German EstSmoke: Estimating adult smoking-related costs and consequences of smoking cessation for Germany

Running head: *German EstSmoke*: Smoking-related costs in Germany

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Abstract

Aims. We compared predicted lifetime health care costs for current, never and ex-smokers in Germany under the current set of tobacco control polices. We compared these economic consequences of the current situation with an alternative in which Germany were to implement more comprehensive tobacco control policies consistent with the WHO Framework Convention for Tobacco Control (FCTC) guidelines.

Design. *German EstSmoke,* an adapted version of the *UK EstSmoke* simulation model, applies the Markov modelling approach. Transition probabilities for (re-)currence of smoking-related disease were calculated from large German disease-specific registries and the German Health Update (GEDA 2010). Estimations of both health care costs and effect sizes of smoking cessation policies were taken from recent German studies and discounted at 3.5%/year.

Setting. Germany

Participants. German population of prevalent current, never and ex-smokers in 2009: 81 million

Measurement. Lifetime cost and outcomes in current, never and ex-smokers

Findings. If tobacco control policies are not strengthened, the German smoking population will incur €41.56 billion lifetime excess costs compared to never smokers. Implementing tobacco control policies consistent with WHO FCTC guidelines would reduce the difference of lifetime costs between current smokers and ex-smokers by at least €1.7 billion.

Conclusions. Modelling suggests that the lifetime healthcare costs of people in Germany who smoke are substantially greater than those of people who have never smoked. However, more comprehensive tobacco control policies could reduce healthcare expenditure for current smokers by at least 4%.

Keywords: smoking cessation, lifetime health care costs, smoking-attributable diseases, cost savings, tobacco control policies, WHO FCTC

What is already known about this topic

- Since health care expenditures increase with age and smoking-related conditions have long latency periods, lifetime estimations of cost are essential to make informed decisions on resource allocation.
- Compared to never smokers, current smokers have higher lifetime and annual health care expenditures.

What important knowledge gaps exist on this topic

- Dynamic modelling frameworks that estimate lifetime benefits of smoking cessation depending on the number of years since quitting.
- Estimations of lifetime economic consequences associated with smoking cessation if Germany implements stronger, more comprehensive or new tobacco control policies consistent with WHO FCTC guidelines.

What this study adds

- The number of years since quitting strongly influences mortality and morbidity risks in ex-smokers and the magnitude of cost savings over lifetime.
- Even tobacco control policies with low effect sizes (3%-4%) result in sizeable future cost savings that outweigh implementation costs.
- *German EstSmoke* supports public policy planners in making informed decisions how to best allocate resources to implement both federal and state tobacco control policies.

1. Introduction

Since smoking is the leading cause of chronic and cost-intensive illnesses, the World Health Organisation (WHO) set out the WHO Framework Convention for Tobacco Control (FCTC) to reduce the health, social and economic consequences of smoking (1). To assist governments to implement the WHO FCTC in a timely and effective manner, WHO introduced MPOWER, a tool to measure tobacco control policy performance based on six policies. These are: 1) monitoring tobacco use and prevention policies, 2) protecting people from tobacco smoke, 3) offering help to quit tobacco use, 4) warning about the dangers of tobacco, 5) enforcing bans on tobacco advertising, promotion and sponsorship, and 6) raising taxes on tobacco (2). However, uniform implementation and application of these policies is currently lacking in the European Union. A large disparity among European countries has been observed by the most recent estimations of the Tobacco Control Scale 2013 (TCS), which quantifies the implementation of tobacco control policies at country level. While countries like the UK have implemented a comprehensive set of tobacco control policies, Germany has been ranked among the most inactive countries in terms of tobacco control (3, 4). Specifically, Germany has largely failed in the TCS categories of "bans on advertising and promotion", "large health warning lables" and "treatment to help smokers quit". Indeed, tobacco advertising is only prohibited on TV, on the radio and in most print publications (based on 2003/33/EU (5)). In contrast, point-of-sale, billboard and outdoor advertising and promotion are allowed (3). Moreover, cessation treatment policies like pharmacotherapies and behavioural interventions involving advice and support by health care providers are not covered by the statutory health insurance in Germany. More importantly, Germany has failed to introduce stronger, more comprehensive or new tobacco control policies following the WHO FCTC. This is mainly because both state and federal governments are responsible for implementing tobacco control policies, resulting in unclear regulations and numerous loopholes (6). This lack of clear jurisdiction may have lead to Germany's current smoking rates, which are stagnating at a high level after decades of decline (3, 7). Moreover, the high prevalance of smoking in Germany imposes substantial health-related economic costs on the country's health care sector (8) (9) (10). In particular, a German study (8) reported 20% higher annual costs in 2009 for smokers than for never smokers, which amounts to €17.9 billion per year. However, the long-term health and economic consequences of Germany´s inactivity are unclear. Similarly, the potential cost savings that Germany would incur if it implemented tobacco control policies in alignment with WHO FCTC guidelines are still not known.

In fact, the only study (11) to date to consider the long-term health consequences of current German tobacco control policies has estimated a decline of smoking prevalence by 17%, which fails to meet WHO FCTC guidelines. However, this study does not consider the long-term economic consequences on the German health care sector. Only a few international cost-of-illness (COI) studies (12) (13) (14) (15) have investigated the long-term economic consequences of smoking in the US and European countries - and their results differ. While the majority of these studies found higher average lifetime health care costs in smokers and ex-smokers compared to never smokers, the study by Barendregt et al. (13) found the opposite. It showed that higher health care costs later in life outweigh the economic benefits of smoking cessation (13). However, this study assumed that costs for all diseases other than heart disease, stroke, chronic pulmonary disease (COPD) and cancers are not related to smoking and does not consider that smokers are also at a higher risk for other cost-intensive diseases (16). Due to differences in the prevalence of smoking, the related costs of health services and the implementation of tobacco control policies in European countries, the economic results of international COI studies are not easily transferable to Germany. Therefore, the primary aim of this study is to predict lifetime health care costs of current smokers, never smokers and ex-smokers in Germany. A second objective is to estimate lifetime economic consequences if Germany strengthens its efforts in implementing WHO FCTC policies, such as marketing bans, health warnings and cessation treatment.

2. Method

In this subsection, we discuss the model parameters, modelling approach and design of *German EstSmoke*.

2.1. Design of German EstSmoke

German EstSmoke is an adapted version of the *UK EstSmoke*, which estimates the lifetime health care cost of smoking in the UK by using Markov modelling (12). Markov modelling is a cohort simulation approach commonly used to model the clinical development of the risks and trajectories of chronic diseases over the course of a lifetime (17). This is particularly relevant for the progression of smoking-related diseases, which are characterised by long latency periods after smoking onset. *German EstSmoke* was developed in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). While Monte Carlo Simulations were programmed in Visual Basic for Application (VBA), further statistical analyses were conducted using Stata version 12.1 (StataCorp. 2011, College Station, TX: StataCorp LP.).

German EstSmoke focuses on the four smoking-related conditions known to have the highest economic and health-related consequences associated with smoking (18, 19): myocardial infraction (MI), stroke, COPD and lung cancer. To model their lifetime trajectories depending on smoking status, we created three base cohorts, one each for current smokers, never smokers and ex-smokers. Modelling clinical pathways separately for each smoking status is in line with other smoking models and a common approach to avoid influences from individual smoking histories (14, 20). In the following, we examine briefly each clinical pathway.

As shown in Figure 1, the base cohort includes healthy adults, i.e. they do not have any of the four clinical conditions explicitly modelled here. During a Markov cycle (here one year), individuals in the base cohort may develop a first-ever acute MI event. Such an event may either be fatal or non-fatal. If fatal, individuals move to the absorbing state “fatal MI”; if non-fatal, they move to the state “non-fatal MI (year 1)”. In the next cycle, individuals may move to the state “non-fatal MI (year 1+)”, have another acute MI event or die from other causes. Beyond year 1 post-MI, individuals may remain in the same health state, have another acute MI or die from other diseases. Individuals who have a second acute MI will follow the same pathway as the first acute MI. Figure 1 shows that the stroke pathway is similar to the MI pathway. By contrast, the COPD pathway has a chronic course and often leads to death. Similarly, once individuals have developed lung cancer, they tend to die from the cancer itself or an opportunistic disease. The model incorporates the increased risk of mortality from lung cancer in individuals with COPD.

We simulated each cohort of current smokers, never smokers and ex-smokers from age 35 until the age 100 to estimate costs and outcomes for each clinical pathway, stratified by sex. Lifetime excess costs of smoking per person were estimated as the difference in projected lifetime costs between a 35-year-old (continuing) smoker and a 35-year-old never smoker. Similarly, the economic consequences of smoking cessation were calculated as the difference in lifetime costs between a 35-year-old smoker and a 35-year-old ex-smoker at given age of quitting for varying smoking cessation rates. The model starts at the age of 35 for three major reasons. Firstly, the absolute risks of developing or dying from MI, stroke, lung cancer and COPD are very low in the general population of adolescence and young adulthood (21). Secondly, the increased relative risk of smoking-attributable conditions accumulates over time, i.e. it has long latency periods and increases with the number of smoking years. Hence, this relative risk is low below the age of 35. Thirdly, the impact of smoking on health care costs is negligible in younger ages due to the long latency periods of smoking-related diseases (15, 20). Finally, modelling the economic consequences of the general adult population (71% of the total population in Germany is ≥35 years) is in line with other model-based economic simulations (22).

2.2 Model Parameters

German EstSmoke uses data on smoking prevalence obtained from the German Health Update (GEDA 2010), which is a nationally representive health survey of 25,000 German adults (age >18) (23) (Table 1). Estimations of mortality rates, incidence rates and relative risks of smoking-related events are taken from the literature, as described below. We evaluated the quality of these data using the STROBE checklist for observational data (24) and the CONSORT checklist for randomised controlled trials (25).

State transition probabilities for MI, stroke, lung cancer and COPD

For state transition probabilities of smoking-related diseases in the general population, we used population-based data from nationally representative German registries for i) MI (26), ii) stroke (27), iii) lung cancer (28) and iv) COPD (29). Following Briggs et al. (30), one-year probabilities of first-ever acute MI, stroke, lung cancer and COPD in the general population were derived using these data (Appendix 1). Since these data include all three smoking-related groups, i.e. current, never and ex-smokers, we subsequently calculated state transition probabilities for each group (Appendices 2a-2d) by applying the previously described approach in our companion paper (12). Specifically, transition probabilities for first-ever MI, stroke, lung cancer and COPD for each group were calculated using relative risk estimations from i) the INTERHEART study (31, 32), which investigated the risk factors associated with first-ever acute MI based on data from 52 countries, including Germany, ii) the two largest and longest running studies of risk factors associated with primary stroke in women (Nurses' Health Studies) and men (Health Professional Follow-up Study) (33), iii) the SYNERGY project (34) using lung cancer data from eight European case-control studies in 11 countries, including Germany, between 1985-2005 and iv) the European Community Respiratory Health Survey (ECRHS), which examines incidence rates for COPD for 12 countries, including Germany (29) (Table 2).

Similar to transition probabilities of first-ever events, we calculated transition probabilities of recurrent MI and stroke among current, never and ex-smokers based on two nation-wide German registries (recurrent MI) (35) and a large German cohort study (recurrent stroke) (36) (Table 2). Beyond year 1, the probability of acute MI or stroke was based on a systematic review by Lip and Kalra (2010) (37). Finally, for state transition probabilities of fatal events (Appendix 3), we used population-based data from i) the MONICA/KORA MI Registry (fatal MI) (26), ii) Erlangen Stroke Project (ESPrO) (fatal stroke) (27), iii) the Association of Population-based Cancer Registries in Germany (GEKID Atlas) (death from lung cancer) (28) and iv) the WHO health statistics (death from COPD) (38). Since patients with lung cancer or COPD can die not only from these diseases but also from comorbidities like asthma, liver disease and previous metastatic cancer, we rescaled the probability of death as previously described in our companion paper (12).

State transition probabilities of death due to other diseases

Similar to disease pathways, we calculated transition probabilities of death from other diseases based on the most recent population life tables for Germany (39). Since these life tables include deaths caused by the four diseases modelled here, we excluded such deaths (Appendix 3). This was taken as mortality due to other diseases in the general population and used to estimate the risk of mortality among never smokers by applying smoking-attributable fractions based on the most relevant German study (21). Finally, since smoking increases the risk of mortality due to other causes, we adjusted the risk of death from other causes for smokers and ex-smokers by using relative risk estimations for mortality for each group (40, 41).

Health care costs for smoking-related diseases and mortality costs from other causes

For the MI and stroke pathways, we considered costs in the acute phase, as well as in the first and subsequent years (year 1+) (Table 2). All estimates of costs were used from two recent and most relevant German bottom-up COI studies (42, 43). In contrast to other German COI studies, these studies provide detailed medical costs per patient after MI and stroke. For the lung cancer pathway, both health care costs per patient and the costs of initial and terminal care were used from the most recent German COI study (44) (Table 2). Since health care costs of COPD vary depending on the severity of the disease, we included annual costs of

COPD and costs of death due to a severe exacerbation of COPD. Data were taken from two German studies (45, 46), which include detailed in- and outpatient COPD costs per patient depending on COPD severity grades. Lastly, although health care costs from other causes were not considered, mortality costs from other causes were calcuated using the most relevant evaluation report by the German Scientific Advisory Committee (47), which is based on the nationally representative health insurance data of 4.8 million individuals covered by statutory health insurance in Germany. Since the data include mortality costs due to smoking-related diseases, these mortality costs were excluded. All costs were indexed to year 2015 euros (€).

Sensitivity and scenario analyses

Probabilistic sensitivity analyses (Monte Carlo Simulations) were used to test the robustness of our results. Specifically, we randomly sampled parameter values from statistical distributions defined by standard error or confidence interval estimates in the literature. We ran 10,000 simulations for the probabilistic sensitivity analysis (PSA) (48). Commonly used statistical distributions were implemented for relative risks (log normal distribution) and costs (gamma distribution) (49). A uniform distribution was used only when the parameter range was available without standard errors. The 95% confidence intervals based on the PSA are reported in the Results section (48).

For scenario analyses, we assumed that Germany strengthens its efforts to implement the WHO FCTC policies that had the lowest ranking in TCS. Specifically, we evaluated an increase of smoking cessation rate by i) 3% (strong health warnings), ii) 4% (comprehensive marketing bans) and iii) 34% (cessation treatment such as pharmaco- and behavioural therapies) (11). Since Germany implemented a telephone quitline in 1999, we followed Levy et al. (11) and assumed a 34% increase in smoking cessation (instead of 39% if no cessation treatment policy had been implemented).

3. Results

We estimated the magnitude of lifetime health care costs of four smoking-related diseases for current smokers, never smokers, and ex-smokers using a cohort modelling approach. Our analysis projected four clinical pathways and associated costs and then estimated potential economic consequences of smoking cessation if Germany strengthens efforts in implementing WHO FCTC policies that had the lowest ranking in TCS.

Lifetime health care costs for smoking-related diseases

Table 3 presents the lifetime health care costs due to MI, stroke, lung cancer and COPD for current smokers, never smokers, and ex-smokers. Smokers have significantly higher lifetime health care costs than never smokers and ex-smokers. Compared to never smokers, the lifetime health care costs for both male and female smokers are twice as high. For the current smoking population in Germany lifetime excess health care costs of smoking were €41.56 billion (2015, discounted at 3.5%). Moreover, compared to ex-smokers, the lifetime health care costs for smokers are 20% higher for males and 30% higher for females (Table 3).

Figure 2 presents the distribution of cumulative health care costs incurred by smokers and ex-smokers by age. It shows that the difference in incurred costs is much more pronounced after the age of 65 years before it stabilises at the age of 80. This variation in costs is likely due to the higher probability of using medical services as smoking-related diseases become clinically relevant in older individuals. Indeed, Figure 3 shows that smoking-attributable deaths increase with age, particularly between the ages of 55 and 85. For example, while 9% of all deaths are attributable to smoking-related diseases in males aged 35-45, 28% of all deaths are attributable to smoking-related diseases in males aged 70-74. Finally, our results confirm that MI and stroke are the top contributors to the overall smoking burden over lifetime, which indicates potential sizeable reductions in costs as MI and stroke events can be prevented (see Appendix 4).

Potential economic consequences of implementing WHO FCTC policies

Table 3 shows the magnitude of the difference in costs between smokers and ex-smokers if Germany implements strong health warnings, comprehensive marketing bans or cessation treatment policies, which are in line with WHO FCTC guidelines. We found that a 3% increase of smoking cessation (which is potentially achievable due to strong health warnings (11)) would reduce the lifetime cost-difference between smokers and ex-smokers by €1.7 billion (discounted). Similarly, this potential difference would decline by €2.2 billion if smoking cessation rates increase by 4% due to an implementation of comprehensive marketing bans (11). Finally, if Germany implements further cessation treatment policies like pharmaco- and behavioural therapies, we predict a reduction in cost-difference by €18.9 billion (discounted) over a lifetime.

3. Discussion

Twelve years after the introduction of the WHO FCTC, Germany still lacks comprehensive tobacco control policies and has implemented only a minimal set of policies (3). By using *German EstSmoke,* we projected that lifetime health care costs of smoking were twice as high in smokers than in never smokers under Germany´s tobacco control policies. Moreover, if it does not strengthen its policies, Germany will impose substantial lifetime excess health care costs of smoking on the population level (€41.56 billion, discounted). These costs underscore the economic and public health relevance of smoking in Germany. More importantly, using *German EstSmoke* we showed that small effect sizes of tobacco control policies (3%-4%) result in sizeable cost-differences (€1.7-2.2 billion) compared to programme costs, which vary between €0.008 billion (50) and €0.4 billion (51). Using *German EstSmoke,* we also demonstrated that larger potential cost savings can be achieved with the help of pharmaco- and behavioural therapies (€18.9 billion, discounted). Therefore we urge swift implementation of stronger health warnings, more comprehensive advertising bans and new cessation therapies, all covered by statutory health insurance, as major components of an effective tobacco control policy in Germany.

A recent systematic literature review (52) provides strong evidence that only few international studies have also estimated lifetime costs of smoking using a dynamic modelling framework. For instance, Hodgson (15) estimated that compared to never smokers, male (female) smokers have a 47% (41%) higher lifetime cost, which is in line with our results. However, it should be noted that Hodgson´s approach (15) to estimating lifetime medical expenditures was based on smoking status (not on clinical pathways, as in our model). A similar approach was applied by the European study on Quantifying Utility of Investment in Protection from Tobacco (EQUIPT) (53), a recent multicentre study which evaluates the cross-context transferability of economic evidence of tobacco control policies among European countries. For Germany, annual health care costs of smoking-attributable diseases (MI, stroke, COPD, lung cancer) were estimated at €15.12 billion (54) which are slightly higher than our estimates (€13.26 billion). This cost difference is mainly due to methodological differences. For instance, the prevalence of smoking-attributable diseases for smokers and ex-smokers was calculated by using population-attributable fractions in the EQUIPT study (53, 55), compared to modelling clinical pathways for each disease. Moreover, morbidity and mortality of ex-smokers depending on the number of years since quitting was modelled in *German EstSmoke* while an average risk for ex-smokers was assumed in the EQUIPT model. With respect to the economic consequences of smoking cessation, our results are consistent with the results of other COI studies (52) but cannot be compared with cost-effectiveness models like the frequently used Benefits of Smoking Cessation on Outcomes (BENESCO) model, which assesses the cost-effectiveness of smoking cessation pharmacotherapies in the US and European countries. All COI studies, except that of Barengregt et al. (13), found that smoking cessation will result in short- and/or long-term cost savings. However, Barengregt et al. (13) concluded that smoking cessation reduces only short-term costs while increasing long-term costs. This conclusion can be challenged for a number of reasons. Firstly, smoking increases the risk of more expensive health conditions (such as lung cancer), which otherwise have lower incidence rates. Secondly, smoking increases the risk of chronic non-fatal conditions that incur ongoing medical costs (such as COPD and asthma). Indeed, our model showed that between ages 50 and 80, there is a higher proportion of the smoker cohort with at least one of the four diseases than the never-smoking cohort. For instance, at age 70, 16% of smokers are alive with at least one smoking-related disease compared to 7% of never smokers. Thirdly, Barengregt et al. (13) restricted their analysis to four conditions and did not include the increased relative risk of other conditions, many of which are non-fatal. Finally, since smoking increases the early onset risk of diseases (including long-term chronic conditions and expensive fatal conditions such as lung cancer), costs incurred earlier in life are valued more than costs incurred later in life when discounting is applied. This impact results in higher discounted costs than those incurred later in life. However, Barengregt et al. (13) did not apply discounting to their COI model. Similar arguments were raised by other authors in response to this paper (see comments of Hodgson; Fries; Heaney; Leistikow and Miller, and Sauter 1998 (16)).

Our study has a number of strengths. It provides the first model, *German EstSmoke*, which is capable of estimating lifetime costs of smoking in Germany. Indeed, modelling clinical pathways which depend on smoking status over the course of a lifetime helps clinicians and health care specialists to make informed decisions on allocating scarce resources based on both clinical and economic relevance. For instance, MI not only has a high clinical relevance but also causes high lifetime health care costs. More importantly, since political decisions are made within four-year electoral cycles, *German EstSmoke* is a useful economic tool in decision-making processes: it predicts the economic consequences of tobacco control policies not merely for a specific year but for longer timeframes. *German EstSmoke* can be thus used to predict long-term economic consequences of a single or combined tobacco control policy at federal or state level. Ranking these consequences provides an important basis for prioritising tobacco control policies according to cost savings. However, we must bear in mind that the implementation of these policies is under the purview of the 16 German states, which enact the WHO FCTC guidelines differently. Thus our model may also help to compare both performances among the states and the economic consequences of inaction at the federal and state level. Another strength of our study is its incorporation of time-dependent transitions within a comprehensive decision analytic framework. In contrast to previous studies (15) (13), our model takes into account that smoking cessation benefits depend on the number of years since quitting. This, in turn, allows a more accurate estimation of future gains from smoking cessation.

Since the limitations of the modelling approach are extensively discussed in earlier work (12), we briefly summarise them and focus here on their implications. Firstly, since smoking increases the risk of chronic (non-)fatal conditions such as asthma, modelling only four clincial conditions according to smoking status, although in line with earlier studies (56) (57) (14) (58), underestimates the costs of smoking-related diseases and the benefits of smoking cessation. Similarly, since good quality epidemiological data about the impact of smoking relapse on the risk of morbidity and mortality of smoking-related conditions are not available, our results are rather conservative. Finally, since *German EstSmoke* does not consider both the costs of implementing tobacco control policies and the impact of these policies on clinical outcomes (e.g. reduced prevalence of smoking-related diseases), it is a partial economic evaluation. In contrast to the BENESCO model (52), explicit investment choices cannot be derived by using *German EstSmoke.*

In summary, by using *German EstSmoke,* we showed that the consequences of Germany´s inaction in implementing stronger, more comprehensive and new tobacco control policies are considerable. Without the implementation of more rigorous policies, adult smoking-related costs will substantially increase. Given that Germany is ranked among the most inactive European countries in terms of tobacco control policies (3, 4), it can expect higher benefits from policies to prevent or stop smoking, compared to countries which already meet WHO FCTC guidelines. Indeed, our analysis shows that even small effect sizes (3-4%) can substantially reduce the health-related costs of smoking in Germany. With the help of models such as *German EstSmoke,* policy planners can make informed decisions to instigate effective tobacco control policies.

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Table and Figure Legend

Table 1: Prevalence of never, current and ex-smokers by age group and sex

Age- and gender-specific prevalences of never smokers, current smokers and ex-smokers.

Table 2: Parameter values for Markov model and distribution of Monte Carlo Simulation

Epidemiological and economic input data for Markov model.

Table 3: Lifetime costs of health care resource use due to MI, stroke, lung cancer, COPD and economic consequences of implementing WHO FCTC policies (2015)

Lifetime health care costs due MI, stroke, lung cancer, COPD, and other causes of death for never smokers, current smokers, and ex-smokers. Smokers have significantly higher lifetime health care costs than never smokers and ex-smokers.

Figure 1: Markov structure for four clinical pathways related to smoking and quitting smoking

German EstSmoke focuses on four smoking-related conditions, i.e. myocardinal infarction (MI), stroke, chronic obstructive pulmonary disease (COPD) and lung cance. Three base cohorts, one each for never smokers, current smokers and ex-smokers, were created.

Figure 2: Cumulative distribution of lifetime health care costs in smokers and ex-smokers

Predicted lifetime health care costs incurred by smokers and ex-smokers, stratified by sex. The difference in incurred costs is much more pronounced beyond the age of 65 before it stabilises at the age of 80.

Figure 3: Predicted survival of smokers and ex-smokers

Predicted survival curves for smokers and ex-smokers. They show that smoking cessation is likely to increase the probability of survival in men and women, particularly between the ages of 55 and 85 years.

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