Appendix 1: Technical appendix

The HealthLumen[1] microsimulation consists of two modules. The first module calculates the predictions of smoking prevalence trends over time based on data from rolling cross-sectional studies. The second module performs the microsimulation of a virtual population, generated with demographic characteristics matching those of the observed data. The health trajectory of each individual from the population is simulated over time allowing them to contract, survive or die from a set of diseases or injuries related to the analysed risk factors. The detailed description of the two modules is presented below.(1)

Module one: Predictions of smoking prevalence over time

Smoking status groups are indicated in Table 1.

Table 1. Description of the categories used for tobacco consumption the risk factor of interest

Smoker status	Number of categories (N)	Categories
Tobacco (initialisation)	3	1 Never smoker 2 Ex-smoker 3 Smoker
Tobacco (changes in smoking over time)	2	1 Non-smoker 2 Smoker

Smoking is the categorical risk factor. Each individual in the population may belong to one of the three possible smoking categories {*never smoked, ex-smoker, smoker*} with their probabilities {p_0, p_1, p_2}. These states are updated on receipt of the information that the person is either a smoker or a non-smoker. They will be a never-smoker or an ex-smoker depending on their original state (an ex-smoker can never become a never-smoker).

The complete set of longitudinal smoking trajectories and the probabilities of their happening is generated for the simulation years by allowing all possible transitions between smoking categories:

$$\{never\ smoked\} \rightarrow \{never\ smoked, smoker\}$$
$$\{ex\text{-}smoker\} \rightarrow \{ex\text{-}smoker, smoker\}$$
$$\{smoker\} \rightarrow \{ex\text{-}smoker, smoker\}$$

When the probability of being a smoker is p the allowed transitions are summarised in the state update equation

[1] Originally developed within UK Health Forum

$$\begin{bmatrix} p_0' \\ p_1' \\ p_2' \end{bmatrix} = \begin{bmatrix} 1-p & 0 & 0 \\ 0 & 1-p & 1-p \\ p & p & p \end{bmatrix} \begin{bmatrix} p_0 \\ p_1 \\ p_2 \end{bmatrix} \tag{0.1}$$

In the initial year of the simulation, a person may be in one of the three smoking categories this is determined by the static trend with three smoking categories. After N updates there will be 3×2^N possible trajectories. These trajectories will each have a calculated probability of occurring; the sum of these probabilities is 1.

In each year the probability of being a smoker or a non-smoker will depend on the forecast smoking scenario which provides exactly that information. In the baseline scenario this is the dynamic trend. Note that these states are two dimensional and cross-sectional {*non-smoking, smoking*}, and they are turned into three dimensional states {*never smoked, ex-smoker, smoker*} as described above. The time evolution of the three-dimensional states are the smoking trajectories necessary for the computation of disease table disease and death probabilities.

Multinomial logistic regression

Measured data consist of sets of probabilities, with their variances, at specific time values (typically the year of the survey). For any particular time the sum of these probabilities is unity. Typically such data might be the probabilities of never smoker, ex-smoker, smoker as they are extracted from the survey data set. Each data point is treated as a normally distributed[2] random variable; together they are a set of N groups (number of years) of K probabilities $\{\{t_i, \mu_{ki}, \sigma_{ki} | k \in [0,K\text{-}1]\} | i \in [0,N\text{-}1]\}$. For each year the set of K probabilities form a distribution – their sum is equal to unity.

The regression consists of fitting a set of logistic functions $\{p_k(a, b, t) | k \in [0,K\text{-}1]\}$ to these data – one function for each k-value. At each time value the sum of these functions is unity. Thus, for example, when measuring smoking status in the three states already mentioned, the $k = 0$ regression function represents the probability of being a never smoker over time, $k = 1$ the probability of being an ex-smoker and $k = 2$ the probability of being a smoker.

The regression equations are most easily derived from a familiar least square minimization. In the following equation set the weighted difference between the measured and predicted probabilities is written as S; the logistic regression functions $p_k(a,b;t)$ are chosen to be ratios

[2] Depending on the circumstances this assumption will be more or less accurate and more or less necessary. In general, it is both extremely useful and accurate. For simple surveys the individual Bayesian prior and posterior probabilities are Beta distributions – the likelihood being binomial. For reasonably large samples, the approximation of the beta distributions by normal distributions is both legitimate and a practical necessity. For complex, multi-PSU, stratified surveys, it is again assumed that these base probabilities are approximately normally distributed and, again, it is an assumption that makes the analysis tractable.

Depending on the nature of the raw data set it may be possible to use non-parametric statistical methods for this analysis. This is possible for the HSE and GHS data sets of this study but when this has been done the authors can report no discernible difference in the results.

of sums of exponentials (This is equivalent to modelling the log probability ratios, p_k/p_0, as linear functions of time.)

$$S(\mathbf{a},\mathbf{b}) = \tfrac{1}{2}\sum_{k=0}^{k=K-1}\sum_{i=0}^{i=N-1}\frac{\left(p_k(\mathbf{a},\mathbf{b};t_i)-\mu_{ki}\right)^2}{\sigma_{ki}^2} \tag{0.2}$$

$$p_k(\mathbf{a},\mathbf{b},t) \equiv \frac{e^{A_k}}{1+e^{A_1}+..+e^{A_{K-1}}}$$

$$\mathbf{a} \equiv (a_0,a_1,..,a_{K-1}), \quad \mathbf{b} \equiv (b_0,b_1,..,b_{K-1}) \tag{0.3}$$

$$A_0 \equiv 0, \quad A_k \equiv a_k + b_k t$$

The parameters A_0, a_0 and b_0 are all zero and are used merely to preserve the symmetry of the expressions and their manipulation. For a K-dimensional set of probabilities there will be $2(K\text{-}1)$ regression parameters to be determined.

For a given dimension K there are K-1 independent functions p_k – the remaining function being determined from the requirement that complete set of K form a distribution and sum to unity.

Note that the parameterization ensures that the necessary requirement that each p_k be interpretable as a probability – a real number lying between 0 and 1.

The minimum of the function S is determined from the equations

$$\frac{\partial S}{\partial a_j} = \frac{\partial S}{\partial b_j} = 0 \qquad \text{for j=1,2,....,k-1} \tag{0.4}$$

noting the relations

$$\frac{\partial p_k}{\partial A_j} = \frac{\partial}{\partial A_j}\left(\frac{e^{A_k}}{1+e^{A_1}+..+e^{A_{K-1}}}\right) = p_k\delta_{kj} - p_k p_j$$

$$\frac{\partial}{\partial a_j} = \frac{\partial}{\partial A_j} \tag{0.5}$$

$$\frac{\partial}{\partial b_j} = t\frac{\partial}{\partial A_j}$$

The values of the vectors a, b that satisfy these equations are denoted $\hat{\mathbf{a}},\hat{\mathbf{b}}$. They provide the trend lines, $p_k(\hat{\mathbf{a}},\hat{\mathbf{b}};t)$, for the separate probabilities. The confidence intervals for the trend lines are derived most easily from the underlying Bayesian analysis of the problem.

Bayesian interpretation

The $2K$-2 regression parameters {a,b} are regarded as random variables whose posterior distribution is proportional to the function exp(-S(a,b)). The maximum likelihood estimate of

this probability distribution function, the minimum of the function S, is obtained at the values $\hat{\mathbf{a}},\hat{\mathbf{b}}$. Other properties of the (2*K*-2)-dimensional probability distribution function are obtained by first approximating it as a (2*K*-2)-dimensional normal distribution whose mean is the maximum likelihood estimate. This amounts to expanding the function *S*(a,b) in a Taylor series as far as terms quadratic in the differences $(\mathbf{a}-\hat{\mathbf{a}}),(\mathbf{b}-\hat{\mathbf{b}})$ about the maximum likelihood estimate $\hat{\mathbf{S}}\equiv S(\hat{\mathbf{a}},\hat{\mathbf{b}})$. Hence

$$\begin{aligned} S(\mathbf{a},\mathbf{b}) &= \tfrac{1}{2}\sum_{k=0}^{k=K-1}\sum_{i=0}^{i=N-1}\frac{\left(p_k(\mathbf{a},\mathbf{b};t_i)-\mu_{ki}\right)^2}{\sigma_{ki}^2} \\ &\equiv S(\hat{a},\hat{b})+\tfrac{1}{2}(a-\hat{a},b-\hat{b})P^{-1}(a-\hat{a},b-\hat{b})+\ldots \\ &\approx S(\hat{a},\hat{b})+\tfrac{1}{2}\sum_{i,j}(a_i-\hat{a}_i)\frac{\partial^2\hat{S}}{\partial\hat{a}_i\partial\hat{a}_j}(a_j-\hat{a}_j)+\tfrac{1}{2}\sum_{i,j}(a_i-\hat{a}_i)\frac{\partial^2\hat{S}}{\partial\hat{a}_i\partial\hat{b}_j}(b_j-\hat{b}_j)+ \\ &+\tfrac{1}{2}\sum_{i,j}(b_i-\hat{b}_i)\frac{\partial^2\hat{S}}{\partial\hat{b}_i\partial\hat{a}_j}(a_j-\hat{a}_j)+\tfrac{1}{2}\sum_{i,j}(b_i-\hat{b}_i)\frac{\partial^2\hat{S}}{\partial\hat{b}_i\partial\hat{b}_j}(b_j-\hat{b}_j) \end{aligned} \tag{0.6}$$

The (2*K*-2)-dimensional covariance matrix *P* is the inverse of the appropriate expansion coefficients. This matrix is central to the construction of the confidence limits for the trend lines.

Estimation of the confidence intervals

The logistic regression functions $p_k(t)$ can be approximated as a normally distributed time-varying random variable $N(\hat{p}_k(t),\sigma_k^2(t))$ by expanding p_k about its maximum likelihood estimate (the trend line) $\hat{p}_k(t)=p(\hat{\mathbf{a}},\hat{\mathbf{b}},t)$

$$\begin{aligned} p_k(\mathbf{a},\mathbf{b},t) &= p_k(\hat{\mathbf{a}}+\mathbf{a}-\hat{\mathbf{a}},\hat{\mathbf{b}}+\mathbf{b}-\hat{\mathbf{b}},t) \\ &= \hat{p}_k(t)+(\nabla_{\hat{a}},\nabla_{\hat{b}})\hat{p}_k(t)\begin{pmatrix}\mathbf{a}-\hat{\mathbf{a}}\\ \mathbf{b}-\hat{\mathbf{b}}\end{pmatrix}+\ldots \end{aligned} \tag{0.7}$$

Denoting mean values by angled brackets, the variance of p_k is thereby approximated as

$$\begin{aligned} &\sigma_k^2(t)\equiv\left\langle\left(p_k(\mathbf{a},\mathbf{b},t)-\hat{p}_k(t)\right)^2\right\rangle=(\nabla_{\hat{a}}\hat{p}_k(t),\nabla_{\hat{b}}\hat{p}_k(t))\left\langle\begin{pmatrix}\mathbf{a}-\hat{\mathbf{a}}\\ \mathbf{b}-\hat{\mathbf{b}}\end{pmatrix}\begin{pmatrix}\mathbf{a}-\hat{\mathbf{a}}\\ \mathbf{b}-\hat{\mathbf{b}}\end{pmatrix}^T\right\rangle\times \\ &(\nabla_{\hat{a}}\hat{p}_k(t),\nabla_{\hat{b}}\hat{p}_k(t))^T=(\nabla_{\hat{a}}\hat{p}_k(t),\nabla_{\hat{b}}\hat{p}_k(t))\ P\ (\nabla_{\hat{a}}\hat{p}_k(t),\nabla_{\hat{b}}\hat{p}_k(t))^T \end{aligned} \tag{0.8}$$

When *K*=3 this equation can be written as the 4-dimensional inner product

$$\sigma_k^2(t) = \begin{pmatrix} \frac{\partial \hat{p}_k(t)}{\partial \hat{a}_1} & \frac{\partial \hat{p}_k(t)}{\partial \hat{a}_2} & \frac{\partial \hat{p}_k(t)}{\partial \hat{b}_1} & \frac{\partial \hat{p}_k(t)}{\partial \hat{b}_2} \end{pmatrix} \begin{bmatrix} P_{aa11} & P_{aa12} & P_{ab11} & P_{ab12} \\ P_{aa21} & P_{aa22} & P_{ab21} & P_{ab22} \\ P_{ba11} & P_{ba12} & P_{bb11} & P_{bb12} \\ P_{ba21} & P_{ba22} & P_{bb21} & P_{bb22} \end{bmatrix} \begin{pmatrix} \frac{\partial \hat{p}_k(t)}{\partial \hat{a}_1} \\ \frac{\partial \hat{p}_k(t)}{\partial \hat{a}_2} \\ \frac{\partial \hat{p}_k(t)}{\partial \hat{b}_1} \\ \frac{\partial \hat{p}_k(t)}{\partial \hat{b}_2} \end{pmatrix} \quad (0.9)$$

where $P_{cdij} \equiv \left\langle (c_i - \hat{c}_i)(d_j - \hat{d}_j) \right\rangle$. The 95% confidence interval for $p_k(t)$ is centred given as $\left[\hat{p}_k(t) - 1.96\sigma_k(t), \mathrm{p_k}(t) + 1.96\sigma_k(t)\right]$.

Module two: Microsimulation

Microsimulation initialisation: birth, disease and death models

Simulated people are generated with the correct demographic statistics in the simulation's start-year. In this year women are stochastically allocated the number and years of birth of their children – these are generated from known fertility and mother's age at birth statistics (valid in the start-year). If a woman has children then those children are generated as members of the simulation in the appropriate birth year.

The microsimulation is provided with a list of relevant diseases. These diseases used the best available incidence, mortality, survival, relative risk and prevalence statistics (by age and gender). At initialisation, the prevalence statistics are used to generate stochastically a simulated person's initial disease state in the simulation start-year. The population of people, so initialised, will stochastically reproduce the national prevalence statistics for each disease. It is assumed that at initialisation the diseases are independent random variables. In the course of their lives, simulated people can die from one of the diseases caused by smoking that they might have acquired or from some other cause. The probability that a person of a given age and gender dies from a cause other than the disease are calculated in terms of known death and disease statistics valid in the start-year. It is constant over the course of the simulation. The survival rates from tobacco-related diseases will change as a consequence of the changing distribution of smoking level in the population.

The microsimulation incorporates a sophisticated economic module. The module employs Markov-type simulation of long-term health benefits, health care costs and non-health care related costs of specified interventions.

This section provides an overview of the initialisation of the microsimulation model and will be expanded upon in the next sections.

Population models

Populations are implemented as instances of the TPopulation C++ class. The TPopulation class is created from a population (*.ppl) file. Usually a simulation will use only one population but it can simultaneously process multiple populations (for example, different ethnicities within a national population).

Distributions

Distribution name	symbol	note
MalesByAgeByYear	$p_m(a)$	Input in year$_0$ – probability of a male having age a
FemalesByAgeByYear	$p_f(a)$	Input in year$_0$ – probability of a female having age a
BirthsByAgeofMother	$p_b(a)$	Input in year$_0$ – conditional probability of a birth at age a| the mother gives birth.
NumberOfBirths	$p_\lambda(n)$	λ≡TFR, Poisson distribution, probability of giving birth to n children
MaleDeathByAge	$p_{\Omega m}(a)$	Input in year$_0$, probability of a male dying at age a
FemaleDeathByAge	$p_{\Omega f}(a)$	Input in year$_0$, probability of a female dying at age a

Birth model

Any female in the child bearing years {*AgeAtChild.lo, AgeAtChild.hi*} is deemed capable of giving birth. The number of children, n, that she has in her life is dictated by the Poisson distribution $p_\lambda(n)$ where the mean of the Poisson distribution is the Total Fertility Rate (TFR) parameter[3].

The probability that a mother (who does give birth) gives birth to a child at age a is determined from the BirthsByAgeOfMother distribution as $p_b(a)$. For any particular mother the births of multiple children are treated as independent events, so that the probability that a mother who produces N children produces n of them at age a is given as the Binomially distributed variable,

$$p_b(n\,at\,a \mid N) = \frac{N!}{n!(N-n)!}\left(p_b(a)\right)^n\left(1-p_{bm}(a)\right)^{N-n} \tag{0.10}$$

The probability that the mother gives birth to n children at age a is

$$p_b(n\,at\,a) = e^{-\lambda}\sum_{N=n}^{\infty}\frac{\lambda^N}{N!}p_b(n\,at\,a \mid N) = e^{-\lambda}\sum_{N=n}^{\infty}\frac{\lambda^N}{n!(N-n)!}\left(p_b(a)\right)^n\left(1-p_b(a)\right)^{N-n} \tag{0.11}$$

Performing the summation in this equation gives the simplifying result that the probability $p_b(n\ at\ a)$ is itself Poisson distributed with mean parameter $\lambda p_b(a)$,

$$p_b(n\,at\,a) = e^{-\lambda p_b(a)}\frac{\left(\lambda p_b(a)\right)^n}{n!} = p_{\lambda p_b(a)}(n) \tag{0.12}$$

[3] This could be made to be time dependent; in the baseline model it is constant.

Thus, on average, a mother at age a will produce $\lambda p_b(a)$ children in that year.

The gender of the children[4] is determined by the probability p_{male}=1-p_{female}. In the baseline model this is taken to be the probability $N_m/(N_m+N_f)$.

The Population editor' menu item Population Editor\Tools\Births\show random birthList creates an instance of the TPopulation class and uses it to generate and list a (selectable) sample of mothers and the years in which they give birth.

Time dependent birth rates

The TFR parameter for future years can be input from file if known – or otherwise modelled. In this project the TFR parameter is kept constant overtime (ONS, 2016). In each year of their simulated life (y at age a), mothers of child bearing age can use the appropriate Poisson parameter $\lambda(a)p_b(a)$ to generate the number of children in that year. Each child is recorded in the mother's Life Event list and processed as part of the current family at the end of the mother's life.

Population dynamics

In some year, Y, the population will consist of N_m males and N_f females with their respective age distributions. In the next year, Y', the numbers will have been depleted by deaths and augmented by the $N_{newborn}$ births. The new, primed, population is determined from the old by the following equation set

$$N_{newborn} = \lambda N_f \sum_{a=AgeAtChild.lo}^{a=AgeAtChild.hi} p_f(a)\left(1-p_f(a)\right)p_b(a) \tag{0.13}$$

$$N'_m = N_m \sum_{a=1}^{a=Age.hi} p_m(a)\left(1-p_m(a)\right) + p_{male}N_{newborn} \tag{0.14}$$

$$N'_f = N_f \sum_{a=1}^{a=Age.hi} p_f(a)\left(1-p_f(a)\right) + p_{female}N_{newborn} \tag{0.15}$$

$$p'_m(a+1) = \frac{N_m}{N'_m} p_m(a)\left(1-p_m(a)\right) \tag{0.16}$$

$$p'_m(a+1) = \frac{N_m}{N'_m} p_m(a)\left(1-p_{\Omega m}(a)\right) \tag{0.17}$$

$$p'_f(a+1) = \frac{N_f}{N'_f} p_f(a)\left(1-p_{\Omega f}(a)\right) \tag{0.18}$$

[4] The probability of child gender can be made time dependent.

$$p'_m(0) = \frac{1}{N'_m} p_{male} N_{newborn} \tag{0.19}$$

$$p'_f(0) = \frac{1}{N'_f} p_{female} N_{newborn} \tag{0.20}$$

Deaths from modelled diseases

The simulation models any number of specified diseases some of which may be fatal. In the start year the simulation's death model uses the diseases' own mortality statistics to adjust the probabilities of death by age and gender. In the start year the net effect is to maintain the same probability of death by age and gender as before; in subsequent years, however, the rates at which people die from modelled diseases will change as modelled risk factors change. This the population dynamics sketched above will be only an approximation to the simulated population's dynamics. The latter will be known only on completion of the simulation.

Multiple population processing

Multiple populations can be used in a simulation provided they are non-overlapping (people cannot belong to both).

In a simulation, Monte Carlo trials are allocated between current different populations in proportion to their total person count (malesCount+femalesCount). The idea being to provide a representative sample of the combined population.

In a simulation, a population (pop) is current if the simulated year Y satisfies

$$pop \to startYear \le Y \le pop \to stopYear \tag{0.21}$$

Open populations

This model is an *open* population model which allows people to enter and to depart from the population (departure probability $p_\delta(t)$).

Open population, births and deaths

In the year y the number of males and females in the population are denoted as {$N_m(a,y)$, $N_f(a,y)$},

And we suppose that they have departure probabilities {$p_{m\delta}(a,y)$, $p_{f\delta}(a,y)$}. The number of new arrivals into each age in the year Y are denoted {$N_{mArr}(a,y)$, $N_{fArr}(a,y)$}.

The following analysis applies equally to males and females and we drop the gender suffix. The male and female populations grow according to the recursion relations

$$N(a+1, y+1) = N(a,y)\left(1 - p_\Omega(a)\right)\left(1 - p_\delta(a,y)\right) + N_{Arr}(a,y) \quad (a > 1) \tag{0.22}$$

$$N(1,y+1)=N_{Newborn}(y)\left(1-p_{\Omega}(0)\right)\left(1-p_{\delta}(0,y)\right)+N_{Arr}(0,y)\quad(a=0)\qquad(0.23)$$

The longitudinal modelling of populations having known cross sectional data

Given a set of X-sectional population projections {$K_m(a,y)$, $K_f(a,y)|0<=a<=100$; $Y_0<=y<=Y_1$} (the K- population) the question arises of how to model the lives of individuals within the population (the N-population). In the absence of precise arrival (immigration) and departure (emigration) statistics, many solutions exist. The population is constructed iteratively: given the population in year Y the next year' population is calculated from the known birth and death rates; the departure probabilities and arrival numbers are found by matching with the projected K-population.

Minimum arrival and departure model

The minimum arrival and departure model fixes the modelled N-population in the start year and compensates in subsequent years either by having non-zero departure statistics (if N>K) or by importing new people (K>N).

From equation (0.22):

$$if\ N(a,y)\left(1-p_{\Omega}(a)\right)>K(a+1,y+1)$$

$$\left(1-p_{\delta}(a,y)\right)=\frac{K(a+1,y+1)}{N(a,y)\left(1-p_{\Omega}(a)\right)}\quad(a>1)$$

$$\Rightarrow$$

$$N(a+1,y+1)=N(a,y)\left(1-p_{\Omega}(a)\right)\left(1-p_{\delta}(a,y)\right)=K(a+1,y+1)\quad(a>1)\qquad(0.24)$$

$$if\ N(a,y)\left(1-p_{\Omega}(a)\right)<K(a+1,y+1)$$

$$N_{Arr}(a,y)=K(a+1,y+1)-N(a,y)\left(1-p_{\Omega}(a)\right)\quad(a>1)$$

$$\Rightarrow$$

$$N(a+1,y+1)=N(a,y)\left(1-p_{\Omega}(a)\right)+N_{Arr}(a,y)=K(a+1,y+1)\qquad(0.25)$$

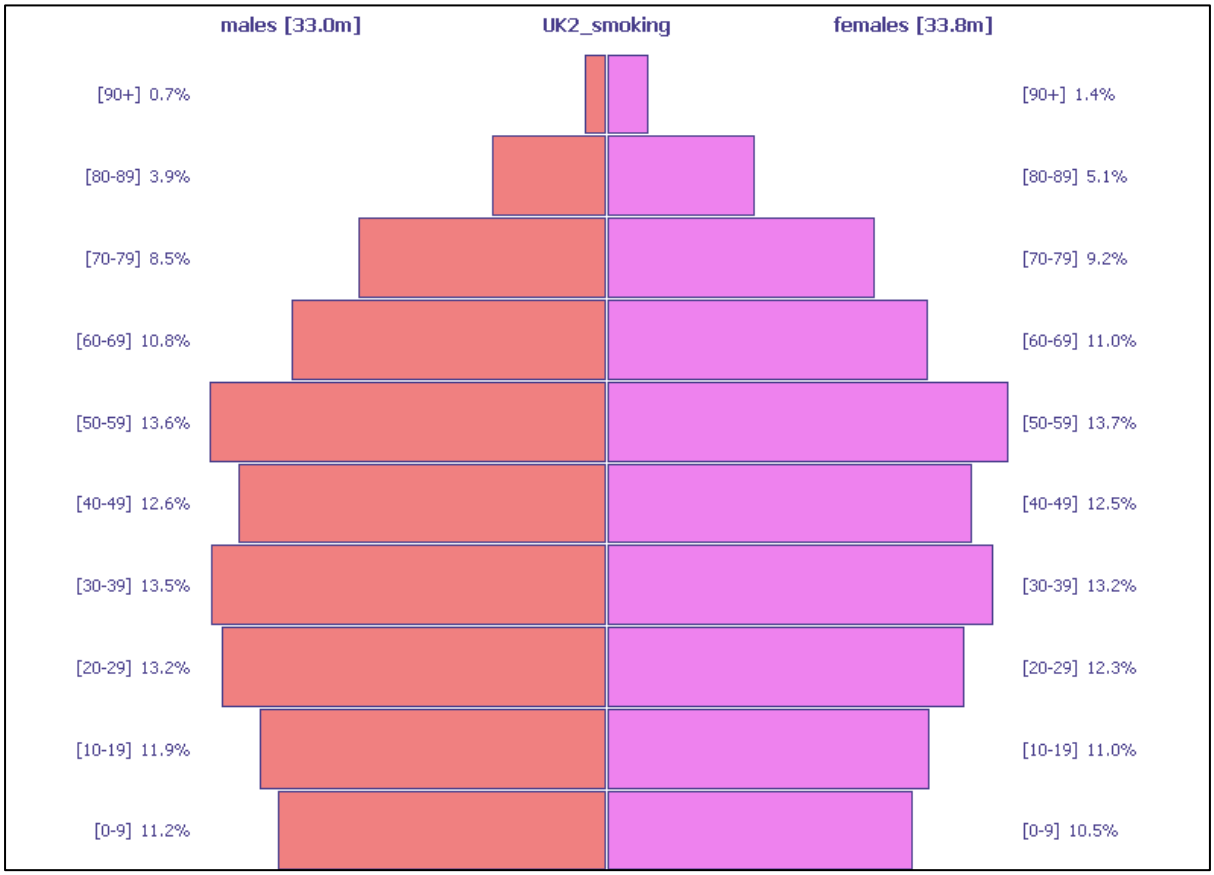
The implementation of this model can be arranged using multiple populations – one population for each year of the simulation. The first population consists of the base line model that matches the N and K populations in the start year; subsequent populations contain the corrections (the arrivals, if any in that year). When arrivals enter the simulated population they have a start year corresponding to this population's start year. They usually will have been modelled from birth in the appropriate risk and disease environment. Arrivals are ordinary members of the modelled population – they simply enter the population at times after the simulation-start time. Arrivals carry with them a population identifier.

The numbers of males and females and their ages are known for all populations. Within the micro simulation multiple populations are sampled at a rate proportional to their population size.

Population assumptions

Error! Reference source not found. shows the population distribution in 2019, in the UK used in the initialisation of the model. The 2019 England population shows a young population with X5% under 50 years of age. The split between males and females shows slightly more females (X%) than males (X%). The pyramid also demonstrates that the women are living longer, of those aged 60 years and over, X% are female.

Figure 1:Population pyramid in 2019 in the UK



Smoking scenarios

The microsimulation framework applied to smoking enables the measurement of the future health impact of changes in rates of tobacco consumption.

In the simulation each person is categorised into one of the three smoking groups: smokers, ex-smokers and people who have never smoked. Their initial distribution is based on the distribution of smokers, ex-smokers and never smokers as predicted by the three smoking category trend.

During the simulation a person may change smoking states and their relative risk will change accordingly. Relative risks associated with smokers and people who have never smoked have been collected from published data. The relative risks associated with ex-smokers ($RR_{\text{ex-smoker}}$) are related to the relative risk of smokers (RR_{smoker}). The ex-smoker relative risks are assumed to decrease over time with the number of years since smoking cessation ($T_{\text{cessation}}$). These relative risks are computed in the model using equations (1.28) and (1.29).(2)

$$RR_{\text{ex-smoker}}\left(A,S,T_{\text{cessation}}\right)=1+\left(RR_{\text{smoker}}\left(A,S\right)-1\right)\exp\left(-\gamma\left(A\right)T_{\text{cessation}}\right) \quad (0.26)$$

$$\gamma\left(A\right)=\gamma_0\exp\left(-\eta A\right) \quad (0.27)$$

where γ is the regression coefficient of time dependency. The constants γ_0 and η are intercept and regression coefficient of age dependency, respectively, which are related to the specified disease (Error! Reference source not found.).

A baseline and three different smoking cessation services in primary care scenarios were simulated in this study. A scenario calculating the attributable burden of smoking was also included. The baseline trends were created in module 1 (the projection program) with cross-sectional Annual Population Survey data from between 2010 to 2017. The other scenarios are described in detail in a further appendix, below shows the flow diagram of the SCS primary care scenarios.

The four smoking cessation scenarios modelled are shown in Figure 2.

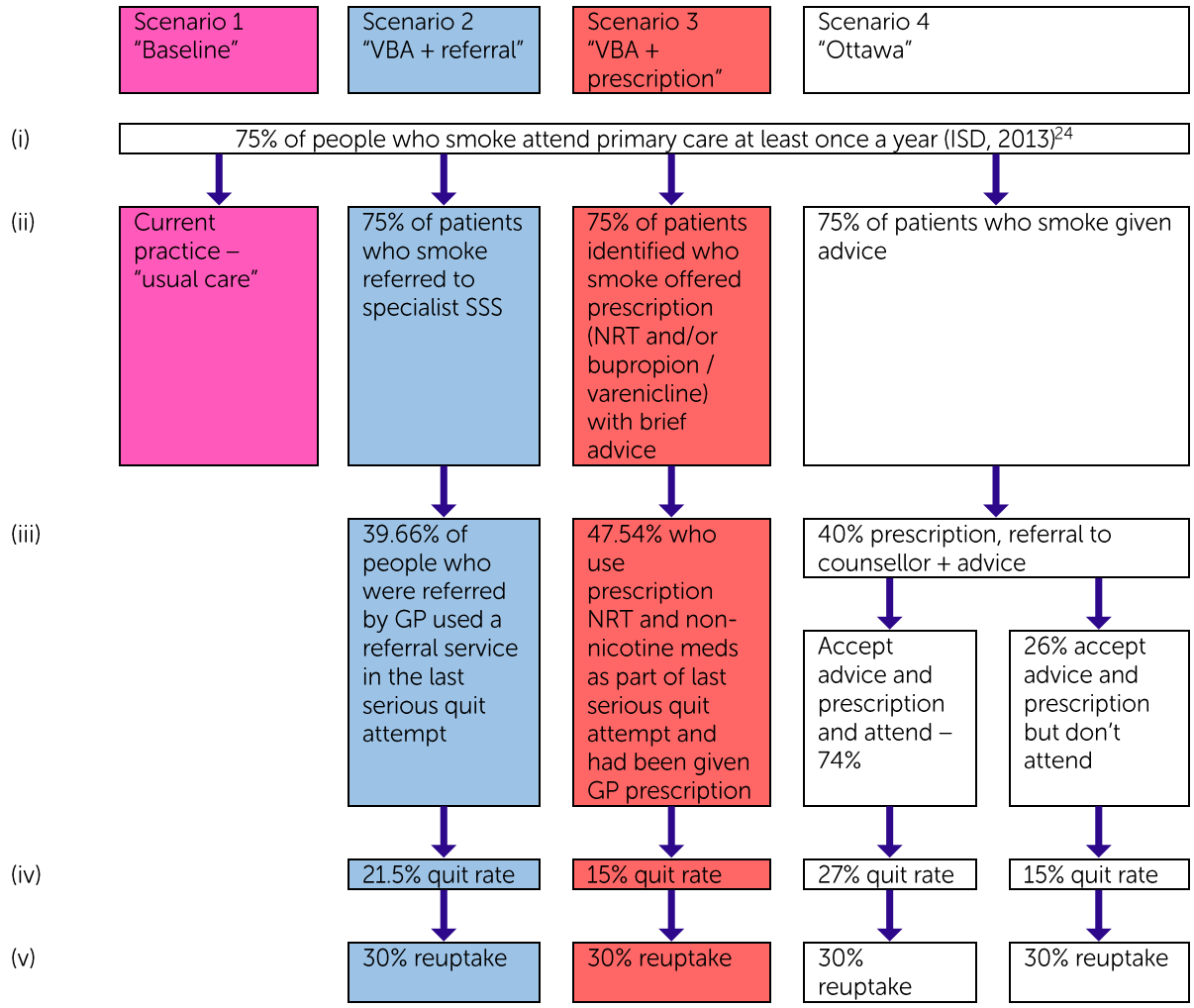


Figure 2: Flow diagram of scenarios modelled.

For each scenario individual Monte Carlo trials sampled from the population are initialised with a smoking status based on the specific scenario trend.

Disease module

Disease modelling relies heavily on the sets of incidence, mortality, survival, relative risk and prevalence statistics. The microsimulation uses risk dependent incidence statistics and these are inferred from the relative risk statistics and the distribution of the risk factor within the population. In the simulation, individuals are assigned a risk factor trajectory giving their personal risk factor history for each year of their lives. Their probability of getting a particular risk factor related disease in a particular year will depend on their risk factor state in that year. The necessary equations are given below.

Once a person has a fatal disease (or diseases) their probability of survival will be controlled by a combination of the disease-survival statistics and the probabilities of dying from other causes. Disease survival statistics are modelled as age and gender dependent exponential distributions.

Relative risks

The reported incidence risks for any disease do not make reference to any underlying risk factor. The microsimulation requires this dependence to be made manifest.

The risk factor dependence of disease incidence has to be inferred from the distribution of the risk factor in the population (here denoted as π); it is a disaggregation process:

Suppose that α is a risk factor state of some risk factor A and denote by $p_A(d|\alpha,a,s)$ the incidence probability for the disease d given the risk state, α, the person's age, a, and gender, s. The relative risk ρ_A is defined by equation (1.30).

$$\begin{aligned} p_{\mathrm{A}}\left(d\,|\alpha,a,s\right) &= \rho_{\mathrm{A}|d}\left(\alpha|a,s\right)p_{\mathrm{A}}\left(d\,|\alpha_0,a,s\right) \\ \rho_{\mathrm{A}|d}\left(\alpha_0|a,s\right) &\equiv 1 \end{aligned} \tag{0.28}$$

Where α_0 is the zero risk state (for example, the moderate state for alcohol consumption).

The incidence probabilities, as reported, can be expressed in terms of the equation,

$$\begin{aligned} p\left(d\,|a,s\right) &= \sum_{\alpha} p_{\mathrm{A}}\left(d\,|\alpha,a,s\right)\pi_A\left(\alpha|a,s\right) \\ &= p_A\left(d\,|\alpha_0,a,s\right)\sum_{\alpha}\rho_{\mathrm{A}|d}\left(\alpha|a,s\right)\pi_A\left(\alpha|a,s\right) \end{aligned} \tag{0.29}$$

Combining these equations allows the conditional incidence probabilities to be written in terms of known quantities

$$p\left(d\,|\alpha,a,s\right) = \rho_{A|d}\left(\alpha|a,s\right)\frac{p\left(d\,|a,s\right)}{\sum_{\beta}\rho_{A|d}\left(\beta\,|\,a,s\right)\pi_A\left(\alpha|a,s\right)} \tag{0.30}$$

Previous to any series of Monte Carlo trials the microsimulation program pre-processes the set of diseases and stores the *calibrated* incidence statistics $p_A(d|\alpha_0, a, s)$.

For each scenario the incidence statistics are calibrated against the baseline smoking trends.

Approximating missing data points

Acquiring survival and mortality data predictions for a particular disease (*d*)

Published disease statistics are frequently incomplete and occasionally inconsistent. The microsimulation program makes use of a number of supporting methods to check and, as necessary, to supply missing disease statistics.

Approximating survival data from mortality and prevalence

An example is provided here with a standard life-table analysis for a disease *d*.

Consider the 4 following states:

state	Description
0	alive without disease *d*
1	alive with disease *d*
2	dead from disease *d*
3	dead from another disease

p_{ik} is the probability of disease *d* incidence, aged *k*

$p_{\omega k}$ is the probability of dying from the disease *d*, aged *k*

$p_{\bar{\omega} k}$ is the probability of dying other than from disease d, aged *k*

The state transition matrix is constructed as follows

$$\begin{bmatrix} p_0(k+1) \\ p_1(k+1) \\ p_2(k+1) \\ p_3(k+1) \end{bmatrix} = \begin{bmatrix} (1-p_{\bar{\omega}k})(1-p_{ik}) & (1-p_{\bar{\omega}k}-p_{\omega k})\,p_{\alpha k} & 0 & 0 \\ (1-p_{\bar{\omega}k})\,p_{ik} & (1-p_{\bar{\omega}k}-p_{\omega k})(1-p_{\alpha k}) & 0 & 0 \\ 0 & p_{\omega k} & 1 & 0 \\ p_{\bar{\omega}k} & p_{\bar{\omega}k} & 0 & 1 \end{bmatrix} \begin{bmatrix} p_0(k) \\ p_1(k) \\ p_2(k) \\ p_3(k) \end{bmatrix} \tag{0.31}$$

It is worth noting that the separate columns correctly sum to unity.

The disease mortality equation is that for state-2,

$$p_2(k+1) = p_{\omega k}\,p_1(k) + p_2(k) \tag{0.32}$$

The probability of dying from the disease in the age interval [*k*, *k*+1] is $p_{\omega k}p_1(k)$ - this is otherwise the (cross-sectional) disease mortality, $p_{mor}(k)$. $p_1(k)$ is otherwise known as the disease prevalence, $p_{pre}(k)$. Hence the relation

$$p_{\omega k} = \frac{p_{mor}(k)}{p_{pre}(k)} \tag{0.33}$$

For exponential survival probabilities the probability of dying from the disease in the age-interval [*k*, *k*+1] is denoted $p_{\Omega k}$ and is given by the formula

$$p_{\omega k} = 1 - e^{-R_k} \quad \Rightarrow \quad R_k = -\ln(1-p_{\omega k}) \tag{0.34}$$

When, as is the case for most cancers, these survival probabilities are known the microsimulation will use them, when they are not known or are too old to be any longer of any use, the microsimulation uses survival statistics inferred from the prevalence and mortality statistics (equation (0.33)).

An alternative derivation equation (0.33) is as follows. Let N_k be the number of people in the population aged k and let n_k be the number of people in the population aged k with the disease. Then, the number of deaths from the disease of people aged k can be given in two ways: as $p_{\omega k} n_k$ and, equivalently, as $p_{mor}(k) N_k$. Observing that the disease prevalence is n_k / N_k leads to the equation

$$\begin{aligned} p_{\Omega k} n_k &= p_{mor}(k) N_k \\ p_{pre}(k) &= \frac{n_k}{N_k} \\ &\Rightarrow \\ p_{\Omega k} &= \frac{p_{mor}(k)}{p_{pre}(k)} \end{aligned} \tag{0.35}$$

Approximating survival data from mortality, incidence and remission data

We begin with the standard 1 year update equation and by defining some probabilities:

$p_i(a,Y)$ the incidence probability of the disease at age a

$p_r(a,Y)$ the remission probability of the disease at age a

$p_\omega(a,Y)$ the probability of dying from the disease at age a, in year Y

$p_{\bar{\omega}}(a,Y)$ the probability of dying from other causes at age a, in year Y

And the probabilities of being in a set of states:

S_0	$p_{\bar{d}}(a,Y)$	the probability of being alive without the disease at age a, in year Y
S_1	$p_d(a,Y)$	the probability of being alive with the disease at age a, in year Y
S_2	$p_\Omega(a,Y)$	the probability of being dead as a result of the disease at age a, in year Y
S_3	$p_{\bar{\Omega}}(a,Y)$	the probability of being dead from other causes at age a, in year Y

The update equation is (the dependence on the year Y is suppressed)

$$\begin{pmatrix} p_{\bar{d}}(a+1) \\ p_d(a+1) \\ p_\Omega(a+1) \\ p_{\bar{\Omega}}(a+1) \end{pmatrix} = \begin{pmatrix} (1-p_{\bar{\omega}})(1-p_i) & (1-p_{\bar{\omega}}-p_\omega)p_r & 0 & 0 \\ (1-p_{\bar{\omega}})p_i & (1-p_{\bar{\omega}}-p_\omega)(1-p_r) & 0 & 0 \\ 0 & p_\omega & 1 & 0 \\ p_{\bar{\omega}} & p_{\bar{\omega}} & 0 & 1 \end{pmatrix} \begin{pmatrix} p_{\bar{d}}(a) \\ p_d(a) \\ p_\Omega(a) \\ p_{\bar{\Omega}}(a) \end{pmatrix} \tag{0.36}$$

Survival

At some age, a_0, the person is alive and gets the disease – at this age the state vector is, $\begin{pmatrix} 0 & 1 & 0 & 0 \end{pmatrix}$.

If we assume the remission probability is zero the person's subsequent life is governed by the equation

$$\begin{pmatrix} p_d(a+1) \\ p_\Omega(a+1) \\ p_{\bar{\Omega}}(a+1) \end{pmatrix} = \begin{pmatrix} 1-p_{\bar{\omega}}-p_\omega & 0 & 0 \\ p_\omega & 1 & 0 \\ p_{\bar{\omega}} & 0 & 1 \end{pmatrix} \begin{pmatrix} p_d(a) \\ p_\Omega(a) \\ p_{\bar{\Omega}}(a) \end{pmatrix} \tag{0.37}$$

At age $a = a_0 + N$ it has the solution

$$p_d(a_0+N) = \prod_{k=1}^{k=N} \left(1-p_\omega(a_k)-p_{\bar{\omega}}(a_k)\right) \tag{0.38}$$

Disease survival probabilities

Disease survival statistics are gathered from those people who do not die from other causes. The probability of surviving N years, given that there is no remission, and that there is no probability of death from other causes is simply

$$p_d(a_0+N) = \prod_{k=1}^{k=N} \left(1-p_\omega(a_k)\right) \tag{0.39}$$

These are longitudinal statistics that, ideally, are gathered by following the life courses of many people who have the disease.

In equation (0.39) it is understood that the disease is contracted at age a_0 and that the death probabilities are the successive probabilities of dying from the disease in the first year - $p_\omega(a_0+1)$, the second year - $p_\omega(a_0+2)$, and so on. These are *disease survival statistics*, closely connected to but not the same as *disease mortality statistics*.

Mortality statistics

In any year, in some population, in a sample of N people who have the disease a subset N_ω will die from the disease.

Mortality statistics record the cross sectional probabilities of death as a result of the disease – possibly stratifying by age

$$p_\omega = \frac{N_\omega}{N} \tag{0.40}$$

Within some such subset N_ω of people that die in that year from the disease, the distribution by year-of-disease is not usually recorded. This distribution would be most useful. Consider two important idealised, special cases

Suppose the true probabilities of dying in the years after some age a_0 are $\{p_{\omega 0}, p_{\omega 1}, p_{\omega 2}, p_{\omega 3}, p_{\omega 4}\}$

The probability of being alive after N years is simply that you don't die in each year

$$p_{survive}(a_0 + N) = (1 - p_{\omega 0})(1 - p_{\omega 1})(1 - p_{\omega 2})..(1 - p_{\omega N-1}) \tag{0.41}$$

The microsimulation's survival models

There are three in use (they are easily extended if the data merit):

Survival model 0: a single probability of dying $\{p_{\omega 0}\}$

$p_{\omega 0}$ is valid for all years

Survival model 1: two different probabilities of dying $\{p_{\omega 0}, p_{\omega 1}\}$

$p_{\omega 0}$ is valid for the first year; $p_{\omega 1}$ thereafter.

Survival model 2: three different probabilities of dying $\{p_{\omega 0}, p_{\omega 1}, p_{\omega 5}\}$

$p_{\omega 0}$ is valid for the first year; $p_{\omega 1}$ for the second to the fifth year; $p_{\omega 5}$ thereafter

Remember that different probabilities will apply to different age and gender groups. Typically the data might be divided into 10 year age groups.

Calculating survival from incidence and mortality

When a person (of a given gender) dies from a disease they must have contracted it at some earlier age. For Survival model 2, this is expressed

$$\begin{aligned}\hat{p}_{mortality}(a) = {} & p_{inc}(a-1)\,p_{\omega 0} + \\ & + p_{inc}(a-2)(1-p_{\omega 0})\,p_{\omega 1} + \\ & + p_{inc}(a-3)(1-p_{\omega 0})(1-p_{\omega 1})\,p_{\omega 1} + \\ & + p_{inc}(a-4)(1-p_{\omega 0})(1-p_{\omega 1})^2\,p_{\omega 1} + \\ & + p_{inc}(a-5)(1-p_{\omega 0})(1-p_{\omega 1})^3\,p_{\omega 1} + \\ & + p_{inc}(a-6)(1-p_{\omega 0})(1-p_{\omega 1})^4\,p_{\omega 5} + \\ & + p_{inc}(a-7)(1-p_{\omega 0})(1-p_{\omega 1})^4(1-p_{\omega 5})\,p_{\omega 5} + \\ & + \ldots\end{aligned} \tag{0.42}$$

The three probabilities $\{p_{\omega 0}, p_{\omega 1}, p_{\omega 5}\}$ are estimated by minimising

$$S = \sum_{a \in AgeGroup} \frac{\left(\bar{p}_{mortality}(a) - \hat{p}_{mortality}(a)\right)^2}{\bar{\sigma}^2} \tag{0.43}$$

When the longitudinal probability of the disease incidence at age a satisfies the recursion relation

$$p_{inc}(a) = (1 - p_i(0))(1 - p_i(1))..(1 - p_i(a-1))\, p_i(a) \tag{0.44}$$

The probabilities of being alive after 1, 5 and 10 years are

$$\begin{aligned} p_{survival}(a_0 + 1) &= (1 - p_{\omega 0}) \\ p_{survival}(a_0 + 5) &= (1 - p_{\omega 0})(1 - p_{\omega 1})^4 \\ p_{survival}(a_0 + 10) &= (1 - p_{\omega 0})(1 - p_{\omega 1})^4 (1 - p_{\omega 5})^5 \end{aligned} \tag{0.45}$$

Rates

It is common practice to describe survival in terms of a survival rate R, supposing an exponential death-distribution. In this formulation the probability of surviving t years from some time t_0 is given as

$$p_{\text{survival}}(t) = 1 - R^{-1} \int_0^t du e^{-Ru} = e^{-Rt} \tag{0.46}$$

For a time period of 1 year

$$\begin{aligned} p_{survival}(1) &= e^{-R} \\ &\Rightarrow \\ R &= -\ln\left(p_{survival}(1)\right) = -\ln(1 - p_{\omega}) \end{aligned} \tag{0.47}$$

For a time period of, for example, 4 years,

$$p_{\text{survival}}(t = 4) = 1 - R^{-1} \int_0^4 du e^{-Ru} = e^{-4R} = (1 - p_{\omega})^4 \tag{0.48}$$

In short, the Rate is minus the natural log of the 1-year survival probability.

Survival models 0, 1 and 2

For any potentially terminal disease MIDRIF can use any of three survival models, numbered {0, 1, 2}. The parameters describing these models are given below.

Survival model 0

Given the 1-year survival probability $p_{survival}(1)$

The model uses 1 parameter {R}

$$R = -\ln\left(p_{survival}(1)\right) \tag{0.49}$$

Survival model 1

The model uses two parameters {p_1, R}

Given the 1-year survival probability $p_{survival}(1)$ and the 5-year survival probability $p_{survival}(5)$

$$\begin{aligned} p_1 &= 1 - p_{survival}(1) \\ R &= -\frac{1}{4}\ln\left(\frac{p_{survival}(5)}{p_{survival}(1)}\right) \end{aligned} \tag{0.50}$$

Survival model 2

The model uses three parameters {p_1, R, $R_{>5}$}

Given the 1-year survival probability $p_{survival}(1)$ and the 5-year survival probability $p_{survival}(5)$

$$\begin{aligned} p_1 &= 1 - p_{survival}(1) \\ R &= -\frac{1}{4}\ln\left(\frac{p_{survival}(5)}{p_{survival}(1)}\right) \\ R_{>5} &= -\frac{1}{5}\ln\left(\frac{p_{survival}(10)}{p_{survival}(5)}\right) \end{aligned} \tag{0.51}$$

Costs module

The cost module developed for this study includes both direct and indirect cost calculations.

Direct costs

The cost model used in the simulation is part of the economics module and, here, simply scales the aggregated individual disease costs according to the relative disease prevalence in years after the start year for which the costs are known.

In any year, the total healthcare cost for the disease *D* is denoted $C_D(year)$. If the prevalence of the disease is denoted $P_D(year)$ we assume a simple relationship between the two of the form

$$C_D\left(year\right) = \kappa P_D\left(year\right) \tag{0.52}$$

for some constant κ.

For each of the trial years, the microsimulation records the prevalence of each disease call it $P_D(year|trial)$ and the trial population size for that year, $N_{pop}(year|trial)$. Further assume that the prevalence in the whole population $N_{pop}(year)$ is a simple scaling of the trial prevalence, then

$$C_D\left(year\right) = \kappa P_D\left(year\right) = \lambda \frac{N_{pop}\left(year\right) P_D(year\,|\,trial)}{N_{pop}(year\,|\,trial)} \tag{0.53}$$

for some constant λ.

By comparing any trial year to some initial year, *year0*, the total disease cost in any year is given as

$$\frac{C_D\left(year\right)}{C_D\left(year0\right)} = \frac{N_{pop}\left(year\right)}{N_{pop}\left(year0\right)} \frac{N_{pop}(year0\,|\,trial)}{N_{pop}(year\,|\,trial)} \frac{P_D(year\,|\,trial)}{P_D(year0\,|\,trial)} \tag{0.54}$$

Indirect costs

Premature mortality cost

The premature mortality costs are calculated by considering the error generated from each age in each year.

For each age *a* in a given year,

$p_a(y) =$ Rate of death at age a in a given year

$\mathrm{d}_a(y) =$ Number of inviduals at age a that die in a given year

$\mathrm{N}_a(y) =$ Total number of individuals at age a in a given year

$$p_a(y) = \frac{d_a(y)}{N_a(y)}$$

$\mathrm{C}_a(y) =$ The cost per case at age a in a given year y

$$\mathrm{C}_a(y) = \sum_{i=a}^{i=LE-1} (Income(i) * discount(y + (i-a)))$$

$R =$ Rate of death at age a in the whole population in a given year

$D(y) =$ Total number of individuals who die in a given year

$$\mathrm{R} = \frac{\mathrm{d}_a(y)}{D(y)}$$

$$95\%\ \text{CI per 100,000 costs at age a} = 1.96\left(\sqrt{\frac{p_a(1-p_a)}{N_a}}\right) * C_a * 100000 \quad (0.55)$$

Where the standard deviation (σ) is calculated as shown in equation

$$\sigma_a = \sqrt{\frac{p_a(1-p_a)}{N_a}} \quad (0.56)$$

For each year the standard deviation for all age groups is calculated as shown in equation. A weighted average of the variance from each age group is calculated.

$$\sigma = \sqrt{\sum_{a=0}^{a=LE-1} RC_a(y)^2 {\sigma_a}^2} \quad (0.57)$$

The 95% CI for the premature mortality costs in a given year will be calculated from

$$\text{PMC } 95\%\text{CI per } 100{,}000 = 1.96\sigma * 100000 \quad (0.58)$$

Premature morbidity costs

The premature morbidity costs refer to the loss of potential earnings incurred when an individual contracts a disease which impacts their productivity. The productivity of an individual represents the amount of working time the individual actually spends working. It is estimated as a function of the patient's age, sex and QoL. The output of this estimate is a measure of the proportion of working time spent actually working. Note that this encompasses all possible reasons for not working, including unemployment, retirement, not being of working age, as well as ill health. This effectively allows the impacts of factors such as retirement and unemployment to be automatically reflected in the estimate of paid production as a function of age, sex and QoL. Estimation of productivity as a function of age and QoL uses a model developed by ScHARR, based on the Understanding Society dataset. This dataset includes information on the respondents' productivity (questions below), and their health (measured using the SF12 instrument), as well as their age and gender.

Premature morbidity costs are calculated annually and are related to an individual's age and quality of life (QoL). The quality of life is related to the type of disease a person may acquire. Each disease in the simulation has a quality of life associated with it. If an individual has multiple diseases it is assumed their quality of life is calculated from the product of the quality of life of each disease. The physical capability (PCS) and mental capability (MCS) are shown in equations (1.2) and (1.3).

$$PCS = \beta_0 + \beta * Age/10 + \beta * QoL + \varepsilon \quad (0.59)$$

$$MCS = \beta_0 + \beta * Age/10 + \beta * QoL + \varepsilon \quad (0.60)$$

The parameter values for these equations are displayed in Table 2.

Table 2 Parameter values for the equations representing physical capability (PCS) and mental capability (MCS) as described in Equations (0.59) and (0.60).

Variable	MCS	PCS
Age/10, β	1.0383	-1.0443
QoL, β	5.0122	25.918
Constant, β_0	32.5459	31.0231

Equation (1.4) is used as an estimate of the logistic function of productivity (*L(p)*). The parameter values are shown in Table 3.

$$L(p) = \beta_0 + \beta * Age/10 + \beta * (Age/10)^2 + \beta * Sex + \beta * PCS + \beta * PCS^2 + \beta * MCS + \beta * MCS^2 + \varepsilon \quad (0.61)$$

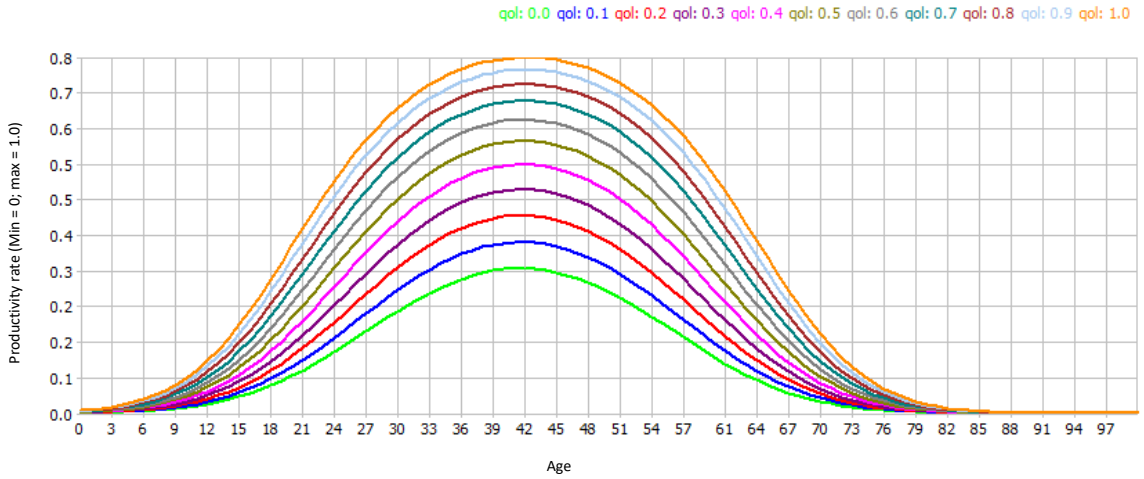
Table 3 Parameter values for the equation representing L(p) as described in Equation (0.61).

Variable	L(p)
Age/10, β	2.95
$(Age/10)^2$, β	-0.35
MCS/10, β	1.19
$(MCS/10)^2$, β	-0.09
PCS/10, β	1.37
$(PCS/10)^2$, β	-0.09
Constant, β_0	-13.2

The productivity (*C*) is calculated in equation (1.5).

$$C = \frac{\exp(L(p))}{1+\exp(L(p))} \tag{0.62}$$

Figure 3: Productivity curve, by age and QoL



The total premature morbidity cost of an individual for each year of the simulation is calculated using the mean yearly income of the individual for a given age (B); the productivity of the individual at full health i.e. QoL=1.0 (C_y); productivity of the individual with the disease (C_z); and overheads associated with employment (D; constant rate of 30%) (1.6).

$$\text{Morbidity cost (year)} = Discount(year) \times \Big((B \times C_y \times D) - (B \times C_Z \times D) \Big) \tag{0.63}$$

Primary care cost-per-case, primary care costs and GP appointments avoided estimation methods

Cost per case estimation

Annual costs of primary care consultations per smoking-related diseases were required. However, this was only available for COPD for which GP surgery contact costs were extracted at patient level. That is, the estimated average patient-level cost of contact with primary care over one year (includes multiple visits per patient). Total annual primary care costs (GP consultations plus all other primary care costs) for stroke, Type 2 diabetes (T2D), Coronary Heart Disease (CHD), Colorectal cancer, Lung Cancer were available in the literature, so were used in this analysis. Annual primary care costs for all of the other conditions were not available, so only a subset of conditions are included. The processing of these data is described in detail below.

COPD

COPD primary care costs data were published by stage for 2009 – to estimate overall cost-per-case a simple average of costs at each stage was estimated.[5] This cost average was then inflated to 2019 (described below).

All other diseases

Total population primary care costs for each condition were extracted from the literature, in Euros (apart from T2DM which was in GBP), for the most recent year available. Costs in Euros were converted to GBP (described below) and inflated to 2019 (described below). These inflated costs were then converted to costs-per-case by applying estimated prevalence, by age, to the estimated 2019 UK population in order to estimate the total expected number of cases in the UK at that time. The total population costs of each disease were then divided by this estimated expected number of cases to estimate costs-per-case for each condition.

Cost per case estimate sources

Disease	Reference
Colorectal cancer	Luengo-Fernandez, R., Leal, J., Gray, A., & Sullivan, R. (2013). Economic burden of cancer across the European Union: a population-based cost analysis. The Lancet Oncology, 14(12), 1165–1174. doi:10.1016/s1470-2045(13)70442-x
Lung cancer	Luengo-Fernandez, R., Leal, J., Gray, A., & Sullivan, R. (2013). Economic burden of cancer across the European Union: a population-based cost analysis. The Lancet Oncology, 14(12), 1165–1174. doi:10.1016/s1470-2045(13)70442-x
COPD	Punekar YS, Shukla A, Müllerova H. COPD management costs according to the frequency of COPD exacerbations in UK primary care [published correction appears in Int J Chron Obstruct Pulmon Dis. 2014;9:247]. *Int J Chron Obstruct Pulmon Dis.* 2014;9:65–73. doi:10.2147/COPD.S54417
CHD	British Heart Foundation, Heart & Circulatory Disease Statistics 2019. https://www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2019
Stroke	British Heart Foundation, Heart & Circulatory Disease Statistics 2019. https://www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2019
T2DM	Hex, N., Bartlett, C., Wright, D., Taylor, M., & Varley, D. (2012). Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabetic Medicine, 29(7), 855–862. doi:10.1111/j.1464-5491.2012.03698.x

Currency conversion

Estimates extracted from the literature in Euros were converted to GBP using an estimated rate of 1.11 for all 2009 estimates[6] based on average published exchange rates for December

[5] Relative prevalence by stage would be needed in order to weight these average costs by prevalence at each stage.

2009 and an estimated rate of 1.38 for all 2015 estimates[7] based on average published exchange rates for December 2015.

Cost inflation

Costs were inflated from the year of the extracted estimates to 2019 using annual CPI inflation rates.[8]

Cost and appointments saved estimates

Total primary care costs for each disease with data available were estimated, by scenario, within the microsimulation, for each year 2019-2039. These total primary care costs avoided (scenario relative to baseline) were then distributed across all GP practices in the UK weighted for registered patients per practice and converted to an estimate of appointments saved. We recognise that for all diseases apart from COPD this reflects total primary care costs (not just GP costs). However, the conversion to appointments saved provides an illustration the potential use of the savings in practical terms.

Cost distribution and costs / appointments avoided by GP practice

The total registered population at each GP practice in the UK (with data available) was extracted separately for each constituent country, using the most recent data available.[6,7,8,9,10,11] This registered population was summed across all GP practices in the UK (denominator) and the total number of registered patients (numerator) at each practice was divided by this to get proportion of patients registered in UK at each practice.

To distribute estimated cost savings under each scenario the total cumulative primary costs avoided (per UK population £ billions) were distributed proportionally to each GP practice based on the registered population. No adjustment was made to account for non-GP costs since the cost savings were translated to GP consultations to provide an illustration of potential uses for savings.

The number of appointments saved at each GP practice was estimated by dividing the costs saved under each scenario and by the estimated average cost of a GP consultation (£30).[10]

The final estimates presented are crude estimates and no discounting was applied to any cost estimate. The summary outputs include:

- Total costs and appointments saved across all GP practices for each scenario and disease - these are the results presented in "Summary" and represent UK-wide estimates

[6] https://freecurrencyrates.com/en/exchange-rate-history/GBP-EUR/2009/cbr
[7] https://freecurrencyrates.com/en/exchange-rate-history/GBP-EUR/2015/cbr
[8] https://www.rateinflation.com/inflation-rate/uk-historical-inflation-rate
[9] https://digital.nhs.uk/data-and-information/publications/statistical/patients-registered-at-a-gp-practice/september-2019

[10] https://www.rateinflation.com/inflation-rate/uk-historical-inflation-rate

[11] https://www.england.nhs.uk/2019/01/missed-gp-appointments-costing-nhs-millions/

- Average number of appointments and costs saved for GP practices taken as arithmetic mean of costs / appointments saved across all GP practices
- Minimum and maximum costs saved included as the lowest and highest cost savings estimated out of all GP practices - lowest and highest values from results for all practices

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