costs were inflated to reflect UK prices in the year 2009 using the 'Hospital and Community Health Services' inflation index for the NHS (PSSRU 2009, table 2 p.175):

$$P_2 = \frac{P_1 * PPI_2}{PPI_1} \qquad (9)$$

Here P_2 refers to the price in the current period and P_1 refers to the baseline price as reported in the original study. PPI_1 and PPI_2 represent the Pay and Price Indices at the two time points respectively. Below we discuss the cost data for the conditions modelled here.

I. Myocardial infarction

The costs associated with myocardial infarction were divided into three periods, i.e. cost of treating the acute phase of MI (modelled as an event), cost of managing MI during the 1st year post-MI, and the cost in subsequent years (year 1+). Costs for individuals experiencing non-fatal MI were equal to the sum of acute phase costs and the cost of management in year 1. These cost estimates are summarised table 5.

The cost of acute MI event was estimated from Hartwell et al (2005) by taking a weighted average of the cost of initial treatment by thrombolysis (figures reported at 2002/03 prices: £3,656.16 and £4,736.76; mean = of £4,196.46) and treatment by angioplasty (range: from £5,915.60 to £6,996.20; mean =£6,455.90). Weighting was done based on the Myocardial Ischaemia National Audit Project report (Health Quality Improvement Partnership 2010) that reports that 47% of acute MI patients received primary angioplasty in England in 2008/9. We assumed that the remaining patients received thrombolysis. The estimated weighted-average was equal to £5,258.40. The costs were inflated to current price using equation (9) to reach £6,609.29.

The cost of MI in the 1st year (post-acute-event) and the subsequent years (year 1+) were estimated using the same approach (see table 5). For year 1 following MI, the annual costs were estimated to be £1,964 (Vergel, 2007) and for year 1+ the cost was £816 (Briggs et al 2007). These were adjusted to current price to arrive at £2,346.67 and £974.99 respectively. Finally the cost of death from MI was also estimated from Briggs et al (2007) at £3015.0 (adjusted to £3602.4).

II. Stroke

Similar to MI, the costs associated with stroke were divided into three periods, i.e. cost of treating acute phase of stroke (modelled as an event), cost of managing stroke during the 1st year post-stroke, and the costs in subsequent years (year 1+). The costs during acute stage and year 1 were estimated from Kalra et al (2005). The study randomised patients to one of the three treatment strategies for the management of stroke. These included stroke unit, stroke team and home care strategies. To derive the costs associated with acute stroke and post-stroke year 1, we assumed that patients had equal probability of receiving any of the three interventions. To estimate the costs associated with stroke year 1+, we used the 5-year stroke management cost from Youman et al (2003) and subtracted the year 1 costs (already estimated) and then divided the remainder by four. Table 5 summarises the costs for each of these pathways.

III. Chronic obstructive pulmonary disease (COPD)

The cost of treating COPD varies depending on severity of the disease. The estimated cost of an acute episode ranges from £8 - £15 for someone with mild COPD, £23 - £95 for mild to moderate COPD patients to £1,600 for patients with severe COPD (British Lung Foundation, 2009). The annual cost of COPD per patient was obtained from Britton et al (2003) which estimates the cost to be £819.42 per patient (£1,120.08 at current price). To estimate the cost of death from COPD, we assumed that patients experience severe exacerbation before death; hence, the cost was severe exacerbation from Britton et al (2003) was used as cost of death from COPD (see table 5).

Table 5: Health care costs associated with MI, stroke, COPD and lung cancer

Condition	Original costs	Year	Adjusted costs to 2009 prices (£)*	Sources
Myocardial Infarction (AMI)				
Initial treatment AMI	£5,258.40	2002-03	£6,609.29	Estimated by taking a weighted average of the cost of thrombolysis and angioplasty based initial management of MI (Hartwell et al 2005) using relative proportions as reported in the MI National Audit Project (2009)
MI state (Year 1)	£1,964.00	2003-04	£2,346.67	Vergel et al (2007)
After MI state (Year 2 and after)	£816.00	2004	£974.99	Briggs et al (2007)
Cost of death from MI	£3,015.00	2004	£3,602.44	Briggs et al (2007)
Stroke				
Acute stroke management	£8825 (Stroke Unit) £5952 (Stroke Team) £3856 (Home care)	1997-98	£9,247.64	Kalra et al (2005). We assumed equal probability of receiving the three treatment options.
Post-stroke (Year 1)	£2625 (Stroke Unit) £3575 (Stroke Team) £2984 (Home Care)	1997-98	£4,558.06	As above
Post-stroke (Year 2 and after)	£855 (Stroke Unit) £1524 (Stroke Team) £2457 (Home Care)	1997-98	£2,400.13	As above
Fatal stroke	£7,041.00	2004	£8,412.87	Youman et al (2003)

Condition	Original costs	Year	Adjusted costs to 2009 prices (£)*	Sources
Lung Cancer				
Annual cost	£5,032.31	2005-06	£5,610.95	Estimated by using annual lung cancer related costs for the NHS (Allender et al 2009) and the prevalence rate in the UK
Lung Cancer (Initial treatment)			£12,902.47	Estimated by applying relative ratio of annual and initial treatment costs for lung cancer in the US (US EPA 2006) to the annual cost of lung cancer in the UK
Lung Cancer (terminal care)			£14,918.94	As above
COPD				
Annual cost	£819.42	2000-01	£1,120.08	Britton et al (2003) adjusted for UK costs by NICE (2004)
Cost of death from COPD	£1,307.10	2000-01	£1,786.70	Assumed to be equal to the cost of severe exacerbation. Sources: As above
Death from other causes			£10,285.00	Briggs et al (2007)

* All unit costs have been inflated to 2009 prices using Hospital and Community Health Services pay and price inflation. See PSSRU 2009 Table 2 page 175.

IV. Lung cancer

Allender et al (2009) estimated that the total cost to the UK NHS for treating lung cancer was £327.1 million. Furthermore, Cancer Research UK estimated that the total number of lung cancer patients in the UK were 65,000 during the year 2008 (Cancer Research UK, 2010). Hence, the average cost per patient was calculated by dividing the total cost by the number of patients with lung cancer to reach an estimated annual cost of £5032.31 per patient (£5,610.95 at 2009 price) (see table 5). Costs of initial and terminal care of lung cancer were estimated by applying the relative ratio of initial and annual treatment costs for lung cancer in the US (US EPA 2006) to the annual cost of lung cancer in the UK. The same approach was taken to estimate the cost of terminal care (see table 5).

5. RESULTS OF THE ECONOMIC ANALYSIS

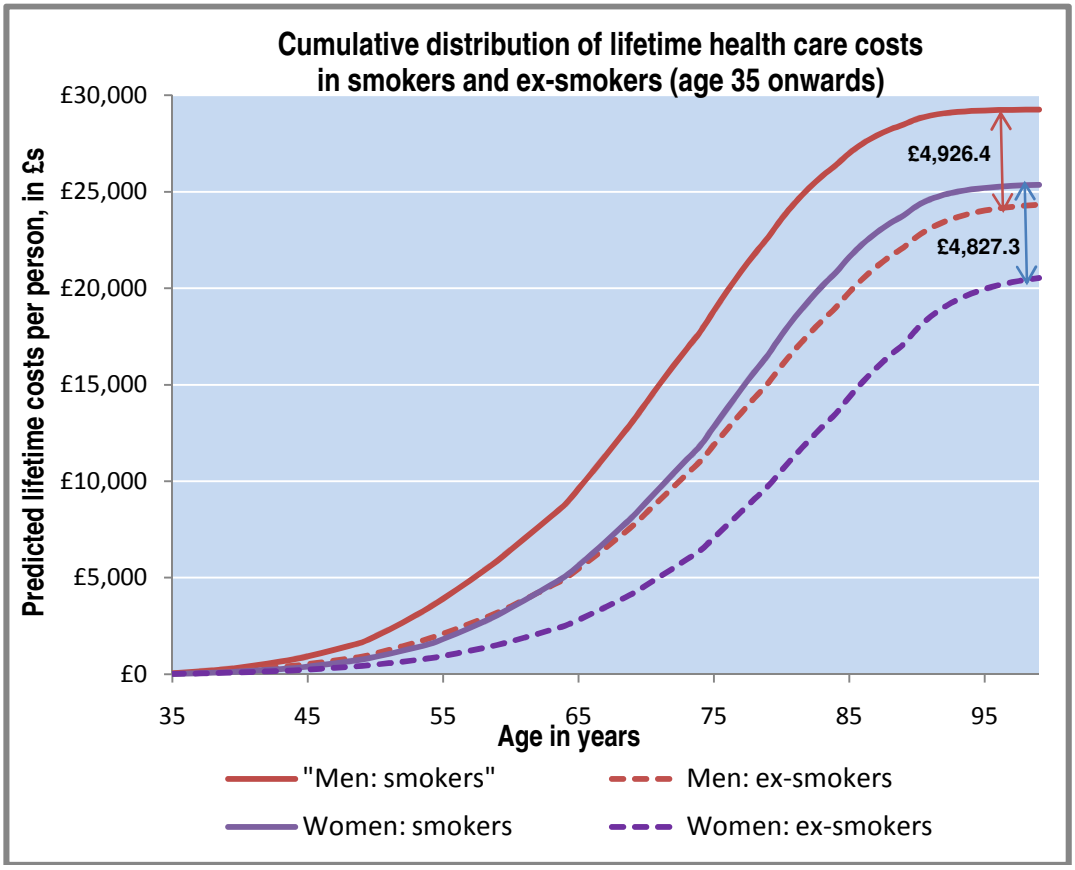
The results of the economic analysis are presented as cost savings and life years gained during the lifetime of a cohort of 1,000 individuals in the population. The results are presented separately for men and women and for current and ex-smokers. The impact of smoking cessation is evaluated on a varying scale of cessation rates achieved for the cohort. Costs and life years gained were discounted at the rate of 3.5% to account for the preference for present over future. Both undiscounted and discounted results are presented.

The cohort entered the model at the age of 35 years; individuals were assumed to be healthy (free from the four smoking-related diseases) and were followed until death or until they reached the age of 100 years, whichever occurred first. Table 6 shows the lifetime health care costs attributable to morbidity and mortality due to the four smoking-related conditions and death due to other causes. The difference between lifetime health care costs for smokers and ex-smokers for a cohort of 1,000 individuals was predicted to be £4,926,398 for men and £4,827,297 for women (not discounted). Figure 6 shows the predicted cumulative distribution of health care costs (per person) incurred by smokers and ex-smokers over their lifetimes. The figure suggests that the difference in incurred costs is much pronounced beyond the age of 65 years and becomes stable beyond the age of 85 years.

Table 6: Lifetime health care costs due to MI, stroke, Lung Cancer, COPD and other causes of death for a cohort of 1,000 individuals (model start age = 35 years)

Smoking group	Discounting	Lifetime costs		10 year costs		20 year costs	
		Men	Women	Men	Women	Men	Women
Non-smokers	No	£20,655,822	£17,515,251	£282,897	£120,926	£1,222,359	£522,409
	Yes (3.5%)	£5,225,998	£3,852,878	£228,571	£97,814	£764,529	£328,486
Smokers	No	£29,255,512	£25,352,486	£766,964	£320,360	£3,460,390	£1,564,607
	Yes (3.5%)	£9,300,053	£7,002,511	£616,323	£257,155	£2,150,373	£969,574
Ex-smokers	No	£24,329,114	£20,525,188	£445,663	£202,089	£1,865,820	£822,517
	Yes (3.5%)	£6,716,501	£4,878,581	£361,744	£163,713	£1,171,410	£519,712
Cost of smoking: difference between non-smokers and smokers	No	£8,599,690	£7,837,235	£484,067	£199,434	£2,238,031	£1,042,198
	Yes (3.5%)	£4,074,056	£3,149,633	£387,752	£159,342	£1,385,844	£641,088
Cessation savings: difference between smokers and ex-smokers	No	£4,926,398	£4,827,297	£321,302	£118,271	£1,594,570	£742,090
	Yes (3.5%)	£2,583,552	£2,123,930	£254,579	£93,442	£978,963	£449,862

Figure 6: Cumulative distribution of lifetime health care costs in smokers and ex-smokers (per person)*



* Costs are not discounted.

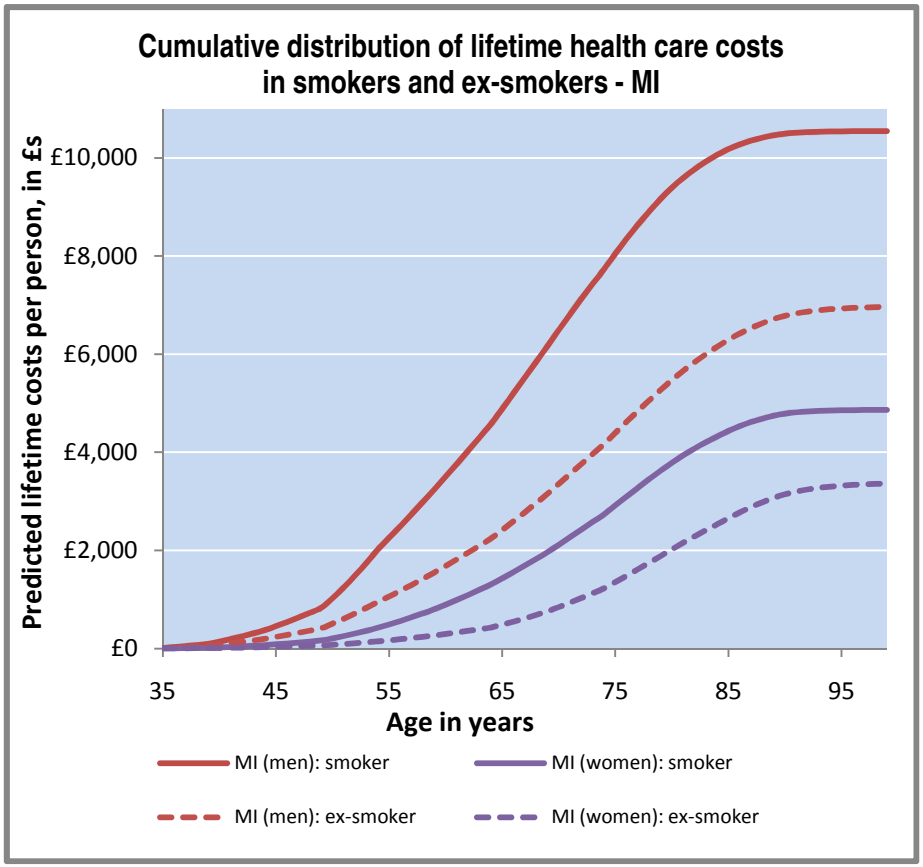
Table 7 shows the cost savings associated with varying levels of smoking cessation in the cohort. For example, if 5% of the cohort of 1,000 men quit smoking at the age of 35 years, the lifetime cost savings for the cohort is predicted to £246,320 (undiscounted) or £129,178 (after discounting at 3.5%) for men and £241,365 (undiscounted) or £106,197 (after discounting at 3.5%) for females. These figures can be useful when evaluating the cost savings associated with current or future smoking cessation programmes with known rates of smoking cessation.

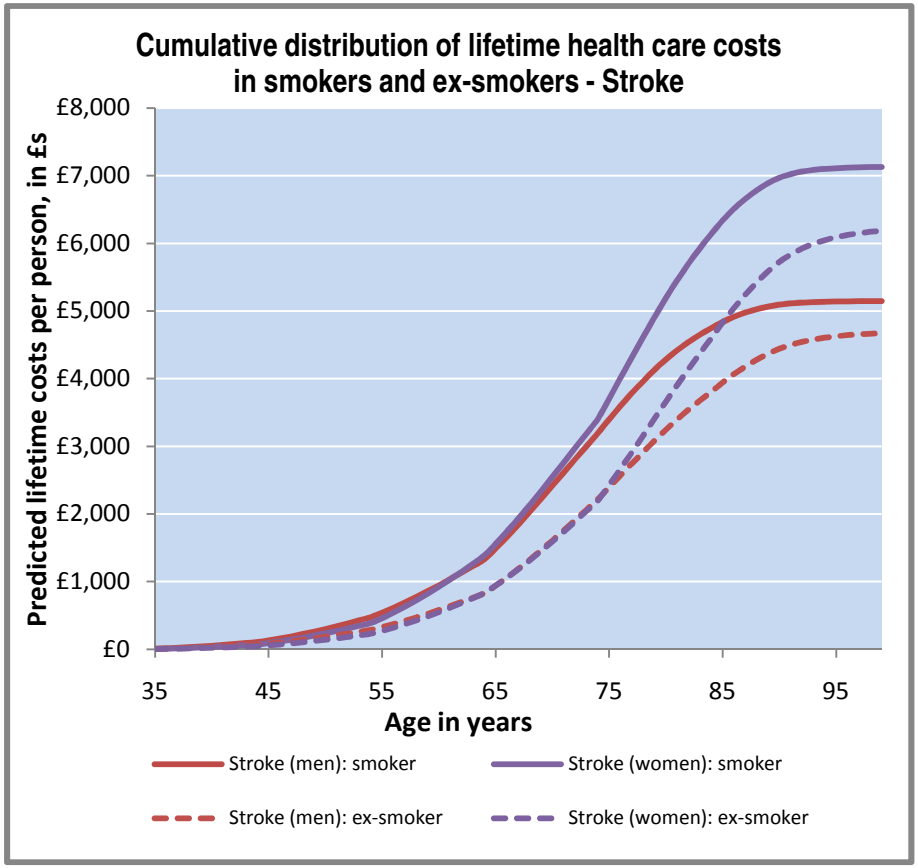
Table 7: Lifetime cost savings (in health care resource use) associated with smoking cessation in a cohort of 1,000 individuals (cohort start age = 35 years)

	Men		Women	
	Cost difference		Cost difference	
Cessation Rate	Not discounted	Discounted (3.5%)	Not discounted	Discounted (3.5%)
5%	£246,320	£129,178	£241,365	£106,197
10%	£492,640	£258,355	£482,730	£212,393
15%	£738,960	£387,533	£724,095	£318,590
20%	£985,280	£516,710	£965,459	£424,786
25%	£1,231,599	£645,888	£1,206,824	£530,983
30%	£1,477,919	£775,066	£1,448,189	£637,179
35%	£1,724,239	£904,243	£1,689,554	£743,376
40%	£1,970,559	£1,033,421	£1,930,919	£849,572
45%	£2,216,879	£1,162,598	£2,172,284	£955,769
50%	£2,463,199	£1,291,776	£2,413,649	£1,061,965
55%	£2,709,519	£1,420,954	£2,655,014	£1,168,162
60%	£2,955,839	£1,550,131	£2,896,378	£1,274,358
65%	£3,202,159	£1,679,309	£3,137,743	£1,380,555
70%	£3,448,479	£1,808,487	£3,379,108	£1,486,751
75%	£3,694,798	£1,937,664	£3,620,473	£1,592,948
80%	£3,941,118	£2,066,842	£3,861,838	£1,699,144
85%	£4,187,438	£2,196,019	£4,103,203	£1,805,341
90%	£4,433,758	£2,325,197	£4,344,568	£1,911,537
95%	£4,680,078	£2,454,375	£4,585,932	£2,017,734
100%	£4,926,398	£2,583,552	£4,827,297	£2,123,930

We further investigate the distribution of the costs associated with each of the four smoking-related conditions explicitly modelled (figure 7). Cumulative costs are functions of cumulative risk of respective disease pathways within the competing risk model. Hence, since lung cancer is a relatively rare event compared with myocardial infarction or stroke, its cumulative probability and hence the cumulative predictive cost per person is smaller than MI or stroke. The results suggest that the greatest cost savings for both men and women after smoking cessation occurs due to reduction in MI events and the smallest gain is due to reduction in the incidence and the associated cost of lung cancer. Note that the vertical axes of the graphs are not drawn to the same scale.

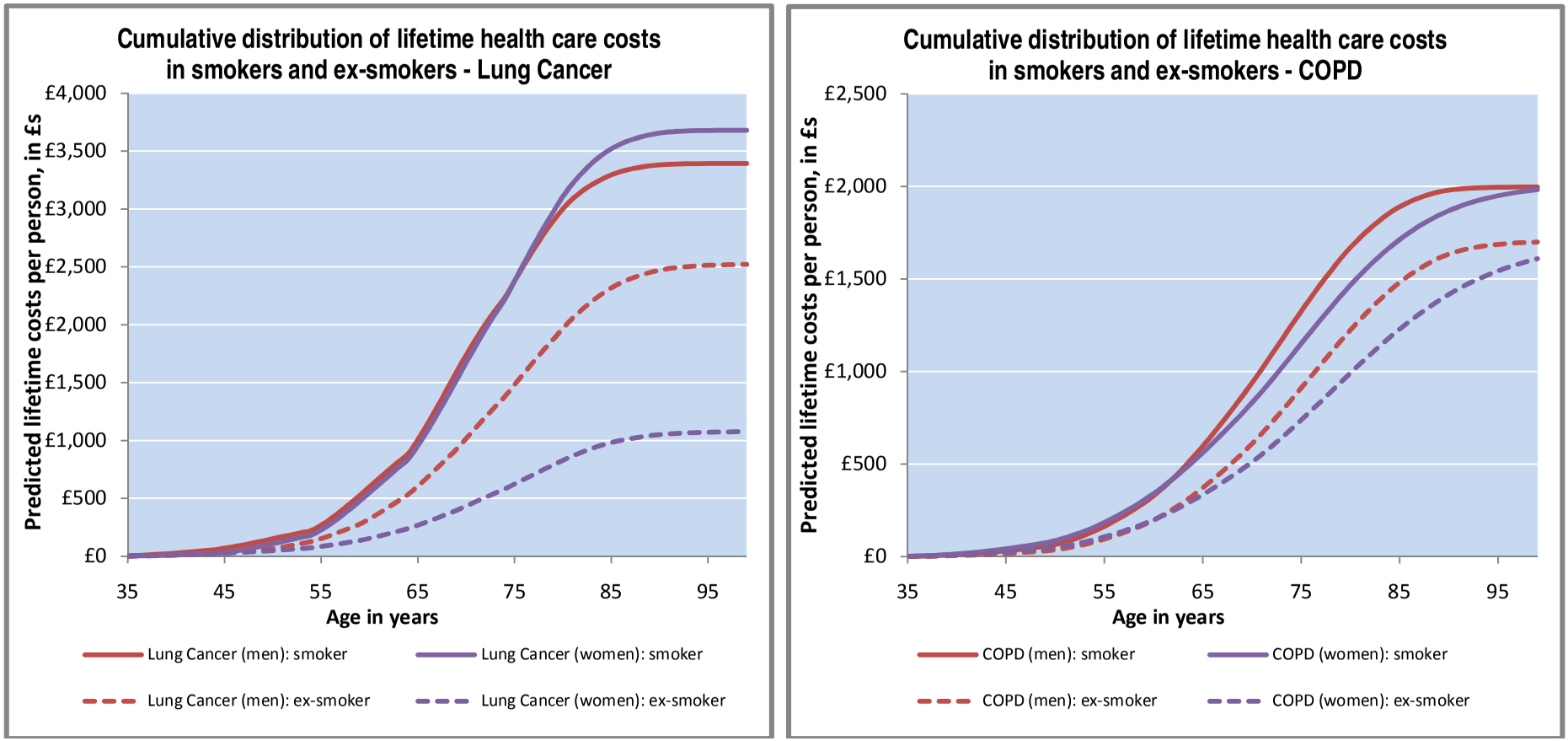
Figure 7 (A): Cumulative distribution of lifetime health care costs (per person) due to the four smoking-related conditions*





* Costs not discounted.

Figure 7 (B): Cumulative distribution of lifetime health care costs (per person) due to the four smoking-related conditions



The model also explores the impact of smoking cessation on life years lived. Figure 8 presents the predicted survival curves for smokers and quitters showing that smoking cessation is likely to increase the probability of survival in men and women. The area between the solid and the dotted lines represents the predicted gain in life years after smoking cessation.

Figure 8: Predicted survival of smokers and ex-smokers by sex

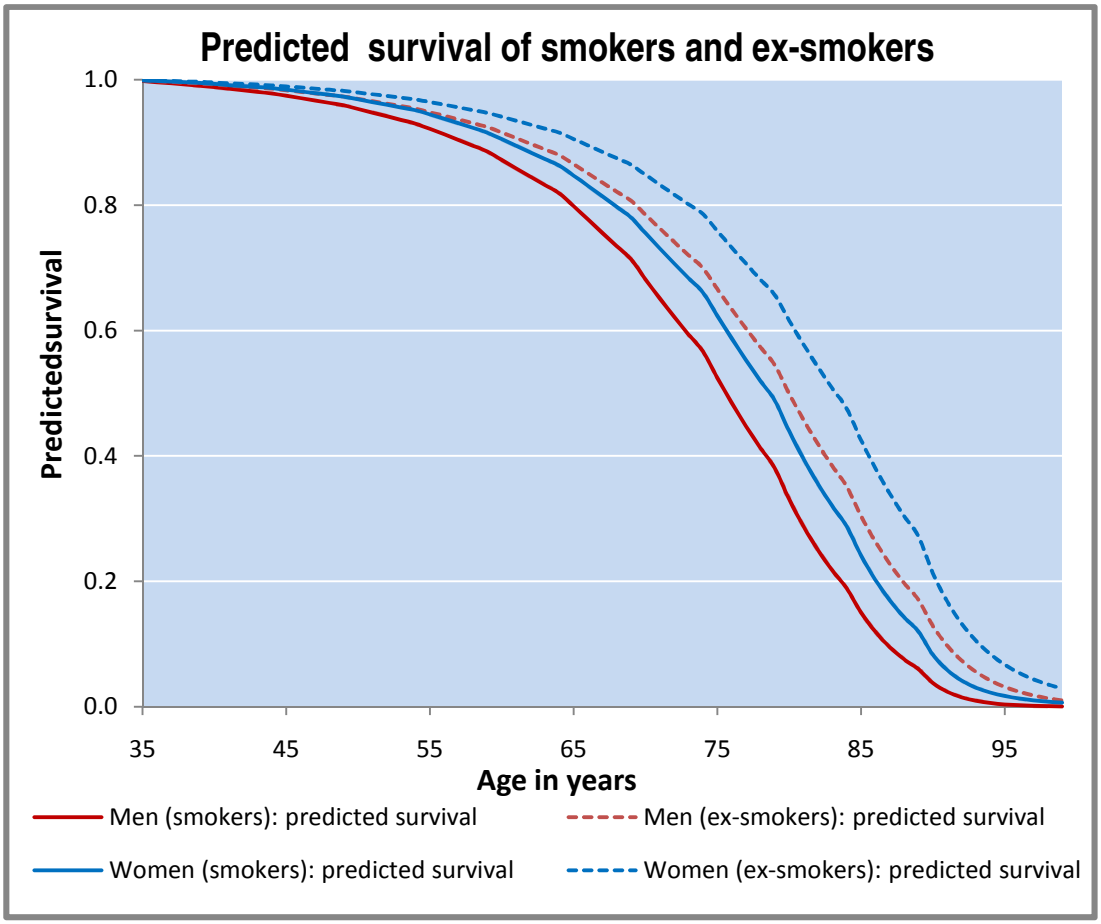


Table 8 summarises the predicted life years lived by randomly selected healthy cohorts of non-smokers, current smokers and ex-smokers (cohort size = 1,000 individuals for each of the smoking-related categories) starting at the age of 35 years. The results predict that smoking cessation would result in life year gain of 4,262 years (undiscounted) or 1,069 years (after discounting at 3.5%) in men and 4,534 (undiscounted) or 1,046 (after discounting at 3.5%) in women for a cohort of 1,000 smokers. We further explored gain in life years for a range of smoking cessation rates. For instance, our model predicts that a 5% cessation rate in a cohort of 1,000 male smokers would result in a gain of 213.1 years (undiscounted) or 53.5 (discounted) years over the lifetime of the cohort. Since the fatal

events averted by smoking cessation were likely to occur in later years of life, the discounted estimates of life years gained are much smaller than the undiscounted estimates.

Table 8: Predicted life years for non-smoker, current smoker and ex-smoker cohorts of 1,000 individuals (model start age = 35 years)

	With and without discounting	Men	Women
Non-smokers	Without discounting	45,823.6	48,575.7
	With discounting (at 3.5%)	22,065.3	22,702.7
Smokers	Without discounting	39,213.7	42,054.7
	With discounting (at 3.5%)	20,461.6	21,227.8
Ex-smokers	Without discounting	43,476.1	46,588.7
	With discounting (at 3.5%)	21,531.1	22,273.7
Difference between current and ex-smokers	Without discounting	4,262.40	4,534.02
	With discounting (at 3.5%)	1,069.48	1,045.94

Table 9: Predicted life years gained (in natural units) as a result of quitting (cohort size = 1,000 individuals; model start age = 35 years)

	Men		Women	
Cessation Rate	**Undiscounted**	**Discounted**	**Undiscounted**	**Discounted**
5%	213.1	53.5	226.7	52.3
10%	426.2	106.9	453.4	104.6
15%	639.4	160.4	680.1	156.9
20%	852.5	213.9	906.8	209.2
25%	1065.6	267.4	1133.5	261.5
30%	1278.7	320.8	1360.2	313.8
35%	1491.8	374.3	1586.9	366.1
40%	1705.0	427.8	1813.6	418.4
45%	1918.1	481.3	2040.3	470.7
50%	2131.2	534.7	2267.0	523.0
55%	2344.3	588.2	2493.7	575.3
60%	2557.4	641.7	2720.4	627.6
65%	2770.6	695.2	2947.1	679.9
70%	2983.7	748.6	3173.8	732.2
75%	3196.8	802.1	3400.5	784.5
80%	3409.9	855.6	3627.2	836.8
85%	3623.0	909.1	3853.9	889.0
90%	3836.2	962.5	4080.6	941.3
95%	4049.3	1016.0	4307.3	993.6
100%	4262.4	1069.5	4534.0	1045.9

We used the model to answer further two questions: 1) what is the total lifetime cost of continued smoking to the NHS for the current (prevalent) population demographics of England; 2) what is the maximum total lifetime cost savings to the NHS for the current (prevalent) population of England if all smokers quit smoking. The first question refers to the additional health care costs due to smoking-related conditions for the current population demographics and smoking prevalence in England, i.e. it estimates the additional lifetime cost of current adult smokers in England (≥35 years of age) compared to non-smokers. Note that the estimate relates to the sum total of additional costs for all smokers currently alive and the time period of cost incurrence is from now until death or reaching the age of 100 years, whichever occurs first. Hence, we do not include the additional cost already incurred in the past due to smoking behaviour. This estimate indirectly indicates the potential cost savings that can be achieved by primary prevention of smoking uptake. The second question refers to the maximum lifetime cost savings in the prevalent population of England after smoking cessation. Again, the estimate relates to the savings from now until death or the age of 100, whichever occurs first. These are important questions for researchers and policy-makers and will help put the cost estimates into perspective. For both analyses, we assumed that non-smokers, smokers and ex-smokers continue their smoking status during their lifetimes. Most recently available population demographics (2009) and smoking prevalence (2008) in England were used for this analysis.

The lifetime cost of smoking was estimated by taking the difference between lifetime health care costs of smokers and non-smokers for each start age in the model and then multiplying the cost difference by the number of individuals in the population of the particular age and further multiplying by smoking prevalence in England for the particular age. The model was then run for all start ages between 35 – 99 years and lifetime costs were estimated for each age cohort until the cohort reached 100 years. Finally, the total lifetime cost of smoking was estimated by taking the sum of additional lifetime cost of smoking for all age groups. Using this approach, we estimate additional health care costs that the NHS will incur if the current prevalent population of England continued their smoking behaviour until death or until they reach the age of 100 years. Similarly, the lifetime cost savings from smoking cessation was estimated by taking the difference between lifetime health care costs of smokers and ex-smokers for each start age in the model and repeating the above calculations. The calculation thus estimates cost savings if all smokers quit today.

The results for cost of smoking and savings from cessation for each age group in the population are presented in appendices 8 and 9 of the report. Table 10 summarises the total lifetime health care cost of smoking and the estimated savings from smoking cessation when applied to the prevalent adult population of England (≥35 years old). Our results show that the total lifetime health care cost of smoking for the prevalent population in England, over and above the health care costs of non-smokers, is estimated to be £23.3 billion for men and £21.4 billion for women, totalling to £44.8 billion for the smoking population of England. When these costs are discounted, the total cost of smoking is predicted to be £29.0 billion at 3.5% and £21.3 billion at 6.0% discount rates. It should be noted that the time horizon for cost calculations is between now and the time of death or until the cohort reaches the age of 100 years.

Table 10: Lifetime health care cost of smoking and savings from smoking cessation applied to the prevalent adult population in England, 35 year old and over *

	Discounting	Men	Women	Total
Lifetime health care cost of smoking	No	£23,346,713,488	£21,418,726,434	£44,765,439,922
	3.5%	£15,759,393,151	£13,233,295,694	£28,992,688,845
	6.0%	£11,730,127,557	£9,544,614,034	£21,274,741,590
Lifetime cost savings from smoking cessation	No	£11,488,311,471	£11,804,906,335	£23,293,217,806
	3.5%	£8,483,900,719	£7,681,536,736	£16,165,437,456
	6.0%	£6,405,762,305	£5,516,869,488	£11,922,631,793

* Note: the time horizon for cost calculations is between now and the time of death or until the cohort reaches the age of 100 years.

We also evaluated the predicted cost savings associated with smoking cessation, attributable to reduced risk of smoking-related conditions. The model predicts that if all smokers in the prevalent population of England quit smoking, the total lifetime cost savings would be £11.5 billion for men and £11.8 billion for women, totalling to £23.3 billion for the adult population of England (population ≥35 years of age). The discounted total savings from cessation are predicted to be £16.2 billion at 3.5% and £11.9 billion at 6.0%. These cost savings are huge when evaluated in the light of total NHS budget.

6. DISCUSSION

The economic model developed for this study aims to predict lifetime health care costs and consequences of adult smoking and the benefits of smoking cessation. The model can be used as a tool to evaluate cost savings to the NHS against the cost of public health interventions aimed at promoting smoking cessation. When data on programme costs and the expected cessation rates are available for a given population, this model can be used to project net monetary savings to the health care system and the benefits in terms of reduced morbidity and mortality.

The report has presented in detail the design, methodology and results from the economic model for adult smoking. The four clinical pathways modelled in this study include myocardial infarction, stroke, chronic obstructive pulmonary disease and lung cancer. These conditions represent the most significant contributors to the smoking-related health care costs and the loss of quality and quantity of life. We further incorporated the increased risk of mortality and costs due to 'other diseases' by allowing smokers and ex-smokers to have higher risk of death and cost incurrence compared to non-smokers. Lifetime costs and consequences were modelled for three population groups, i.e. never smokers, current smokers and ex-smokers (quitters). The probability of events in the latter two groups was modelled using relative risk estimates from the published literature. Risk reduction in quitters was modelled, where possible, as a function of time since quitting smoking.

The model is developed using competing risk approach that allows individuals to develop any of the four conditions over the course of their lifetimes. The transition to a disease state is dictated solely by age and sex specific probability in the smoking-related group. Once a particular condition is developed, the patient then follows the pathway dictated by the disease. The model uses estimates of incidence rates in the general population of England or the UK (depending on the sources available) to derive the incidence in non-smokers. The probability of disease in smokers and ex-smokers was derived using relative risk estimates from the published literature.

The model results predict that smoking cessation in a cohort of 1,000 individuals at the age of 35 is likely to save £4.9 million for men and £4.8 for women and a gain of 4,262 years in men and 4,534 years in women. The results also show the distribution of cost savings and the life years gained over the lifetime of individuals. The model also allows us to predict the

benefits for varying levels of smoking cessation rates in the population. However, one should note that the results of the model may underestimate cost savings and life year gains because the model does not allow development of concurrent disease conditions. However, the model can be further developed to incorporate concurrent risk, which will result in further cost savings. Also, because the model primarily focuses on four most common smoking-related conditions, it provides a conservative estimate of the overall benefits of quitting. One should also note that the model evaluates only the direct impact of smoking and ignores the environmental effect of passive smoking. However, the current model can be extended to include evidence on additional benefits of smoking cessation.

The results of our models are consistent with the results of other models in the literature. All models, except for Barengregt et al (1997), found that smoking cessation will result in short and/or long-term cost savings. However, Barengregt et al (1997) conclude that smoking cessation only reduces short term costs whilst increasing long term costs. Based on the description provided in the published paper, we were not able to critically appraise their modelling methodology generally, and more specifically, the risk modelling after smoking cessation. The results of all other studies are in agreement with our findings in terms of the direction of impact on costs and life years.

In terms of the magnitude of the benefit of smoking cessation, we compared our results with the previously published studies. Hurley and Matthews (2007) estimated that the cost savings after 10 years of smoking cessation in 1,000 individuals were equal to A$408,000 for men and A$328,000 for women. These estimates are broadly comparable with our estimates of cost savings of £321,302 for men and £118,271 for women (table 6). We further estimated that life year gain predicted by our model during 10 years of smoking cessation (not shown in the table) was equal to 40.3 years for men which is directly comparable with Hurley and Matthews estimate of 47 life years saved. However, one should note that the gain in life years after quitting will be lower in the earlier years of life because the underlying risk of smoking-related conditions is low. Therefore, as the cohort ages, the risk of smoking-related conditions increases and therefore the benefit of cessation becomes more pronounced. This provides further argument for lifetime modelling of costs and health consequences.

We also compared our estimates of the lifetime cost of smoking for the prevalent population of England with previous estimates in the literature. The HECOS model (Orme et al 2001) estimated that the total cumulative health care costs associated with smoking related diseases

in the UK over 20 years was equal to £28.3 billion (discounted at 6%). Our model estimated that the lifetime health care costs of adults ≥ 35 years in England is approximately £44.8 billion (undiscounted), £26.5 billion (discounted at 3.5%) and £21.3 billion (discounted at 6%) [table 10]. Again, these figures are broadly in agreement with the estimates of Orme et al (2001). It should however be noted that our model estimates costs for adult who are ≥ 35 years (representing 70% of the total adult population in England) and the population size was limited to England (not the UK, as in Orme et al 2001). Our model also estimates cost savings associated with smoking cessation in the general adult population of England. The analysis suggests smoking cessation could potentially save up to a maximum of £23.3 billion over the lifetime of the prevalent population of England. Our analysis also supports the idea of investing in preventive programmes that reduce the uptake of smoking at an earlier age. When lifetime health care costs of non-smokers are compared with smokers, the potential savings for non-starters of smoking are estimated to be approximately £8,600 per person compared to savings of £4,926 after smoking cessation at the age of 35 (table 6).

When compared with previously published economic models, the current model is a leap forward, both in terms of the modelling approach used and its relevance to the context of England. For instance, Hodgson (1992) focused primarily on incremental health care costs for smokers compared with never smokers (appendix 2) and does not distinguish between current and ex-smokers for modelling purposes. Such studies are only useful in allowing assessment of the impact of becoming a smoker versus not becoming a smoker, but do not address the impact of smoking cessation on medical care expenditures. As a result, it would not be possible to estimate future cost savings associated with smoking cessation and in turn the cost-effectiveness of cessation interventions in a given population.

Our model evaluated the impact of smoking cessation on the lifetime of a cohort to estimate long-term costs and consequences. This is in line with the approach taken by many other economic models in the literature, except for Lightwood & Glantz 1997, Orme et al 2001 and Hurley and Matthews 2007 that estimated costs and outcomes between 1 and 20 year periods. Taking a lifetime approach would dispel misconceptions such as continuing smokers may save money to the health care system by dying sooner than the non-smokers. Our results clearly show that models that estimate cost savings over shorter periods, for instance, over 10 year period in Hurley and Matthews 2007, significantly underestimate the benefits of smoking cessation. Table 6 clearly shows that the cost savings in the first 10 years of

smoking cessation represent only 6.5% of the lifetime cost savings among men aged 35 years. Similarly, cost savings in the first 20 years represented 32.4% of the lifetime cost savings. These findings stress the need for lifetime modelling since most smoking-related conditions develop in later years of life; hence, taking a short-term approach to cessation modelling may produce incorrect estimates of the analysis.

The model presented in this report focused on four clinical conditions that are responsible for the majority of smoking-related costs and health consequences. While this may potentially underestimate the overall benefit of smoking cessation, our conservative estimates demonstrate that the benefits of cessation in terms of cost savings are huge for the health care system. This approach is in line with earlier models of smoking cessation that also concentrated on the most important smoking-related disease conditions. The advantage of modelling specific disease pathways is that it allows analysts to use more specific and precise data on relative risk estimates and allows specification of disease pathways in line with what is clinically observed. Consequently, with changes in underlying disease epidemiology, either as a result of changes in incidence/prevalence/relative risks of specific conditions or due to treatment advancements for certain conditions. The current approach will facilitate the model to be dynamic in allowing it to incorporate such disease specific changes. The non-disease-specific approach used by Hodgson (1992) uses crude estimates of relative risk based on life tables; as a result, individual level consequences are estimated based on population level non-disease-specific estimates that may not be precise, are potentially amenable to confounding and may not allow incorporation of epidemiological changes in incidence of specific conditions or disease progression (and treatment) pathways. Hence, we preferred the more flexible, albeit computational more intensive, approach to model the impact of smoking cessation on disease-specific morbidity and mortality. It should be noted that we have further incorporated increased smoking-related risk of mortality and costs due to 'other diseases' by allowing smokers and ex-smokers to have higher risk of death and cost incurrence compared to non-smokers (in line with the evidence from the literature, see Jha *et al* 2008).

The economic model in this study is also significant in terms of its relevance to the context of England. Except Orme et al (2001), all others models identified during the literature review focused on the impact of smoking cessation outside of the UK. Since economic models are driven by the underlying population-specific epidemiological data, the results cannot be transferred to other countries without changing the underlying risk and cost equations.

7. LIMITATIONS OF THE STUDY

Decision analytic models inevitably make assumptions and have to be selective with respect to the pathways modelled and the costs and consequences captured. The assumptions made in this model are highlighted in the relevant sections. Here we summarise some of the limitations of the model. It should be noted that the modelling framework developed for the current project can be adapted during future research to overcome some of these limitations by adding further degree of complexity to the modelling framework. Below we summarise some of the limitations of the model.

[a] Standard Markov models used in health economics research typically concentrate on one disease condition in a given model. However, the smoking cessation model required us to model multiple disease pathways in a Markov framework. This was a modelling challenge because of the large number of health states that will arise as a result of interaction of disease pathways. If all possible interactions of pathways are allowed, the model will be extremely difficult to construct and unfold within a population cohort framework. Therefore, this model takes a competing risk approach which allocates individuals to different disease pathways based on age and sex-specific transition probabilities for each disease condition. Once a patient develops one of the four conditions, s/he follows the model pathway for the particular disease. Hence, patients are not allowed to have concurrent conditions, even though they may still die from other causes.

It should also be noted that the model concentrates on four clinical conditions. As a result, the model may underestimate the costs associated with smoking-related diseases and the benefits of smoking cessation. However, the results (albeit possibly underestimated) clearly demonstrate the benefits of smoking cessation in terms of cost savings and life years gained.

[b] The economic model does not distinguish between smokers in terms of the number of years of smoking or the intensity of smoking (or pack years). Hence, dose response relationship was not explored in the current study. Furthermore, the model assumed that the decline in risk following smoking cessation is independent of the years and intensity of smoking. This approach was taken due to the limitations of data availability. Taking this into account, one should be careful when comparing cost savings associated with smoking cessation in a younger cohort with an older cohort

because those quitting smoking at the age of 65 (after 40 years of smoking) are likely to have higher risk of post-quitting risk compared to individuals who quit smoking at the age of 35. If further data becomes available on the relationship between disease risk and intensity/duration of smoking, then the current model can be adapted to reflect smoking history of individuals and transition probabilities within the Markov model.

[c] The Markov model does not allow for smoking relapses once an individual has quit smoking. This is primarily because of scarcity of data on relative risk of diseases for individuals who relapse to smoking. When further data becomes available, a relapse state can be introduced within the Markov framework to estimate time-dependent transition probabilities that are functions of smoking and relapse histories. However, it should be noted that incorporating relapse state would require structural changes to the current modelling framework.

[d] For quitters the relative risk of smoking-related conditions is assumed to be independent of the number of years of smoking before quitting. As before, these parameters can be built into the modelling framework during future research, if relevant data becomes available.

[e] Finally, the model does not take account of passive smoking in the population. Passive smoking may influence relative risk in non-smokers and ex-smokers (and possibly current smokers). The costs associated with passive smoking can be modelled using current modelling framework by introducing separate cohorts for non-smoker and ex-smokers based on exposure to passive smoking. However, this would require reasonable amount of additional work to find relevant epidemiological evidence and to incorporate changes in the current modelling framework. However, once relevant data is available, the model can be adapted to estimate the additional cost burden associated with passive smoking.

8. CONCLUSION

The economic model presented here can be used as a decision tool by policy-makers who will be able to predict the impact of an intervention in terms of cost savings and life years saved. The modelling approach makes use of the available evidence on morbidity and mortality associated with smoking-related conditions to predict the impact of potential scenarios arising from the implementation of smoking cessation strategies on the lifetime of a pre-defined

cohort. Moreover, the modelling framework has the potential to be adapted to accommodate evidence from smoking cessation trials to predict long-term costs and consequences of cessation strategies. Finally, the model also has the flexibility to accommodate, at a later stage, any epidemiological changes in the underlying incidence and prevalence rates and the risk of morbidity and mortality in the population of interest.

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10.APPENDICES

Appendix 1: Search strategy used to identify economic models of smoking

Database searched: Ovid MEDLINE(R)

Item no.	Strategy
1	Smoking/ec (1178)
2	Smoking/pc (11286)
3	Smoking Cessation/ec (479)
4	Economics/ (25675)
5	"costs and cost analysis"/ (36960)
6	Cost allocation/ (1854)
7	Cost-benefit analysis/ (43514)
8	Cost control/ (17900)
9	Cost savings/ (6016)
10	Cost of illness/ (10634)
11	Cost sharing/ (1403)
12	"deductibles and coinsurance"/ (1193)
13	Medical savings accounts/ (389)
14	Health care costs/ (16882)
15	Direct service costs/ (854)
16	Drug costs/ (8619)
17	Employer health costs/ (988)
18	Hospital costs/ (5623)
19	Health expenditures/ (10212)
20	Capital expenditures/ (1835)
21	Value of life/ (5039)
22	exp economics, hospital/ (15520)
23	exp economics, medical/ (11752)
24	Economics, nursing/ (3839)
25	Economics, pharmaceutical/ (1930)
26	exp "fees and charges"/ (23871)
27	exp budgets/ (9860)
28	(low adj cost).mp. (10486)
29	(high adj cost).mp. (5060)
30	(health?care adj cost$).mp. (1764)
31	(fiscal or funding or financial or finance).tw. (44917)
32	(cost adj estimate$).mp. (866)
33	(cost adj variable).mp. (23)
34	(unit adj cost$).mp. (880)
35	(economic$ or pharmacoeconomic$ or price$ or pricing).tw. (97802)
36	or/4-35 (314742)
37	or/1-3 (12287)
38	36 and 37 (1451)
39	from 38 keep 1-1451 (1451)

Appendix 2: Summary of the key features of previous economic models of adult smoking

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco-unting	Results	Comments
Hodgson 1992	To estimate lifetime medical expenditure for smokers and never smokers	Never smokers, moderate smokers (<25 cigs/ day) and heavy smokers (≥25 cigs/day)	US general population (men and women evaluated separately)	Not specific	Life time (from 17 years to death)	Longitudinal lifetime cost profiles estimated using multiple US surveys and databases	Direct medical care costs	Yes (3%)	Men: $5,615 (21%) higher for moderate smokers and $12,911 (47%) higher than never-smokers. Women: $6,135 (14%) higher for moderate smokers and $17,564 (41%) higher than never-smokers.	Current and former smokers were grouped together as ever-smokers. Study did not address the impact of quitting smoking on expenditure.
Barendg-redt et al 1997	To analyse health care costs for smokers and non-smokers and the consequence of smoking cessation	Smokers, non-smokers and mixed group with smokers and non-smokers	Dutch general population	Heart disease, stroke, lung and other cancers and COPD	Life time	Population life tables were used and risk ratios applied to incorporate smoking-related risk	Direct medical care costs	Yes (3%, 5% and 10%)	Costs for smokers at a given age were 40% higher than those for non-smokers. However, if all smokers quit, health care costs would initially drop but after about 15 years costs would increase beyond current levels	Study found that smoking cessation saves costs only in short term but increases costs in long-term. Method used to estimate cost savings associated with smoking cessation are not clearly documented.

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco-unting	Results	Comments
Lightwood & Glantz 1997	To simulate the impact of 1% absolute reduction in smoking prevalence associated with prevented acute myocardial infarctions and strokes.	Smokers and non-smokers	US General population aged 35-64 years old	Acute myocardial infarction and stroke	1 year and 7 year periods	Simulation of the impact of 1% reduction in smoking prevalence	Direct medical care costs	Yes (2.5%)	In the first year, 924 fewer hospitalisations for AMI and 538 for stroke will occur resulting in cost savings of $44 million. After seven years, 63 840 fewer hospitalizations for AMI and 34,261 fewer for stroke will occur resulting in cost savings of $3.20 billion.	Life time costs were not considered in the study. Focus limited to two conditions. However, the study modelled risk reduction as a function of time since quitting.
Orme et al 2001	To describe the health and economic consequences of smoking and the benefits of smoking cessation	Current smoker, recent quitter and long-term quitter	UK general population split into following age and sex groups: male (female): 0–34, 35–69, and 70+	COPD, asthma, coronary heart disease (CHD), stroke, lung cancer and low-birth weight pregnancy	5, 10, 15 and 20 years	Markov model for a UK cohort of smokers who either stay as smokers or quit and rebound or quit for long term. Study follows the cohort for 20 years	Direct medical care costs	Yes (6% and then varied betwe-en 0% and 10%)	Smoking cessation is predicted to reduce health care spending by £35 million, and a reduction in mortality of 10 239 cases.	Lifetime perspective was not taken. Cohort split into large age-related categories assuming constant risk within a group. Deaths from non-smoking related causes not captured. Relative risk of each disease is not explicitly stated for smokers and short/ long-term quitters.

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco-unting	Results	Comments
van Genugten et al 2003	To estimate the impact of reduced smoking prevalence on disability adjusted life-years (DALYs) and costs.	Never smokers, smokers and former smokers	Dutch general population	Lung cancer, coronary heart disease, stroke, and COPD	Until death or until year 2050, which-ever occurs first	Dutch population in 1994 is divided into birth cohorts and followed until 2050. In a dynamic framework, individuals may start or quit smoking, and may develop morbidity or die.	Disease specific costs	No	In short-run, quitting was projected to save 40,000 life years for males by 2025 and a maximum of 50,000 by 2035 for females. Costs to be avoided will be almost €80 million for males and €100 million for females. However, eventually the health gain and avoided costs of the 'don't start' scenario is predicted to go beyond the yield of the quitting scenario.	Risk in ex-smokers is not specified explicitly as a function of years of quitting. This is likely to result in higher predicted morbidity and mortality in the ex-smoker population than actually observed. Also, the model did not evaluate the underlying risk in non-smokers; hence, any direct comparison between smokers and non-smokers is not possible. Finally, the paper does not include details of how the model is formulated and how these projections are made.
Rasmuss-en et al 2005	To estimate the direct and indirect lifetime health care	Smokers and ex-smokers	Danish general population	Cancer (ICD code: C00-C99), vascular disease	Lifetime horizon	Crude population attributable risks based on age, sex, smoking status and quantity of smoking were estimated	Health care and producti-vity costs	Yes (5%)	The total lifetime health cost savings of smoking cessation are highest at the	Crude estimates based on population attributable risks, smoking attributable costs and population

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco-unting	Results	Comments
	cost savings associated with smoking cessation			(I00-I99), respiratory disease (J00–J99) and all other diseases		using Danish population data and multiplied by age, sex and disease-based costs.			younger ages. The total, direct and productivity lifetime cost savings of smoking cessation in moderate smokers who quit smoking at the age of 35 years were €24,800, €7,600, and €17,200 in men, and €34,100, €12,200, and €21,800 in women respectively.	demographic proportions were used to estimate cost savings. Disease specific costs and relative risks were not used.
Chung et al 2007	To estimate the lifetime financial burden national health insurance (NHI) system, life expectancy and years of life expectancy	Never smokers and current smokers	Taiwanese general population of never smokers and current smokers	Cancers (ICD-9CM code: 140-151, 154-156, 162, 180), Stroke (430, 431, 434, 436), AMI (410), COPD (491, 492, 496)	Lifetime horizon	Smoking-related incidence was estimated using population incidence rate for each disease and smoking-attributable fractions. Years lost due to smoking were calculated using survival analysis results, the smoking attributable fractions and the annual disease incidences for	Direct medical care costs	Yes (1% and 3%)	Out of 241,280 incidents of the 10 study diseases in 2001, 53,648 cases (22.2%) were attributable to smoking, with total years of life expectancy lost of 191,313. The total lifetime financial burden	Savings estimated as cost difference that would be expected if smokers had not started smoking. Consequences of smoking cessation in current smokers not explored.

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco-unting	Results	Comments
	lost (YLEL) attributable to smoking					each of the ten selected disease areas. Lifetime medical expenditures for the study diseases were estimated by integrating the survival curve for each disease area, with disease costs being derived from NHI reimbursement records.			on the national insurance due to smoking was estimated to be between $291 million (3% discount) and $336 million (1% discount) in 2001, equal to about 24.6% of the total estimated lifetime medical expenditure for all incidents of the 10 study diseases.	
Hurley and Matthews 2007	To estimate the benefits of smoking cessation in terms of life-years, QALYs and costs.	Current smokers and recent quitters	Adult general population of Australia	Acute myocardial infarction, stroke, lung cancer and COPD	Ten years	A Markov cycle tree model was developed for four disease pathways. All individuals in the model start off in disease-free state, and then develop one of the four conditions based on the underlying transition probabilities that are function of age, sex and smoking status. Accumulated costs and life years over 10 years	Direct health care costs.	Yes (3.5% and 5.0%)	The results suggest that the average savings in health care costs for a cohort of 1,000 individuals in the first ten years following quitting is A$408,000 for men, A$328,000 for women (average: A$373,000). In terms of disease	We found that Hurley and Matthews model is more analytically advanced and developed compared to previous models. However, the model has some limitation. Firstly, the model uses a limited time horizon of 10 years that is not long enough to capture lifetime benefits of smoking cessation.

Study	Aim of the study	Smoking -related groups	Population	Clinical conditions	Time horizon	Modelling approach	Costs included	Use of disco- unting	Results	Comments
						were evaluated and compared for smokers and ex-smokers.			diagnosis, overall 40 of these quitters will be spared a diagnosis of AMI, COPD, lung cancer and stroke in the first ten years following quitting, resulting in an estimated 47 life-years saved and 75 QALYs.	The model does not explicitly allow for recurrence of primary events and also does not explicitly incorporate excess risk of other conditions.

Appendix 3: Incidence rate and probability of first-ever acute MI, stroke, lung cancer or COPD in the general population, by age and sex

		MI		Stroke		Lung Cancer		COPD	
Sex	**Age groups**	**Incidence per 1,000 person years**	**1 - year probability in the general population**	**2-year incidence rate of stroke per person**	**1 - year probability in the general population**	**Incidence per 100,000 person years**	**1 - year probability in the general population**	**Incidence per 1,000 person years**	**1 - year probability in the general population**
Men	35-39	0.89	0.00089	0.00054	0.00027	2.58	0.00003	0.21	0.0002
	40-44	1.94	0.00194	0.00054	0.00027	6.26	0.00006	0.21	0.0002
	45-49	3.63	0.00222	0.00146	0.00073	16.58	0.00017	0.21	0.0002
	50-54	6.42	0.00791	0.00146	0.00073	42.12	0.00042	1.62	0.0016
	55-59	7.83	0.00508	0.00354	0.00177	87.91	0.00088	1.62	0.0016
	60-64	11.16	0.00507	0.00354	0.00177	157.46	0.00157	3.69	0.0037
	65-69	15.53	0.00922	0.01293	0.00649	260.18	0.00260	3.69	0.0037
	70-74	14.86	0.01220	0.01293	0.00649	347.16	0.00347	6.33	0.0063
	75-79	17.25	0.01806	0.01885	0.00947	474.96	0.00475	6.33	0.0063
	80-84	21.41	0.02118	0.01885	0.00947	573.92	0.00574	7.03	0.0070
	85+	26.14	0.02580	0.03944	0.01992	527.19	0.00527	7.03	0.0070
Women	35-39	0.08	0.00008	0.00031	0.00016	2.23	0.00002	0.26	0.0003
	40-44	0.36	0.00036	0.00031	0.00016	6.93	0.00007	0.26	0.0003
	45-49	0.61	0.00037	0.00108	0.00054	15.39	0.00015	0.26	0.0003
	50-54	1.09	0.00135	0.00108	0.00054	33.80	0.00034	1.16	0.0012
	55-59	2.19	0.00142	0.00350	0.00175	68.05	0.00068	1.16	0.0012
	60-64	3.97	0.00180	0.00350	0.00175	112.65	0.00113	1.82	0.0018
	65-69	6.68	0.00397	0.00815	0.00408	171.11	0.00171	1.82	0.0018
	70-74	7.41	0.00610	0.00815	0.00408	211.18	0.00211	3.37	0.0034
	75-79	9.45	0.00993	0.02101	0.01056	263.96	0.00264	3.37	0.0034
	80-84	12.89	0.01281	0.02101	0.01056	291.72	0.00292	3.46	0.0035
	85+	18.05	0.01789	0.03015	0.01519	228.40	0.00228	3.46	0.0035

Appendix 4: Probability (expressed as percentage chance) of developing first-ever MI, based on age, sex and smoking status

Sex	Age groups	Non-Smokers	Smokers	Ex-smokers: time since quitting					
				>1-3 yrs	>3 - 5 years	>5 - 10 years	>10 - 15 years	>15 - 20 years	>20 years
Men	35-39	0.05%	0.16%	0.09%	0.08%	0.08%	0.08%	0.07%	0.07%
	40-44	0.11%	0.35%	0.20%	0.18%	0.18%	0.17%	0.15%	0.15%
	45-49	0.13%	0.44%	0.25%	0.22%	0.22%	0.21%	0.19%	0.19%
	50-54	0.46%	1.55%	0.87%	0.77%	0.77%	0.75%	0.67%	0.67%
	55-59	0.33%	0.83%	0.61%	0.54%	0.54%	0.53%	0.47%	0.47%
	60-64	0.34%	0.86%	0.64%	0.56%	0.56%	0.55%	0.49%	0.49%
	65-69	0.63%	1.59%	1.18%	1.04%	1.04%	1.01%	0.91%	0.91%
	70-74	0.83%	2.10%	1.56%	1.37%	1.37%	1.34%	1.20%	1.20%
	75-79	1.30%	3.26%	2.41%	2.12%	2.12%	2.07%	1.85%	1.85%
	80-84	1.52%	3.83%	2.82%	2.49%	2.49%	2.43%	2.17%	2.17%
	85+	1.85%	4.66%	3.42%	3.02%	3.02%	2.95%	2.64%	2.64%
Women	35-39	0.00%	0.02%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%
	40-44	0.02%	0.08%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
	45-49	0.02%	0.09%	0.04%	0.03%	0.03%	0.03%	0.03%	0.03%
	50-54	0.07%	0.33%	0.14%	0.12%	0.12%	0.12%	0.10%	0.10%
	55-59	0.08%	0.36%	0.15%	0.13%	0.13%	0.13%	0.12%	0.12%
	60-64	0.10%	0.47%	0.20%	0.17%	0.17%	0.17%	0.15%	0.15%
	65-69	0.30%	0.65%	0.57%	0.50%	0.50%	0.49%	0.44%	0.44%
	70-74	0.47%	1.00%	0.87%	0.77%	0.77%	0.75%	0.67%	0.67%
	75-79	0.79%	1.70%	1.48%	1.31%	1.31%	1.27%	1.14%	1.14%
	80-84	1.02%	2.19%	1.91%	1.68%	1.68%	1.64%	1.47%	1.47%
	85+	1.43%	3.06%	2.66%	2.34%	2.34%	2.29%	2.05%	2.05%

Appendix 5: Probability (expressed as percentage chance) of developing first-ever stroke, based on age, sex and smoking status

Sex	Age groups	Non-Smokers	Smokers	Ex-smokers: time since quitting				
				< 2 years	2-4 years	5-9 years	10-14 years	≥ 15 years
Men	35-39	0.02%	0.04%	0.03%	0.02%	0.02%	0.02%	0.02%
	40-44	0.02%	0.04%	0.03%	0.02%	0.02%	0.02%	0.02%
	45-49	0.06%	0.12%	0.09%	0.07%	0.07%	0.07%	0.07%
	50-54	0.06%	0.12%	0.09%	0.07%	0.07%	0.07%	0.07%
	55-59	0.14%	0.29%	0.21%	0.17%	0.17%	0.17%	0.17%
	60-64	0.14%	0.29%	0.21%	0.17%	0.17%	0.17%	0.17%
	65-69	0.54%	1.09%	0.80%	0.65%	0.65%	0.65%	0.65%
	70-74	0.54%	1.09%	0.80%	0.65%	0.65%	0.65%	0.65%
	75-79	0.84%	1.68%	1.23%	1.00%	1.00%	1.00%	1.00%
	80-84	0.84%	1.68%	1.23%	1.00%	1.00%	1.00%	1.00%
	85+	1.76%	3.54%	2.61%	2.12%	2.12%	2.12%	2.12%
Women	35-39	0.01%	0.03%	0.02%	0.02%	0.02%	0.02%	0.02%
	40-44	0.01%	0.03%	0.02%	0.02%	0.02%	0.02%	0.02%
	45-49	0.04%	0.10%	0.08%	0.06%	0.06%	0.06%	0.06%
	50-54	0.04%	0.10%	0.08%	0.06%	0.06%	0.06%	0.06%
	55-59	0.14%	0.35%	0.26%	0.21%	0.21%	0.21%	0.21%
	60-64	0.14%	0.35%	0.26%	0.21%	0.21%	0.21%	0.21%
	65-69	0.33%	0.85%	0.62%	0.50%	0.50%	0.50%	0.50%
	70-74	0.33%	0.85%	0.62%	0.50%	0.50%	0.50%	0.50%
	75-79	0.91%	2.36%	1.73%	1.40%	1.40%	1.40%	1.40%
	80-84	0.91%	2.36%	1.73%	1.40%	1.40%	1.40%	1.40%
	85+	1.31%	3.39%	2.50%	2.03%	2.03%	2.03%	2.03%

Appendix 6: Probability (expressed as percentage chance) of developing lung cancer, based on age, sex and smoking status

Sex	Age groups	Non-Smokers	Smokers	Ex-smokers: time since quitting		
				0 - <5 years	5 - <10 years	≥10 years
Men	35-39	0.00%	0.01%	0.00%	0.00%	0.00%
	40-44	0.00%	0.01%	0.01%	0.01%	0.01%
	45-49	0.00%	0.04%	0.03%	0.02%	0.02%
	50-54	0.01%	0.11%	0.07%	0.04%	0.04%
	55-59	0.02%	0.23%	0.15%	0.09%	0.09%
	60-64	0.04%	0.42%	0.26%	0.16%	0.16%
	65-69	0.07%	0.71%	0.44%	0.28%	0.28%
	70-74	0.10%	0.95%	0.59%	0.37%	0.37%
	75-79	0.15%	1.47%	0.92%	0.58%	0.57%
	80-84	0.18%	1.78%	1.11%	0.70%	0.69%
	85+	0.17%	1.63%	1.02%	0.64%	0.64%
Women	35-39	0.00%	0.01%	0.00%	0.00%	0.00%
	40-44	0.00%	0.02%	0.01%	0.01%	0.00%
	45-49	0.01%	0.04%	0.03%	0.02%	0.01%
	50-54	0.01%	0.09%	0.06%	0.04%	0.02%
	55-59	0.03%	0.19%	0.12%	0.08%	0.03%
	60-64	0.04%	0.32%	0.20%	0.13%	0.06%
	65-69	0.07%	0.52%	0.32%	0.21%	0.09%
	70-74	0.08%	0.64%	0.39%	0.26%	0.11%
	75-79	0.12%	0.93%	0.57%	0.38%	0.17%
	80-84	0.14%	1.03%	0.63%	0.42%	0.18%
	85+	0.11%	0.80%	0.49%	0.33%	0.14%

Appendix 7: Probability (expressed as percentage chance) of developing COPD, based on age, sex and smoking status

Sex	Age groups	Non-Smokers	Smokers	Ex-smokers
Men	35-39	0.01%	0.04%	0.02%
	40-44	0.01%	0.04%	0.02%
	45-49	0.01%	0.05%	0.03%
	50-54	0.06%	0.35%	0.20%
	55-59	0.06%	0.34%	0.19%
	60-64	0.13%	0.77%	0.43%
	65-69	0.13%	0.77%	0.43%
	70-74	0.22%	1.32%	0.74%
	75-79	0.23%	1.41%	0.79%
	80-84	0.25%	1.57%	0.88%
	85+	0.25%	1.57%	0.88%
Women	35-39	0.01%	0.06%	0.03%
	40-44	0.01%	0.06%	0.03%
	45-49	0.01%	0.06%	0.03%
	50-54	0.04%	0.28%	0.15%
	55-59	0.04%	0.28%	0.15%
	60-64	0.07%	0.43%	0.24%
	65-69	0.07%	0.46%	0.26%
	70-74	0.14%	0.84%	0.47%
	75-79	0.15%	0.95%	0.53%
	80-84	0.16%	0.98%	0.55%
	85+	0.16%	0.98%	0.55%

Appendix 8: Cost of smoking for adult population in England, 35 year old and over *

	Men		Women	
Age	**Cost of smoking per 1,000 individuals**	**Total cost of smoking for each age group in England**	**Cost of smoking per 1,000 individuals**	**Total cost of smoking for each age group in England**
35	£8,599,690	£1,023,001,041	£7,837,235	£794,095,280
36	£8,497,389	£1,057,403,117	£7,746,616	£826,235,041
37	£8,450,942	£1,096,927,849	£7,730,592	£872,992,971
38	£8,406,648	£1,123,657,077	£7,715,310	£894,477,556
39	£8,364,580	£1,114,025,949	£7,700,794	£881,308,639
40	£8,324,845	£1,139,151,191	£7,687,072	£905,001,346
41	£8,240,876	£1,140,001,500	£7,657,526	£903,458,715
42	£8,160,258	£1,153,532,748	£7,629,269	£918,640,464
43	£8,083,042	£1,133,418,484	£7,602,322	£916,741,059
44	£8,009,273	£1,126,192,860	£7,576,703	£918,823,308
45	£7,938,928	£814,722,841	£7,552,423	£730,194,337
46	£7,842,831	£786,568,750	£7,503,811	£715,258,922
47	£7,750,989	£756,008,366	£7,457,080	£690,764,732
48	£7,663,531	£730,795,549	£7,412,304	£668,357,581
49	£7,580,631	£695,274,505	£7,369,577	£637,648,702
50	£7,502,683	£675,959,377	£7,329,067	£619,819,356
51	£7,234,627	£643,773,638	£7,235,359	£602,025,260
52	£6,973,867	£596,403,853	£7,145,824	£572,753,446
53	£6,720,870	£553,568,402	£7,060,606	£545,942,535
54	£6,476,105	£518,447,449	£6,979,861	£524,636,410
55	£6,239,928	£397,560,159	£6,903,832	£414,681,652
56	£6,103,442	£381,303,080	£6,755,650	£397,897,563
57	£5,972,368	£368,040,886	£6,611,556	£386,303,067
58	£5,847,259	£361,159,052	£6,471,916	£379,822,445
59	£5,728,851	£362,159,349	£6,337,192	£382,186,854
60	£5,618,716	£365,836,980	£6,208,286	£383,871,145
61	£5,542,857	£385,029,603	£6,088,807	£402,635,063
62	£5,474,403	£396,648,049	£5,974,442	£413,760,917
63	£5,414,154	£315,723,405	£5,865,693	£329,698,986
64	£5,363,001	£302,489,798	£5,763,131	£315,247,397
65	£5,322,075	£216,082,843	£5,667,696	£242,935,463
66	£5,118,788	£197,066,705	£5,486,960	£226,252,821
67	£4,914,206	£169,231,844	£5,308,277	£197,169,282

	Men		Women	
Age	**Cost of smoking per 1,000 individuals**	**Total cost of smoking for each age group in England**	**Cost of smoking per 1,000 individuals**	**Total cost of smoking for each age group in England**
68	£4,710,403	£150,279,632	£5,133,088	£178,089,525
69	£4,510,413	£147,668,979	£4,963,327	£178,213,473
70	£4,320,777	£139,767,600	£4,802,420	£171,122,030
71	£4,209,727	£132,382,010	£4,692,043	£163,888,026
72	£4,099,198	£123,445,946	£4,584,386	£155,528,738
73	£3,991,857	£114,531,149	£4,481,082	£146,944,921
74	£3,891,142	£105,594,472	£4,384,170	£137,883,748
75	£3,802,131	£44,379,295	£4,296,870	£75,842,539
76	£3,612,706	£40,461,418	£4,074,263	£70,508,224
77	£3,399,731	£36,634,654	£3,835,008	£65,485,959
78	£3,166,474	£32,471,660	£3,582,108	£60,261,500
79	£2,920,053	£27,592,234	£3,320,666	£53,470,963
80	£2,679,077	£23,108,233	£3,061,483	£46,270,637
81	£2,625,312	£20,386,395	£2,940,119	£41,214,052
82	£2,555,716	£18,421,760	£2,799,802	£37,745,042
83	£2,472,710	£16,101,014	£2,642,181	£33,797,588
84	£2,382,266	£13,607,346	£2,471,034	£29,203,162
85	£2,298,361	£11,443,571	£2,295,923	£25,127,675
86	£2,290,660	£9,906,733	£2,243,298	£22,557,324
87	£2,241,258	£8,674,897	£2,160,467	£20,548,785
88	£2,142,433	£7,448,876	£2,046,086	£18,347,488
89	£1,992,697	£5,491,921	£1,903,313	£14,164,338
90 and over	£2,744,238	£19,747,395	£2,498,406	£60,872,385
Total cost		**£23,346,713,488**		**£21,418,726,434**

* Calculated as the difference between lifetime health care costs of smokers and non-smokers for each start age in the model and then multiplying the cost difference with population distribution and adjusting for smoking prevalence in England for each age category. The calculation thus estimates additional health care cost incurred due to smokers taking up and continuing to smoke.

Appendix 9: Cost savings from smoking cessation for adult population in England, 35 year old and over †

	Men		Women	
Age	**Cost savings after smoking cessation per 1,000 individuals**	**Total cost savings for each age group in England**	**Cost savings after smoking cessation per 1,000 individuals**	**Total cost savings for each age group in England**
35	£4,926,398	£586,033,956	£4,827,297	£489,118,178
36	£4,843,473	£602,714,920	£4,771,388	£508,904,541
37	£4,781,746	£620,668,118	£4,754,926	£536,959,788
38	£4,722,300	£631,196,426	£4,739,083	£549,427,476
39	£4,665,409	£621,356,547	£4,723,930	£540,624,835
40	£4,575,997	£626,168,041	£4,692,242	£552,419,086
41	£4,498,290	£622,270,882	£4,662,539	£550,100,911
42	£4,421,684	£625,048,549	£4,633,788	£557,954,525
43	£4,348,233	£609,717,010	£4,606,206	£555,448,479
44	£4,270,741	£600,513,679	£4,572,555	£554,511,683
45	£4,167,335	£427,667,706	£4,518,709	£436,884,410
46	£4,083,451	£409,535,114	£4,470,003	£426,078,091
47	£3,980,659	£388,261,628	£4,418,774	£409,320,199
48	£3,880,277	£370,023,799	£4,369,015	£393,948,216
49	£3,783,611	£347,022,310	£4,320,993	£373,871,627
50	£3,539,463	£318,890,395	£4,228,805	£357,630,165
51	£3,345,930	£297,737,706	£4,143,346	£344,751,220
52	£3,165,676	£270,728,032	£4,060,819	£325,483,524
53	£2,992,204	£246,454,619	£3,981,910	£307,890,580
54	£2,813,245	£225,215,533	£3,889,654	£292,363,169
55	£2,713,182	£172,863,083	£3,720,145	£223,452,152
56	£2,617,197	£163,505,341	£3,584,960	£211,148,742
57	£2,526,386	£155,685,898	£3,452,602	£201,730,260
58	£2,439,988	£150,707,137	£3,324,254	£195,093,087
59	£2,358,754	£149,112,797	£3,200,731	£193,031,414
60	£2,307,853	£150,265,289	£3,086,618	£190,851,974
61	£2,272,693	£157,870,610	£2,978,960	£196,989,940
62	£2,233,200	£161,806,560	£2,867,735	£198,605,437
63	£2,199,258	£128,248,545	£2,761,345	£155,209,733
64	£2,135,293	£120,437,077	£2,637,869	£144,293,301
65	£1,896,414	£76,996,784	£2,409,183	£103,265,258
66	£1,765,894	£67,984,645	£2,277,463	£93,910,350

	Men		Women	
Age	**Cost savings after smoking cessation per 1,000 individuals**	**Total cost savings for each age group in England**	**Cost savings after smoking cessation per 1,000 individuals**	**Total cost savings for each age group in England**
67	£1,635,908	£56,336,193	£2,146,756	£79,738,572
68	£1,506,119	£48,050,875	£2,019,506	£70,065,573
69	£1,379,450	£45,162,610	£1,897,674	£68,138,001
70	£1,285,623	£41,587,055	£1,793,616	£63,910,953
71	£1,234,537	£38,822,119	£1,722,624	£60,169,418
72	£1,177,821	£35,469,666	£1,648,555	£55,928,471
73	£1,125,166	£32,282,355	£1,579,552	£51,797,126
74	£1,066,263	£28,935,320	£1,474,823	£46,383,728
75	£845,822	£9,872,620	£1,124,980	£19,856,620
76	£746,558	£8,361,269	£1,016,536	£17,591,921
77	£641,875	£6,916,684	£904,056	£15,437,506
78	£524,818	£5,381,917	£785,533	£13,214,953
79	£401,571	£3,794,538	£665,022	£10,708,501
80	£327,349	£2,823,531	£548,064	£8,283,330
81	£340,178	£2,641,596	£516,235	£7,236,484
82	£351,739	£2,535,360	£473,392	£6,381,947
83	£362,985	£2,363,568	£425,091	£5,437,570
84	£351,732	£2,009,073	£361,866	£4,276,602
85	£233,653	£1,163,361	£178,963	£1,958,658
86	£252,976	£1,094,081	£182,997	£1,840,117
87	£265,249	£1,026,660	£182,267	£1,733,593
88	£252,643	£878,398	£169,524	£1,520,143
89	£216,570	£596,871	£148,558	£1,105,557
90 and over	£1,041,838	£7,497,015	£858,570	£20,918,639
Total cost savings		**£11,488,311,471**		**£11,804,906,335**

† Calculated as the difference between lifetime health care costs of smokers and ex-smokers for each start age in the model and then multiplying the cost difference with population distribution and adjusting for smoker and ex-smoker prevalence in England for each age category. The calculation thus estimates cost savings if all smokers quit today.