



# The IMPACT<sub>NCD</sub> technical appendix

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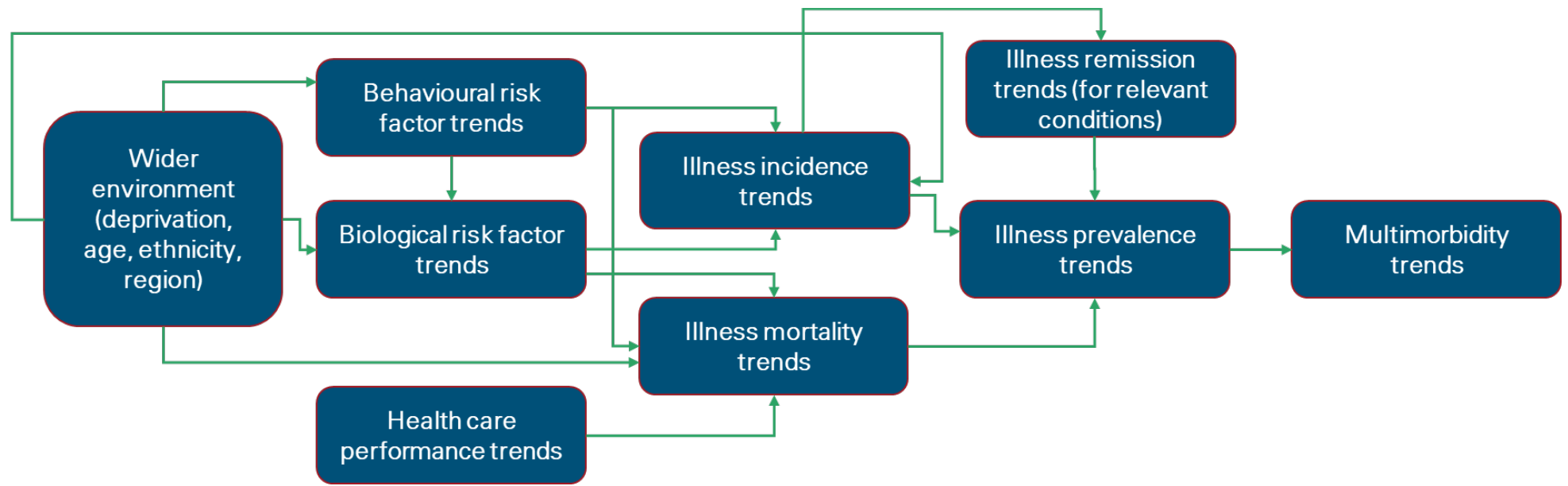
# 1. Introduction

IMPACT<sub>NCD</sub> is an open-source microsimulation modelling framework for public health policy planning and decision making in non-communicable disease (NCD) prevention. The epidemiological engine of the modelling framework translates changes in the trends of disease risk factors into changes in disease incidence and case fatality and subsequent disease prevalence. The policy layer of the framework complements the epidemiological engine and translates policy changes (hypothetical or real) into changes in the trends of disease risk factors.

IMPACT<sub>NCD</sub> has been used extensively to model primary prevention policies nationally in England, Brazil, and the US, and locally in Liverpool. [1–10] A simplified diagram of the model structure is presented in [Figure 1-1](#). At the core of the model is an epidemiological engine which includes age, sex, area deprivation (English Index of Multiple Deprivation (IMD)), smoking, environmental tobacco smoke exposure, alcohol consumption, fruit and vegetable consumption, physical activity, body mass index (BMI), systolic blood pressure (SBP), and total serum cholesterol, as risk factors. The diseases modelled from risk factor trends include coronary heart disease (CHD), stroke, hypertension, type 2 diabetes mellitus (T2DM), lung cancer, colorectal cancer, breast cancer, prostate cancer, chronic kidney disease (CKD), dementia, atrial fibrillation (AF), asthma, and chronic obstructive pulmonary disease (COPD), plus thirteen additional conditions that are modelled from past trends in disease incidence and mortality. Notably, diseases can be risk factors for other diseases (i.e. type 2 diabetes mellitus is a risk factor for coronary heart disease). The policy layer is dedicated to modelling either a specific public health policy formulation or a hypothetical scenario and consists of a mathematical/statistical model of the policy.

This iteration of IMPACT<sub>NCD</sub> uses data from the Health Survey for England (HSE) to inform trends in risk factors and linked primary care records (Clinical Practice Research Datalink (CPRD) Aurum linked to Hospital Episode Statistics (HES) inpatient, HES outpatient, and Office for National Statistics (ONS) mortality records; described in the [Disease module](#) section) to inform trends in disease incidence, prevalence, and disease-specific mortality. ONS population estimates and projections are used to inform estimates of the population size and structure and to calibrate mortality.

Figure 1-1 - Conceptual structure of IMPACT<sub>NCD</sub>



The IMPACT<sub>NCD</sub> framework is modular and can grow in several directions, with contributions from us and others. For example, it allows third parties to develop policy layers independently and hook them to the epidemiological engine. The open-source licence (GPLv3) ensures transparency and accountability while promoting collaborative work throughout development and deployment. The source code of the current implementation is available at [https://github.com/ChristK/IMPACTncd\\_Engl/tree/Report\\_1](https://github.com/ChristK/IMPACTncd_Engl/tree/Report_1).

## 2. Epidemiological engine

### High-level description

The epidemiological engine of IMPACT<sub>NCD</sub> is a discrete-time, dynamic, stochastic microsimulation consisting of three modules: the **Sociodemographic** module, the **Exposure** module, and the **Disease** module.

Within the IMPACT<sub>NCD</sub> epidemiological engine, each unit is a synthetic individual (simulant) represented by a record containing a unique identifier and a set of associated attributes. The microsimulation then projects the life course of each synthetic individual.

The attributes of each synthetic individual include sociodemographic characteristics, exposures to risk factors, acquired diseases, and cause of death if relevant.

Specific attributes include:

1. Age, sex, ethnicity, region, and index of multiple deprivation deciles as sociodemographic exposures.
2. Alcohol intake, smoking status (current smoker/ ex-smoker/ never-smoker), smoking duration, smoking intensity, environmental tobacco exposure, fruit consumption, vegetable consumption, and physical activity as behavioural risk exposure variables.
3. Body mass index, systolic blood pressure, and total serum cholesterol as biological risk exposures.
4. The risk for thirteen diseases is modelled explicitly: asthma, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, coronary heart disease, hypertension, dementia, stroke, type 2 diabetes mellitus, breast cancer, colorectal cancer, lung cancer, and prostate cancer. The risk for these conditions is modelled from relevant exposures to sociodemographic, behavioural, and biological risk factor attributes, as well as certain prevalent conditions. For instance, the risk of heart failure depends on age, sex, ethnicity, region, IMD, and prevalent CHD, COPD, T2DM and hypertension. Finally, the risk for a further 13 conditions – alcohol misuse, anxiety and depression, connective tissue disorders, constipation, epilepsy, hearing loss, heart



failure, irritable bowel syndrome (IBS), other cancers, pain, psychosis and bipolar disorders, rheumatoid arthritis, and type 1 diabetes – is directly driven by past trends in disease incidence and sociodemographic exposures. Some of these conditions are combined in post hoc analyses to derive the 20 conditions for the Cambridge Multimorbidity Score (CMS). [11] The [Disease module](#) section summarises the modelling approach, and [Supplementary materials A: Disease module details](#) gives more detail on the modelling and data sources for each condition. Based on their risk of developing any of these conditions, simulants may develop some conditions during their life course.

5. Mortality from the diseases listed in 4 or any other cause is recorded if it occurs.

All these attributes are updated in discrete annual steps according to a set of stochastic rules. We structured these rules based on well-established epidemiological principles. Specifically, behavioural risk exposures are conditional on sociodemographic exposures; biological risk exposures are conditional on behavioural and sociodemographic exposures, and diseases are conditional on biological, behavioural, and sociodemographic exposures, as well as diagnosis of other conditions. Finally, mortality is conditional on sociodemographic, behavioural, biological and disease exposures.

The life course of synthetic individuals is simulated as many times as the number of scenarios to be modelled (one for this report), using the same random numbers for all policy scenarios to reduce stochastic noise. One of the scenarios is always the ‘baseline’ scenario with which all remaining policy scenarios are compared. In this report, the baseline scenario is that of continuing trends in risk factors. Comparing the disease outcomes from the life courses under the baseline scenario versus the policy scenarios generates the health impact of the policy scenarios. The output of the epidemiological engine is a dataset containing the adult life course of the simulated synthetic individuals with all the attributes mentioned above recorded annually for every scenario. From this dataset of life course trajectories, summary measures such as average CMS, mortality, disease incidence and prevalence can be calculated annually.

As we mentioned above, the epidemiological engine of IMPACT<sub>NCD</sub> consists of three modules: the **sociodemographic** module, the **exposure** module, and the **disease** module. In the following paragraphs, we will describe these three modules. [Table 2-1](#) summarises the key assumptions and limitations of the IMPACT<sub>NCD</sub> microsimulation model.

Table 2-1 IMPACT<sub>NCD</sub> key assumptions and limitations

| Model component                | Key assumptions   |
|--------------------------------|---|
| <b>Sociodemographic module</b> | <p>Migration is not modelled explicitly in the model. However, the model outputs are calibrated to ONS population projections by local authority (LA), which take into account migration. Nevertheless, we assume that migrants have similar characteristics to the local population.</p> |
|                                | <p>Social mobility is not considered.</p>   |
|                                | <p>Decile groups of the index of multiple deprivation (DIMD) is a relative marker of (area) deprivation with several versions since 2003. We have used the 2015 version and assume it is constant throughout the simulation.</p>  |
| <b>Exposure module</b>         | <p>We assume that the surveys used are truly representative of the population. For example, the adjustments for selection bias in the Health Survey for England are adequate.</p>   |
|                                | <p>On average, simulants remain in the same exposure quantile throughout their life (see <a href="#">Exposure module</a> section on p7).</p>  |
|                                | <p>The linear correlations in exposure quantiles remain constant over time (i.e. the clustering of exposures in some subpopulations) (see <a href="#">Exposure module</a> section on p7).</p>   |
|                                | <p>We assume that trends in risk factor exposures continue and follow log-linear trends.</p>  |
| <b>Disease module</b>          | <p>We assume multiplicative risk effects (see <a href="#">Disease incidence</a> section on p10).</p>  |
|                                | <p>We assume log-linear exposure-response for the continuous risk factors.</p>  |
|                                | <p>We assume that the effects of the risk factors on incidence and case fatality are equal (see <a href="#">Mortality</a> on p17).</p>  |
|                                | <p>We assume a mean lag time between exposure and outcome of about 4-5 years for most exposure/outcome pairs, except for cancers, for which we assume a mean lag time of 9 years (see <a href="#">Table 2-3</a> and <a href="#">Disease incidence</a> section on p10).</p>                |
|                                | <p>We assume 100% risk reversibility for all exposures except smoking. We allow smoking to have a cumulative effect on the risk for COPD and lung, breast, and colorectal cancers.</p>  |
|                                | <p>We assume that trends in disease incidence are attributable only to trends of the relevant modelled risk factors or other diseases modelled.</p>   |
|                                | <p>We assume that the linked primary care data used to model disease trends over time represents England's adult population.</p>  |
|                                | <p>We assume that trends in disease incidence continue to follow log-linear trends (other than pain, see below).</p>  |
|                                | <p>For cancers, we assume that survival ten years after diagnosis equals remission.</p>   |
|                                | <p>For all conditions other than cancer (see point above), pain, constipation, asthma, alcohol problems, and anxiety and depression, we assume conditions are chronic.</p>  |

|  |   |
|--|---|
|  | For pain, we modelled the incidence of pain based on the incidence in 2013 due to data quality issues over time with the prescription data.                     |
|  | For anxiety and depression and constipation, we did not calibrate to the observed trends in incidence rates because their projections led to implausible rates. |

## Sociodemographic module

The first year of every simulation in IMPACT<sub>NCD</sub> is 2013, so we could use the overlapping period 2013-19 to calibrate and validate the model.

For each simulation, the algorithm in the module:

1. Identifies the Lower Super Output Areas (LSOAs) that constitute the user area selection; for this report, this was set to the whole of England.
2. Draws 200,000 synthetic individuals, aged 30 to 99, from the joint age-sex distribution of the identified LSOAs. This is a default value that can be modified by the user. The joint age-sex distribution for each LSOA for 2013 is informed by the ONS population estimates. [12]
3. Assigns to each synthetic individual an IMD score based on their LSOA.
4. Probabilistically assigns to each synthetic individual an ethnicity based on their age group, sex, and LSOA. The ethnicity mixture of each LSOA is informed by the 2011 Census. [13] We include nine ethnicities in the model (white, Indian, Pakistani, Bangladeshi, other Asian, Black Caribbean, Black African, Chinese, and others).
5. Assigns to each synthetic individual a Strategic Health Authority (SHA) based on their LSOA. SHA is the smallest geographical area accessible in the Health Survey for England series and is mostly aligned with English regions. We use this in the exposure module, as we describe in the next section.

So far, the algorithm has created a synthetic population that is a snapshot of the population of England in 2013. The following steps of the algorithm create backward and forward projections of the synthetic population that are essential to model exposure time trends and time lags between exposures and diseases.

The backward projection of the synthetic population goes back to 2003; therefore, the maximum time lag we allow in the model is ten years. As everyone alive and older than 30 years old in 2013 was alive in 2003, the algorithm simply creates the back projections by

appropriately reducing the age of the synthetic individuals while keeping constant all other variables.

Similarly, for the forward projections, we project until 2043, and the algorithm increases the age of the synthetic individuals while keeping all other variables constant. For forward projections, mortality needs to be considered. We describe mortality with the disease module as disease-specific mortality is closely related to disease prevalence. IMPACT<sub>NCD</sub> follows an open cohort approach. Every simulated year from 2013 onwards, a new cohort of 30-year-old synthetic individuals enters the model. The same sources inform the cohort size and the joint age-sex-ethnicity distribution we described above. For example, in 2014, the new 30-year-old cohort will be informed by the population size and the joint age-sex-ethnicity distribution of those who were 29 years old in 2013. The approach may be crude; however, the final model outputs are directly standardised to ONS national or local authority population projection estimates as applicable. [14,15]

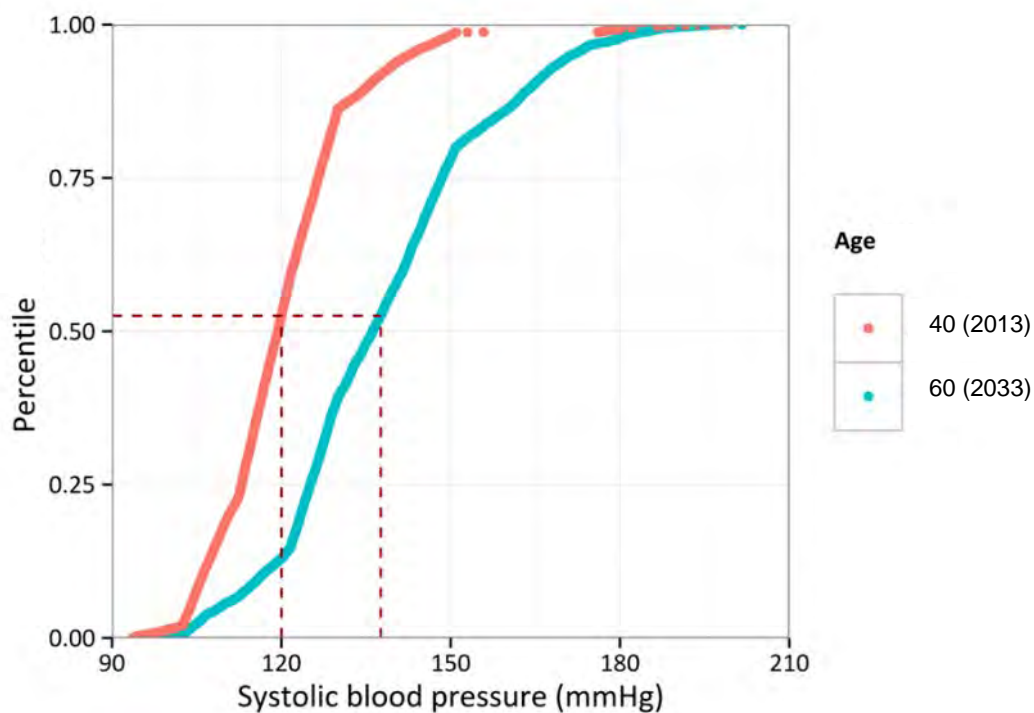
### Exposure module

This module simulates the adult life course exposures of synthetic individuals based on the HSE series between 2003 and 2014. [16–27] We followed the same general principles for all simulated exposures. First, we fit an appropriate statistical model to the HSE data with the exposure of interest as the dependent variable and some functions of the year, age, sex, quintiles of IMD (QIMD; deciles are not available in HSE), ethnicity, and SHA as independent variables. Then, we use the statistical model to predict the exposure level of every synthetic individual in the simulation based on their sociodemographic characteristics estimated from the sociodemographic module.

Including year as an independent variable in our exposure model allows us to extract the trends from the HSE series and project them into the future. Furthermore, it allows us to make backward projections of exposures when we simulate time lags. For example, for a synthetic female aged 30 in 2013, we can estimate her BMI in 2003, when she was 20 and in 2033 when she would be 50. To avoid excessively fast changes in exposure trends and to reflect our belief that decays and growths in natural phenomena are rarely linear, we included the natural logarithm of years in the statistical models assuming logarithmic trends.

We used logit ordinal regression to model exposures that were recorded as ordinal categorical variables in HSE. We used generalised additive models for location, scale, and shape (GAMLSS) for all other exposures. [28,29] These are flexible statistical models that can make all parameters of an assumed distribution for the dependent variable conditional to some function of the independent variables. For example, GAMLSS can model the mean and the standard deviation of a normally distributed dependent variable conditional on the predictors, while a linear regression only models the mean. [Table B-1](#) summarises our modelling approach for all the exposures in the model.

Figure 2-1 – Example of risk factor assignment for the synthetic population: Plot of the systolic blood pressure quantiles of a male synthetic individual living in QIMD 3 area for ages 40 and 60



The approach described above provides us with equations to estimate the distribution of the exposure to a risk factor for a given time and the sociodemographic characteristics of a synthetic individual. When the synthetic individual enters the simulation, a vector of random numbers between 0 and 1 and of size equal to the number of the modelled exposures is allocated to them. Each one of the numbers represents the quantile of the relevant exposure distribution. The principle is that synthetic individuals retain their quantiles throughout their life course (this is known as the rank stability assumption). [30] For example, in 2013, a 40-year-old male synthetic individual living in a QIMD 3 area with an SBP of 120 mmHg has a SBP

quantile of 0.52. Twenty years later, the same synthetic individual retained their quantile score for SBP. However, their SBP is now estimated to be 137.6 mmHg because the SBP distribution has changed to reflect the SBP of 60-year-old men living in a QIMD 3 area in 2033 ([Figure 2-1](#)). In IMPACT<sub>NCD</sub>, we allow the quantile of the synthetic individuals to fluctuate every year using random walks to relax the rank stability assumption. But on average the large majority of synthetic individuals will have minimal changes to their exposure quantile throughout their lives.

### Clustering of risk factors

Finally, exposures in individuals are correlated. For example, people with a high BMI may also have high total cholesterol and hypertension. Some of these correlations reflect strong and well-established causal mechanisms, but the cross-sectional design of HSE may bias these correlations. The method we described above captures some of these correlations by including exposures as independent variables in the statistical models for estimating exposures. For example, we included BMI as a predictor for T2DM. Going a step further, we model the full correlation structure in HSE using the following approach:

1. We used the exposure models to impute missing variables in HSE.
2. We used the quantile function of the distribution estimated by the exposure models to convert exposures in HSE to quantiles. Because the distributions were conditional on the independent variables used in each model, the quantiles are adjusted for these variables (i.e. age, sex, quintiles of IMD, etc.).
3. We estimated the linear correlation matrix of the quantiles of the exposures of interest in HSE using Pearson's correlation.
4. We used the linear correlation matrix from #3 to generate streams of uniform random numbers between 0 and 1 with a correlation structure similar to the one observed in HSE. [31]
5. We used the correlated streams of random numbers from #4 as the exposure quantiles for the synthetic individuals.

For simplicity, we assumed that the correlation structure of the exposure quantiles remains constant over time.

### Disease module

The previous two modules for demographics and exposure generate a dynamic close-to-reality synthetic population composed of the adult life course exposures of each synthetic individual. The disease module then translates these exposures to disease incidence using a population-attributable risk fraction approach (PARF). [32] We will first describe how the disease incidence is simulated in the model and then how the model simulates mortality.

We have modelled conditions in several different ways depending on the disease and the currently accepted causal associations between risk factors and diseases. The included risk factors and the modelled relationships between risk factors and disease incidence are those where sufficient, good quality data on relative risks were available and where there is sufficient evidence of a causal relationship between a risk factor and incidence of disease. Relative risks were obtained from published systematic reviews and meta-analyses supplemented with systematic literature searches. [Supplementary materials A: Disease module details](#) includes a summary of all data sources. Furthermore, we have modelled conditions at a more granular level for some of the conditions within the Cambridge Multimorbidity Score and then aggregated them. [Table 2-2](#) summarises the modelling approach for each condition, and further detail is given in [Supplementary materials A: Disease module details](#).

#### Disease incidence

To estimate the individualised annual probability of a synthetic individual developing a specific disease conditional on their cumulative risk exposures, we follow a 3-step approach:

**Step 1.** The incidence proportion attributable to each modelled risk factor by age, sex, and DIMD is estimated, assuming a specific time lag between exposure and disease. The relationships between exposures and disease incidence included in the model are outlined in [Table 2-2](#). The time lags in the model vary stochastically between 1 and 10 years following a shifted binomial distribution. We set the mean lag time for each pair of risk exposure and disease combination according to the best possible empirical data based on the observation period of cohort studies and time to risk reversal in randomised clinical trials (see [Table 2-3](#) and [Supplementary materials A: Disease module details](#)). For example, the mean lag time between alcohol intake and an increase in breast cancer risk is 9 years. That means that a change in alcohol intake will take 9 years on average to be translated to a change in breast cancer risk.

**Step 2.** The portion of the disease incidence attributable to all the modelled risk factors is estimated and subtracted from the total incidence for 2013, assuming multiplicative risks. By multiplicative risk we mean, for example, that if the relative risk (RR) of obesity on CHD is 2 and the RR of smoking on CHD is 3, then the RR of an obese smoker is assumed to be  $2 * 3 = 6$ .<sup>1</sup>

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<sup>1</sup> An alternative approach would be to assume additive risks. Under this assumption and using the previous example, the RR of an obese smoker would be  $2 + 3 - 1 = 4$ . This multiplicative risk assumption is commonly used for epidemiological modelling. [33–36]

Table 2-2: Overview of how individual conditions are modelled

| CMS condition                            | Modelled condition                | Recovery and recurrence                | Causal relationships |                                 |
|--|-----------------------------------|--|----------------------|---------------------------------|
|  |                                   |  | Risk factors         | Conditions                      |
| <b>Dementia</b>                          | Dementia                          | No recovery                            | Y                    | Y                               |
| <b>Cancer</b>                            | Breast cancer                     | Recovery after 10 years; no recurrence | Y                    | Y                               |
|  | Colorectal cancer                 | Recovery after 10 years; no recurrence | Y                    | Y                               |
|  | Lung cancer                       | Recovery after 10 years; no recurrence | Y                    | Y                               |
|  | Prostate cancer                   | Recovery after 10 years; no recurrence | Y                    | N                               |
|  | Other cancers                     | Recovery after 10 years; can recur     | N                    | Y                               |
| <b>COPD</b>                              | COPD                              | No recovery                            | Y                    | N                               |
| <b>Atrial fibrillation</b>               | Atrial fibrillation               | No recovery                            | Y                    | Y                               |
| <b>Heart failure</b>                     | Heart failure                     | No recovery                            | N                    | Y                               |
| <b>Constipation</b>                      | Constipation                      | Recovery is stochastic; can recur      | N                    | Y + past constipation           |
| <b>Epilepsy</b>                          | Epilepsy                          | No recovery                            | N                    | Y                               |
| <b>Chronic pain</b>                      | Chronic pain                      | Recovery is stochastic; can recur      | N                    | Y + past chronic pain           |
| <b>Stroke/transient ischaemic attack</b> | Stroke/transient ischaemic attack | No recovery                            | Y                    | Y                               |
| <b>Diabetes (type I or II)</b>           | Diabetes Type 1                   | No recovery                            | N                    | N                               |
|  | Diabetes Type 2                   | No recovery                            | Y                    | N                               |
| <b>Alcohol problems</b>                  | Alcohol problems                  | Recovery is stochastic; can recur      | N                    | Past alcohol problems           |
| <b>Psychosis/ bipolar disorder</b>       | Psychosis/bipolar disorder        | No recovery                            | N                    | Y                               |
| <b>Chronic kidney disease</b>            | Chronic kidney disease            | No recovery                            | Y                    | N                               |
| <b>Anxiety and depression</b>            | Anxiety and depression            | Recovery is stochastic; can recur      | N                    | Y + past anxiety and depression |
| <b>Coronary heart disease</b>            | Coronary heart disease            | No recovery                            | Y                    | Y                               |
| <b>Connective tissue disorders</b>       | Rheumatoid arthritis              | No recovery                            | N                    | N                               |
|  | Other connective tissue disorders | No recovery                            | N                    | N                               |
| <b>Irritable bowel syndrome</b>          | Irritable bowel syndrome          | No recovery                            | N                    | N                               |
| <b>Asthma</b>                            | Asthma                            | Recovery is stochastic; can recur      | Y                    | Past asthma                     |
| <b>Hearing loss</b>                      | Hearing loss                      | No recovery                            | N                    | N                               |
| <b>Hypertension</b>                      | Hypertension                      | No recovery                            | Y                    | N                               |



**Step 3.** The probability of developing the disease is estimated for each individual in the synthetic population and is used in an independent Bernoulli trial to select those who finally develop the disease.

Table 2-3 Causal relationships included in the model between risk factors and disease incidence; the number corresponds to the time lag (in years) between exposure and outcome.

|                   | Breast cancer | CHD | Colorectal cancer | Stroke | AF | T2DM | Asthma | CKD | Dementia | COPD | Lung cancer | Prostate cancer | Mortality from non-modelled diseases |
|-------------------|---------------|-----|-------------------|--------|----|------|--------|-----|----------|------|-------------|-----------------|--------------------------------------|
| Physical activity | 9             | 4   | 9                 | 4      | -  | 4    | -      | -   | -        | -    | -           | -               | 5                                    |
| Alcohol           | 9             | 4   | 9                 | 4      | 4  | 5    | -      | -   | -        | -    | -           | -               | 5                                    |
| BMI               | 9             | 4   | 9                 | 4      | 4  | 5    | 5      | 5   | 9        | -    | -           | -               |                                      |
| ETS               | 1             | 1   | -                 | 1      | -  | 1    | -      | -   | -        | 1    | 1           | -               |                                      |
| Fruit             | -             | 4   | -                 | 4      | -  | 4    | -      | -   | -        | -    | 9           | -               |                                      |
| SBP               | -             | 4   | -                 | 4      | 4  | -    | -      | 4   | -        | -    | -           | -               | 5                                    |
| Smoking           | 9             | 4   | 9                 | 4      | 4  | 5    | 5      | -   | 9        | 5    | 9           | 9               | 5                                    |
| Cholesterol       | -             | 4   | -                 | 4      | -  | -    | -      | -   | -        | -    | -           | -               |                                      |
| Vegetable         | -             | 4   | -                 | 4      | -  | -    | -      | -   | -        | -    | -           | -               |                                      |

BMI = body mass index; ETS = environmental tobacco smoke; SBP = systolic blood pressure;

The implementation of the above method is described in more detail using CHD as an example. The same process is used for all modelled diseases except type 1 diabetes mellitus, rheumatoid arthritis, other connective tissue disorders, irritable bowel syndrome, and hearing loss, which will be described separately.

### Step 1

The population-attributable risk fraction (PARF) is an epidemiological measure that estimates the proportion of the disease attributable to an associated risk factor. It depends on the relative risk associated with the risk factor and the prevalence of the risk factor in the population. In a

microsimulation context where exposures to risk factors are known at the individual level and assuming multiplicative risk factors, PARF can be estimated using the formula:

$$PARF = 1 - \frac{n}{\sum_{i=1}^n (RR_{i1} * RR_{i2} * \dots * RR_{ik})}$$

where  $n$  is the number of synthetic individuals in the population, and  $RR_{i1...ik}$  are the relative risks of the risk factors associated with CHD for each individual  $i$ . We calculated PARF based on the above formula stratified by age, sex, DIMD, ethnicity and SHA. Consistent with findings from the respective meta-analyses used for IMPACT<sub>NCD</sub> (Supplementary materials A [Table A-2](#)), on average SBP below 115 mmHg, total cholesterol below 3.8 mmol/l and BMI below 22 Kg/m<sup>2</sup> were considered to have a relative risk of 1.[37] Similarly, consumption of eight or more portions of fruit and vegetables and five or more active days (more than 30 minutes of moderate to vigorous activity) per week were also considered to have a relative risk of 1. All the relative risks were taken from published meta-analyses and empirical studies (for references, see [Supplementary materials A: Disease module details](#) where we describe each disease).

## Step 2

The incidence of CHD not attributable to the modelled risk factors can be estimated by the formula:

$$I_{Theoretical\ minimum} = I_{Observed} * (1 - PARF)$$

Where  $I_{Observed}$  is the CHD incidence and  $PARF$  is from Step 1.  $I_{Theoretical\ minimum}$  represents CHD incidence if all the modelled risk factors were at optimal levels. The theoretical minimum incidence is calculated by age, sex, and QIMD only in the initial year of the simulation, and it is assumed to be stable after that.

## Step 3

Assuming that  $I_{Theoretical\ minimum}$  is the annual baseline probability of a synthetic individual to develop CHD for a given age, sex, DIMD, ethnicity and SHA due to risk factors not included in the model (i.e. genetics, air pollution, dietary exposures beyond fruit and vegetables etc.), the individualised annual probability of developing CHD,  $\mathbb{P}(\text{CHD} \mid \text{age, sex, DIMD, ethnicity SHA, exposures})$ , given their risk factors were estimated by the formula:

$$\begin{aligned} \mathbb{P}(\text{CHD} \mid \text{age, sex, DIMD, ethnicity SHA, exposures}) &= \\ &= I_{Theoretical\ minimum} * RR_{i1} * RR_{i2} * RR_{i3} * \dots * RR_{ik} \end{aligned}$$

Where  $RR_{i1 \dots ik}$  are the relative risks that are related to the specific risk exposures of the synthetic individual, the same as in step 1.

#### *Estimating the observed incidence probability $I_{observed}$*

To estimate the observed incidence probability  $I_{observed}$  we fitted a binomial GAMLSS model to the linked primary care data (CPRD, HES, ONS) with disease incidence probability as the dependent variable and year, age, sex, DIMD, ethnicity and SHA as the independent variables. For type 1 diabetes mellitus, rheumatoid arthritis, other connective tissue disorders, irritable bowel syndrome, and hearing loss that do not depend on any risk factors, we used these models to project their future incidence, assuming log-linear trends. To account for biases in the data, we injected uncertainty of  $\pm 5\%$  (relative) to the estimated disease incidence probability during the simulation.

#### *Initial prevalence*

For the initial simulation year, some synthetic individuals must be allocated as prevalent cases for each modelled disease. We fitted a binomial GAMLSS model to the linked primary care data (CPRD, HES, ONS) with disease prevalence probability as the dependent variable and year, age, sex, DIMD, ethnicity and SHA as the independent variables. We used these models to allocate the initial year disease prevalence in the simulation.

#### *Conditions with recovery and recurrence: asthma, anxiety and depression, constipation, pain, alcohol problems and cancers*

Asthma, anxiety and depression, constipation, pain, and alcohol problems were treated as short-term conditions that can go into remission and reoccur. Spell duration was stochastically derived from observed durations in the CPRD data. In addition to the risk factor relationships described in [Table 2-3](#), incident cases of these five conditions were associated with a previous history of the condition. Cancers were assumed to go into remission after 10 years, but recurrence was not modelled conditional on cancer history. All other conditions were treated as life-long.

#### *Dependencies between conditions*

As the Cambridge Multimorbidity Score (CMS) is a composite measure, it is derived from the combination of conditions an individual has. We, therefore, modelled dependencies between conditions with strong correlations based on our epidemiological understanding and the correlation structure in our linked CPRD data using GAMLSS models to derive relative risks for the effect of prevalent condition A on the incidence of condition B. [Figure 2-2](#) displays the dependencies modelled between a prevalent condition (on the y-axis) and the subsequent incidence of another condition (on the x-axis). Disease dependencies modelled for each incident condition are summarised in [Supplementary materials A: Disease module details](#).



Figure 2-2 - Modelled relationships between conditions<sup>2</sup>



### Disease duration

For existing prevalent conditions among simulants at the start of the simulation (2013), the number of years lived with each condition is assigned based on sociodemographic characteristics and duration of the condition derived from administrative data, as derived from GAMLSS models fitted in the linked CPRD data. For the five conditions with remission and recurrence, these models also inform the duration of each disease occurrence.

<sup>2</sup> The darker the blue, the stronger the association. Prevalent CKD was associated with a reduced risk of pain. This is likely to be because we measured pain using prescription data in CPRD, and many pain medications are contra-indicated for CKD.

## Mortality

All synthetic individuals are exposed to the risk of dying from any of their acquired modelled conditions or any other non-modelled cause. We treat the latter as a condition that everyone is a prevalent case of. That allows us to treat it like any other condition in the model. Hearing loss, IBS, asthma, anxiety and depression, constipation, pain, hypertension, and alcohol problems have very low case fatality; hence, we assume that mortality from these conditions is 0. Furthermore, our dataset had very few CKD deaths, and we could not estimate CKD case fatality accurately. Hence, we assume that CKD mortality is 0 as well. For all other conditions, we fitted GAMLSS models to estimate their case fatality (the probability of a prevalent case of a condition dying of this condition), conditional on year, age, sex, and DIMD. For conditions with high mortality (i.e. CHD), we additionally decomposed case fatality to the first-year post-diagnosis case fatality and the second-year onwards post-diagnosis case fatality. For all potentially fatal conditions, we applied the same PARF approach described above for incidence to the case fatality. For instance, if the RR of smoking on CHD is 3, we assume that smokers have 3 times the risk of never-smokers to develop CHD and when they do, they have 3 times the risk of never-smokers to die from CHD. Therefore, we allow exposures to risk factors to influence the mortality probability of the simulants. The exception is conditions with explicit first-year case fatality, for which we assumed it is independent of exposure to risk factors and is only conditional on age, sex, and DIMD.

Additionally, using a similar approach to the one we used to model disease incidence, we allowed prevalent cases of T2DM, synthetic individuals with SBP higher than 140 mmHg, active smokers, those with one or less active day per week, and those with excessive alcohol intake to experience higher non-modelled cause mortality rates. [38]

### *Mortality calibration*

All-cause mortality in our linked CPRD dataset was lower than the official mortality estimates that the ONS reports. This appears to be a known issue in CPRD. [39] We, therefore, calibrated the CPRD-driven mortality in the model to the ONS estimates. We first fitted functional demographic models by sex and DIMD to the ONS mortality rate estimates by single year of age from 2001 to 2019. [40,41] Using the R package 'demography', we projected all-cause mortality rates to the simulation horizon (2043). [42] Functional demographic models are generalisations of the Lee-Carter demographic model, influenced by ideas from functional data analysis and non-parametric smoothing. [43] We then inflated the case fatality rates of potentially fatal diseases in the simulation by an age/sex/DIMD-specific calibration factor to track the projections of the functional demographic model.

### 3. Population-attributable risk fraction (PARF)

The IMPACT<sub>NCD</sub> model allows for changes in the exposures of synthetic individuals based on defined ‘what if’ scenarios. The change in exposures allows us to calculate the individual risk factor effects on trends in modelled incidence. We can then compare the disease-related events between the counterfactual life courses.

#### PARF calculations

We can use the alternative scenario function to estimate PARFs - the proportion of incidence of a condition attributable to specific risk factors. The PARF analysis runs from 2013 and compares the baseline model scenario with scenarios where each risk factor is set to the optimal level in 2013 (see [Table 3-1](#)). As the lag time between exposure and incidence differs by condition, for each condition, we compare the baseline and optimal scenario incidences at the latest lag time ([Table 3-2](#)). The proportion of the baseline incidence removed under the optimal level scenario gives the PARF. As PARFs are multiplicative and not additive, an additional scenario where all risk factors are set to optimal levels is used to apply a correction factor. Note that in the current implementation, we did not consider the mediated effects of some of the risk factors. i.e. when BMI is reduced, we would expect total cholesterol and SBP to be reduced by some degree for physiological reasons, which we currently ignore.

Table 3-1 Optimal levels for risk factor exposures<sup>3</sup>

| Risk Factor               | Optimal level   |
|---------------------------|---|
| Smoking                   | Never smoker, no current smoking, no second-hand exposure |
| BMI                       | 15  |
| Alcohol consumption       | 0g  |
| Fruit and veg consumption | 400g (5 portions) of each daily                           |
| SBP                       | 90  |
| Total Cholesterol         | 2   |
| Physical activity         | 7 active days/week  |

Table 3-2 Year for PARF calculation

| Condition           | Year of PARF calculation |
|---------------------|--------------------------|
| Atrial fibrillation | 2017                     |
| CHD                 | 2017                     |
| Stroke              | 2017                     |
| Asthma              | 2018                     |

<sup>3</sup> We used optimal levels for the exposures that were well below the minimum level of exposure considered harmful.

|                                 |      |
|---------------------------------|------|
| <b>CKD</b>                      | 2018 |
| <b>Type 2 Diabetes Mellitus</b> | 2018 |
| <b>COPD</b>                     | 2018 |
| <b>Dementia</b>                 | 2022 |
| <b>Breast Cancer</b>            | 2022 |
| <b>Colorectal Cancer</b>        | 2022 |
| <b>Lung Cancer</b>              | 2022 |
| <b>Prostate Cancer</b>          | 2022 |

## 4. Model outputs

The population in the model for this report was set for England. The model has a time horizon of 30 years, from 2013 to 2043. The simulation begins in 2013 to allow for validation and calibration with the linked primary care data used to inform the model. The model outputs produce life-course trajectories for each simulant, including CMS scores. From these, annual summary measures such as incidence, prevalence and mortality rates are calculated. These measures can then be compared across time and between scenarios to estimate the effects and equity of different scenarios. All outcome measures can be standardised to the 2013 European Standard Population or not, and stratification is possible by year, sex, DIMD and age group, allowing examination of how effects differ across sub-populations.

From the estimated mortality rates of the model, we can also estimate life expectancy as follows. The 2010 and 2019 estimates for period life expectancy use historical ONS mortality rates, [44] and the 2040 estimates use projected mortality changes from the microsimulation model applied to 2019 ONS mortality rates. We then apply REAL Centre estimates of the proportion of people in different health states by 5-year age bands to the mortality rates to get estimates for the time spent in different states of ill health in 2010 and 2019. For 2040, we use REAL Centre estimates of the proportion of people in different health states by age group and sex from 2019 for those aged under 30 and assume no changes to these proportions until 2040. For those aged 30 and over for 2040, we use the projected estimates of the proportion of people in different health states by age group and sex from the microsimulation model. We use the same methods for estimating the projected absolute numbers of people with and without illness, based on ONS historical mid-year population estimates for 2019 and ONS 2020 projected population estimates for 2040. [45,46]

Crucially, the model is a dynamic, open-cohort microsimulation model. That means the model is trying to estimate the actual impact of the scenarios within a dynamic population where people are born, people age, people's risk factors change, and people die. The detailed



modelling of the population dynamics in our model is thus different from many economic models, which are often closed-cohort, meaning they follow the same population cohort over time and often have a lifetime horizon.

#### Uncertainty and probabilistic sensitivity analysis

IMPACT<sub>NCD</sub> implements a 2<sup>nd</sup> order Monte Carlo approach to estimate uncertainty intervals (UI) for each scenario. [47,48] For each iteration, a different set of input parameters is used by sampling from the respective distributions of input parameters. We assumed log-normal distributions for relative risks and hazard ratios, normal distributions for coefficients of linear regression equations, and uniform distributions for estimates of incidence, prevalence, and case fatality rates. Specifically, for relative risks and hazard ratios, the distributions were bounded above 1 when the mean was above 1 and vice versa.

IMPACT<sub>NCD</sub> allows stochastic uncertainty, parameter uncertainty, individual heterogeneity, and to some extent, structural uncertainty to be propagated in the reported UI. In IMPACT<sub>NCD</sub>, we minimise stochastic uncertainty by using the same random numbers for all scenarios when appropriate. The following example illustrates the different types of uncertainty considered in the model. Let us assume that the annual risk for CHD is 5%. Suppose we apply this risk to all individuals and randomly draw from a Bernoulli distribution with  $p = 5\%$  to select those who will manifest CHD. In that case, we only consider stochastic uncertainty. Our model minimises stochastic uncertainty when we compare different policy scenarios by using the same random numbers for all scenarios, where appropriate. If we allow the annual risk for CHD to be conditional on individual characteristics (i.e. age, sex, exposure to risk factors), then individual heterogeneity is considered. Finally, when the uncertainty of the relative risks due to sampling errors is considered in estimating the annual risk for CHD, the parameter uncertainty is considered. From these three types of uncertainty, only the parameter uncertainty could be reduced by better studies in the future.

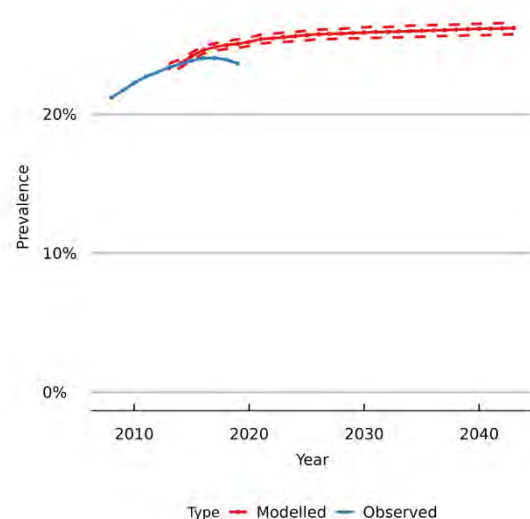
The structure of the model is grounded in fundamental epidemiological ideas and well-established causal pathways on which exposures are causally related to the specific NCDs which are explicitly modelled. For example, hypertension is causally related to CVD but not lung cancer. Hence, structural sensitivity analysis is not necessary to explore the possibility of hypertension being a risk factor for lung cancer. Therefore, we considered this type of uncertainty relatively small and did not study it in detail, with one exception: the discrete-time bias that arises from the fact that time in IMPACT<sub>NCD</sub> is not continuous. A synthetic individual within the model may die of multiple causes within one year; however, the discrete-time nature of the simulation does not allow the identification of the cause that 'killed' the simulant first. Every time this happens to a simulant, we randomly select a cause of death from the list of all

the terminal events that occurred for the simulant that year. Hence, we propagate discrete-time uncertainty to the output.

## 5. Validation and calibration

We validated the IMPACT<sub>NCD</sub> epidemiological engine using internal validation plotting the modelled exposures' prevalence and disease incidence against the observed exposures' prevalence and disease incidence in HSE and linked primary care data, respectively. Mortality in the model is calibrated to mortality projections as described above ([Mortality](#)). We present the relevant validation plots for modelled exposures in [Supplementary materials B: exposure modelling details and validation](#) stratified by year and age group and by quintiles of IMD and age group. [Figure 5-1](#) shows the modelled prevalence of CMS > 1.5 (defined as 'major illness' in this report) against the observed CPRD Aurum prevalence. The decline from 2017 in the observed data is an artefact caused by the case definition and consequent prevalence of pain. Validation plots (age-sex-dimd standardised) for incidence, case fatality, and prevalence of individual conditions are shown in [Supplementary materials A: Disease module details](#). Additionally, we have produced and inspected plots for multiple combinations of stratification levels that are available on request. Overall, the plots suggest that IMPACT<sub>NCD</sub> captures exposure trends and translates them to disease incidence and mortality reasonably well for the purpose of this project.

Figure 5-1 - Validation plot for the prevalence of CMS > 1.5 (age-sex-dimd standardised)



## 6. Definition of the Cambridge Multimorbidity Score and defining conditions in primary care data

The Cambridge Multimorbidity Score (CMS) is used to define levels of ill health for an individual and for the population. [11] The CMS assigns a weight or 'score' to 20 conditions on the basis of how the illness affects their use of primary care, emergency health services and the patient's likelihood of death (see [Table 6-1](#) below for the exact weight of each condition).

Our projections draw on detailed patient-level administrative data linked to primary care (CPRD Aurum) and secondary care (Hospital Episode Statistics) from a sample of 1.7 million patients. The data include chronic conditions diagnosed in primary care and the Index of Multiple Deprivation (IMD) score for each patient's local area, age, sex, ethnicity and region. Since our analysis relies on diagnosis data from patient records, all our projections refer to *diagnosed* prevalence, incidence and illness throughout the report. Due to our focus on the long-term trends in ageing and health and due to our data sample being available up to 2019/20, we do not include COVID-19 and its impacts in our analysis.

The use of diagnosed conditions in administrative primary care data to measure levels of illness has several advantages over using survey data. Administrative data tend to have larger and more representative patient samples and are less subjective than self-reported measures of health in surveys. [49] It is, however, important to note that rates of diagnosis can be impacted by patients' access to care and changes in diagnosis policy and practices over time. Several studies have found underdiagnosis in COPD, [50] hypertension, [51] type 2 diabetes, [52] and dementia, [53] so it is likely that the true burden of illness will be higher than what we estimate in this report.

The CMS is used to define levels of ill health for an individual and for the population. [11] The score provides a metric which allows comparisons of levels of illness across conditions and over time. The CMS assigns a weight or 'score' to 20 conditions based on how the illness affects their use of primary care, emergency health services and the patient's likelihood of death ([Table 6-1](#)). For instance, cancer and heart failure are given higher scores than hypertension (high blood pressure) or hearing loss because they are more likely to lead to death, unplanned hospital admissions or greater primary care needs. For those with multimorbidity, scores are added together, meaning individuals with the same score can have a different number and combination of conditions.

We use the CMS rather than other multimorbidity indices such as Charlson [54] and Elixhauser, [55] as it is more representative of conditions that are highly prevalent today and because it outperforms the Charlson index in predicting primary care consultations and hospital admissions and, to a lesser extent, mortality. [11]

Table 6-1 Cambridge Multimorbidity Score conditions and their weights

| Condition                               | Primary care consultations <sup>1</sup> | Unplanned admissions <sup>2</sup> | Mortality <sup>2</sup> | General outcome <sup>3</sup> |
|---|---|-----------------------------------|------------------------|------------------------------|
| Dementia                                | 1.81                                    | 156.9                             | 124.42                 | <b>2.50</b>                  |
| Cancer                                  | 2.58                                    | 104.8                             | 62                     | <b>1.53</b>                  |
| COPD                                    | 3.43                                    | 134.51                            | 42.5                   | <b>1.46</b>                  |
| Atrial fibrillation                     | 5.94                                    | 105.21                            | 22.14                  | <b>1.34</b>                  |
| Heart failure                           | 2.9                                     | 73.2                              | 43.47                  | <b>1.18</b>                  |
| Constipation                            | 3.42                                    | 72.73                             | 35.42                  | <b>1.12</b>                  |
| Chronic pain                            | 3.43                                    | 84.93                             | 16.46                  | <b>0.92</b>                  |
| Epilepsy                                | 2.13                                    | 113.42                            | 18.26                  | <b>0.92</b>                  |
| Stroke/transient ischaemic attack (TIA) | 1.54                                    | 90.84                             | 20.63                  | <b>0.80</b>                  |
| Diabetes (type 1 or 2)                  | 3.77                                    | 55.33                             | 10.23                  | <b>0.75</b>                  |
| Alcohol problems                        | 0.97                                    | 93.59                             | 12.72                  | <b>0.65</b>                  |
| Psychosis/bipolar disorder              | 2.24                                    | 77.28                             | 7.2                    | <b>0.64</b>                  |
| Chronic kidney disease                  | 0.98                                    | 52.13                             | 16.61                  | <b>0.53</b>                  |
| Anxiety/depression                      | 2.12                                    | 46.61                             | 7.04                   | <b>0.50</b>                  |
| Coronary heart disease                  | 1.49                                    | 70.87                             | 4.22                   | <b>0.49</b>                  |
| Connective tissue disorders             | 3.1                                     | 28.87                             | -0.39                  | <b>0.43</b>                  |
| Irritable bowel syndrome                | 1.82                                    | 8.55                              | -1.33                  | <b>0.21</b>                  |
| Asthma                                  | 1.32                                    | 22.78                             | -2.73                  | <b>0.19</b>                  |
| Hearing loss                            | 1.04                                    | 8.93                              | -3.94                  | <b>0.09</b>                  |
| Hypertension                            | 0.66                                    | 10.76                             | -2.09                  | <b>0.08</b>                  |

Note: 1. Per person-year. 2. Per 1000 person-years. 3. Unit change associated with a change of 1 standard deviation in each of the 3 outcomes. Negative weights can be interpreted as reflecting a negative association with the outcome of interest after controlling for other conditions. Constipation, when diagnosed in primary care data, is likely linked to the side effects of taking opioid analgesics (strong pain killers such as codeine phosphate) and other medication. Chronic pain that leads to opioid prescribing tends to be worse, and therefore constipation could be linked with higher care needs.

Of the 20 conditions in our analysis, most are considered “permanent” because there is no cure: once someone is diagnosed with a condition, like atrial fibrillation, they will forever have that condition. For six of the conditions observed to be more transient in the data, we allow

patients to go into remission: cancer, asthma, anxiety and depression, alcohol problems, constipation and chronic pain.

The code lists used for the CMS, available online, [56] have been developed using CPRD GOLD based on read codes, medcodes and prodcodes. In this report, we use data from CPRD Aurum. [Table 6-2](#) summarises the definitions for each condition used in this report and in the original CMS paper. We use code lists for CPRD developed by Anna Head, available on GitHub [57] and adapted from code lists from the CALIBER algorithms<sup>4</sup>. [58] [Table 6-3](#) and [Figure 6-1](#) summarise the sample inclusion and exclusion criteria along with the cleaning rules applied to the initial 2 million random sample of patients from CPRD Aurum.

Table 6-2 Definition of the conditions in the Cambridge Multimorbidity Score

| Condition  | In this report  |
|--|---|
| <b>Alcohol problems</b>                                | At least one code recorded (in CPRD Aurum or HES) in the last 12 months. Remission after 12 months without new diagnosis. The code list for alcohol misuse excludes 'alcoholic liver disease'.  |
| <b>Asthma</b>  | At least one code recorded (in CPRD Aurum or HES) in the last 12 months. Remission after 12 months without new diagnosis.   |
| <b>Anxiety/depression</b>                              | At least one code recorded for anxiety OR depression in the last 12 months (in CPRD Aurum or HES). Remission after 12 months without new diagnosis.   |
| <b>Atrial fibrillation</b>                             | At least one code ever recorded (in CPRD Aurum or HES).   |
| <b>All cancers</b>                                     | At least one code recorded (in CPRD Aurum or HES) for either bowel, lung, prostate or any other cancer. Remission after 10 years since the first diagnosis of the last cancer, if more than one.  |
| <b>Chronic kidney disease</b>                          | Based on at least two records (in CPRD Aurum) of test values (eGFR) < 60ml/min, corresponding to a diagnosis of CKD of stage 3 or above. The two records must be at least within a 90-day interval.<br>OR<br>At least one CKD observation code ever recorded (in CPRD Aurum or HES) |
| <b>Chronic pain</b>                                    | At least four prescriptions (in CPRD Aurum) for painkiller drugs in the span of a year (analgesics or epilepsy drugs if not diagnosed with epilepsy). Remission after 12 months without new prescriptions.  |
| <b>Connective tissue disorder/rheumatoid arthritis</b> | At least one code ever recorded for connective tissue disorder OR rheumatoid arthritis (in CPRD Aurum or HES).  |
| <b>Constipation</b>                                    | Four or more laxative prescriptions in last 12 months (in CPRD Aurum). Remission after 12 months without new prescriptions.   |
| <b>Chronic obstructive pulmonary disease</b>           | At least one code ever recorded (in CPRD Aurum or HES).   |
| <b>Coronary heart disease</b>                          | At least one code ever recorded (in CPRD Aurum or HES).   |
| <b>Dementia</b>  | At least one code ever recorded (in CPRD Aurum or HES).   |
| <b>Diabetes (any type)</b>                             | At least one code ever recorded for diabetes type 2 OR other type of diabetes (in CPRD Aurum or HES).   |
| <b>Epilepsy</b>  | At least one code ever recorded (in CPRD Aurum or HES).   |

<sup>4</sup> Available here <https://www.caliberresearch.org/portal/phenotypes/chronological-map> and in machine-readable format here <https://github.com/spiros/chronological-map-phenotypes>.

|  |   |
|--|---|
| <b>Hearing loss</b>                            | At least one code ever recorded (in CPRD Aurum or HES).                   |
| <b>Heart failure</b>                           | At least one code ever recorded (in CPRD Aurum or HES).                   |
| <b>Hypertension</b>                            | At least one code ever recorded (in CPRD Aurum or HES).                   |
| <b>Irritable bowel syndrome (IBS)</b>          | At least one code ever recorded (in CPRD Aurum or HES).                   |
| <b>Psychosis</b>                               | At least one code ever recorded (in CPRD Aurum or HES).                   |
| <b>Stroke/Transient ischaemic attack (TIA)</b> | At least one code ever recorded for stroke OR TIA (in CPRD Aurum or HES). |

Table 6-3 Sample exclusions and cleaning rules

| <b>Type</b>                          | <b>Rule</b>   |
|--------------------------------------|---|
| <b>Sample inclusion/exclusion</b>    | Exclude duplicate CPRD patient IDs, keep the most recent one*   |
|                                      | Exclude if not eligible (linkable) for all 5 datasets (CPRD, ONS, HES, cancer registry, mental health) (linkage eligibility file)**   |
|                                      | Exclude if entered the study after 31 March 2020 (as the data contain no HES records after 31st October 2020)   |
|                                      | Exclude implausible linkage**, ie. different number of linkages to HES and ONS registry data  |
|                                      | Exclude implausible linkage, ie. end of registration or death before patient's start of registration with the practice ( <i>regstartdate</i> )  |
|                                      | Exclude patients who are active in the sample for less than one year**, unless they are <1 year old (to be used to calculate infant mortality rates)  |
|                                      | Exclude if missing IMD (deprivation) and missing ethnicity  |
| <b>Cleaning of patient variables</b> | Use ONS' date of death ( <i>dod</i> ) if recorded; otherwise, use date of death recorded in CPRD ( <i>emis_ddate</i> ) or estimated by CPRD ( <i>cprd_ddate</i> ) if ONS date of death is missing and if the CPRD date of death is between 1 Nov 2019 - 31 Oct 2020 (i.e. one year before end of sample eligibility) to account for ONS delays in transmitting death information. |
|                                      | Use earliest of: CPRD registration end date ( <i>regenddate</i> in patient file), date of death (ONS file's date of death ( <i>dod</i> ) if available, or <i>cprd_ddate</i> (CPRD patient file) if between 1 Nov 2019 and 31 Oct 2020), practice last collection date ( <i>lcd</i> in practice file), 31 October 2020 (HES data not available after this)                         |
|                                      | Use most common ethnicity recorded across all sources (CPRD, HES inpatient, outpatient, A&E); unless it is 'Unknown', use non-unknown record of ethnicity.  |
|                                      | If tie in most common ethnicity, use the most recently recorded.  |
|                                      | Where date of observation ( <i>obsdate</i> ) is recorded, use <i>obsdate</i> ; use the date the event was entered into the practice system ( <i>enterdate</i> ) otherwise.  |
|                                      | If date of observation ( <i>obsdate</i> ) is before 1900 or after 2021, and the date the event was recorded ( <i>enterdate</i> ) is between 1900-2021, use  |

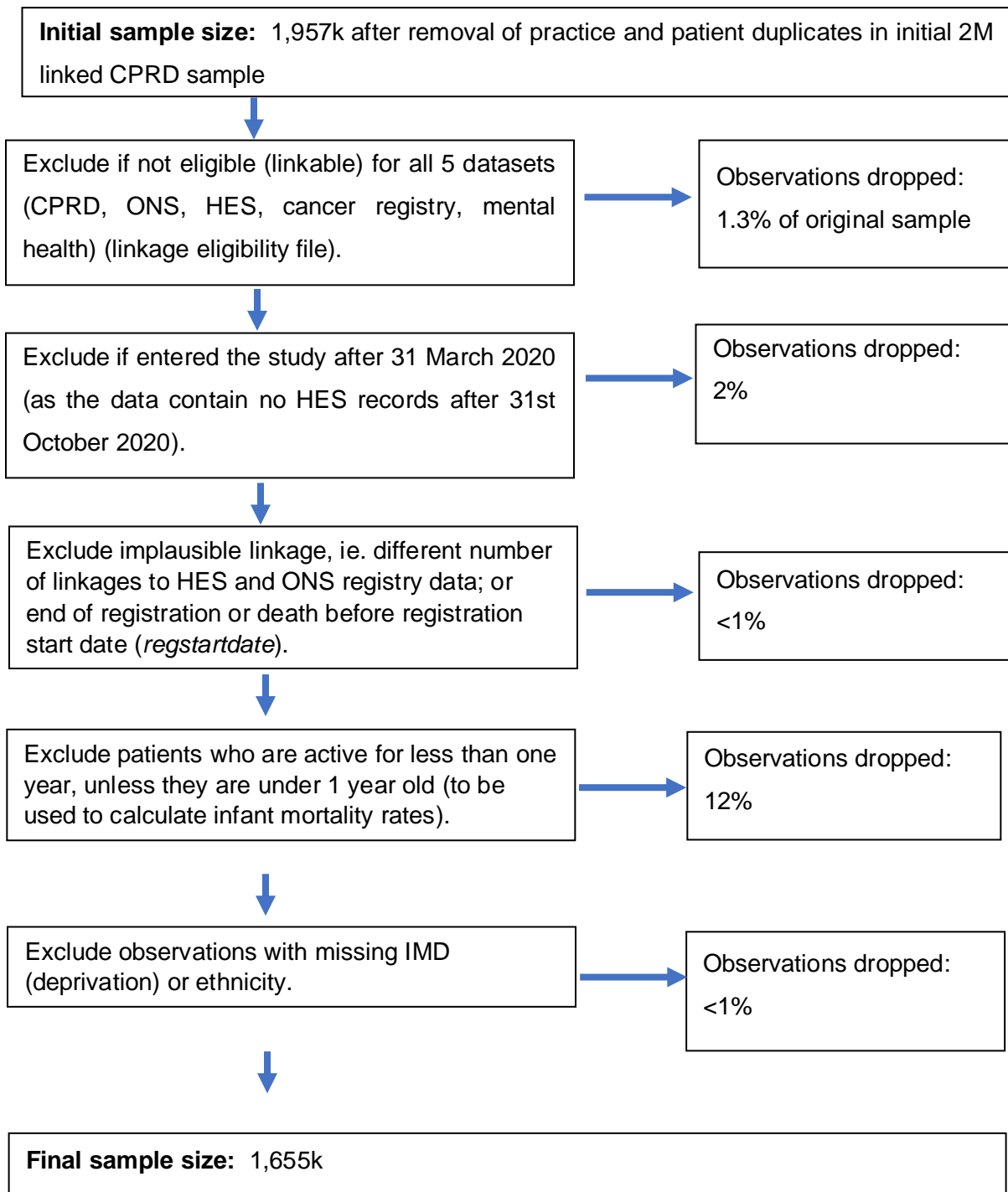
|                             |   |
|-----------------------------|---|
|                             | <i>enterdate</i> ; if <i>enterdate</i> is outside of 1900-2021, we drop the observation <sup>5</sup> .  |
|                             | If date of observation ( <i>obsdate</i> ) is before patient's year of birth, but the date the event was recorded ( <i>enterdate</i> ) is after, we use the latter. If both dates are before year of birth, we drop the observation. |
|                             | Remove observations of type 'family history'  |
|                             | If missing date of the start of the hospital episode ( <i>epistart</i> in HES files), we replace it with date of the end of the hospital episode ( <i>epiend</i> ).   |
|                             | If missing date of the procedure ( <i>evdate</i> ), we replace it with date of the start of the hospital episode ( <i>epistart</i> ).   |
|                             | Recode as prevalence if a new diagnosis takes place within a year of registration with a new practice.  |
| <b>Prevalence modelling</b> | For resolving conditions, if the date of a new diagnosis is within 365 days of the remission date of the previous disease spell, we recode it to be part of the same disease episode.   |

Note: \* this is identified by the highest CPRD patient ID number; \*\* these are cleaning rules commonly implemented when using CPRD (e.g. see (1)).

---

<sup>5</sup> This is because a diagnosis will likely be picked up in other primary or secondary care activity while inferring diagnosis dates wrongly will introduce errors in our age-specific prevalence rates.

Figure 6-1 Flowchart for the sample exclusions





## 7. Strengths and limitations of this modelling approach

The IMPACT<sub>NCD</sub> model is an advanced, validated, flexible microsimulation of the dynamics of NCDs in a population, including important NCDs that are amenable to prevention and provide support to a range of capabilities to conduct state-of-the-art effectiveness and equity analysis.

The complex dynamic generated by reductions in risk factors and disease trends needs to be modelled for a more realistic estimate of the future burden of illness from a societal perspective, which includes competing causes of illness and death. For instance, the model factors in that if CHD incidence is delayed, people may live longer and be more likely to get any of the other modelled diseases. This was evident in our projections, where, for example, the number of COPD cases increased because of people living longer. The modelling of individual conditions allows in-depth exploration of how trends in risk factors may impact the future burden of multimorbidity.

All such modelling analyses have limitations. This iteration of the model uses exposure data from HSE waves up to 2014; however, we know that there have been changes in more recent years to both overall trends and socioeconomic inequalities. Furthermore, the data that informs our model is from before the coronavirus pandemic and therefore does not capture any of the impacts of the coronavirus or pandemic-related restrictions. The use of HSE data from 2003-2014 was based on several reasons. Most importantly, during this time period there is consistent recording of risk factors based on age, decile of IMD, ethnicity and geographic region over time. This allows us to separately model the projected incidence of long-term illness for different population subgroups. Although later versions of HSE are available, differences in survey methodology meant it was not possible to include them in this model. As we have used data from HSE for the period between 2003-2014, some trends in risk factors differ from those reported by OHID and PHE Fingertips for the period between 2014-present day.

We derived trends in disease incidence, prevalence, and mortality, from CPRD data (GP practices) linked to HES (secondary care data) and ONS (cause of death) records. CPRD and HES data only provide information from where individuals have accessed healthcare and diagnostic information has been recorded. Whilst CPRD data is collated directly from GP records, HES data is an administrative summary of each episode of care. As such, our analyses measure only diagnosed cases of conditions and do not capture unmet needs. Whilst this linked primary care data largely represents the population of England registered with primary care providers, it is slightly less representative compared to the overall population of England: marginalised groups and those from the most deprived areas are underrepresented.

We have modelled dependencies between certain diseases based on the strength of the correlations and clinical understanding. In future iterations of the model, we plan to improve the modelling of disease clusters by including additional disease-disease interactions.

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## A) Supplementary materials A: Disease module details

The following subsections present the assumptions, data sources, structural diagram, and validation plots for each condition.

Incidence, prevalence, case-fatality and mortality trends are modelled using GAMLSS models fitted to the CPRD data by sex, age group, deprivation decile, and year.

Disease dependencies are where the incidence of the condition of interest is associated with the prevalence of other condition(s). These were included based on the strength of correlations and known plausible directional associations and modelled as relative risks by sex, age group, and deprivation decile, using logistic regression.

For some conditions, calibration factors were applied based on visual inspection of the simulated data against the observed data. Two types of calibration factors were used: intercept and trend. The intercept calibration factor is multiplied by the simulated incidence to shift it up (calibration factor > 1) or down (calibration factor < 1). The trend calibration factor is applied as an exponential based on the number of years since the start of the simulation. For all case fatality rate plots, the model output is post-calibrated to the ONS mortality; therefore, it is expected to be higher than the CPRD observed mortality.

### Model structure

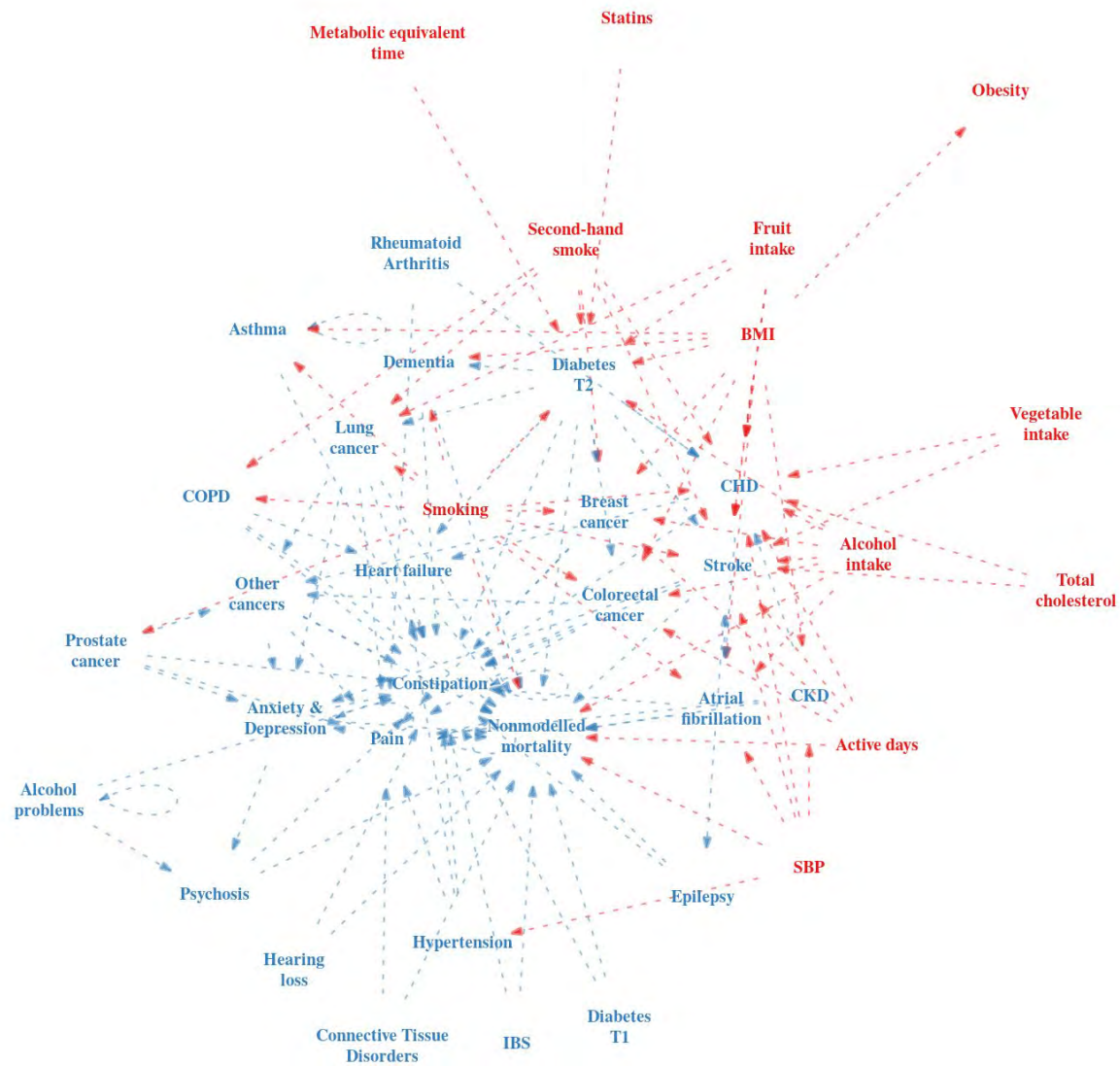
Figure A-1 is a 'birds-eye' diagrammatic presentation of all the relationships modelled between risk factors and conditions and between pairs of conditions, as described in the above sections. As this is difficult to read and interpret, the structural diagram for the relationships affecting each modelled condition is presented alongside the individual condition summaries in the following sub-sections.

In all the diagrams, conditions are in blue and modelled exposures are in red. Modelled associations between risk factors and conditions are shown by the red arrows; modelled associations between prevalent condition x and incident condition y are shown by the blue arrows.

In the disease-specific sub-sections, the incident condition of interest is in black text in the centre, and all direct relationships modelled between exposures and other conditions are shown by the arrows pointing towards the middle.



Figure A-1 Relationships modelled between exposures and conditions.



## Coronary Heart Disease (CHD)

Table A-1 Modelling assumptions for incident CHD

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery  |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke, systolic blood pressure, total cholesterol, body mass index, physical activity, alcohol intake, fruit and vegetable intake |
| <b>Disease dependencies</b>     | Chronic kidney disease, diabetes mellitus type 2, rheumatoid arthritis   |
| <b>Calibration factor</b>       | Intercept: 0.97  |

Figure A-2 - Causal structure of risk factor associations and disease dependencies for incident CHD

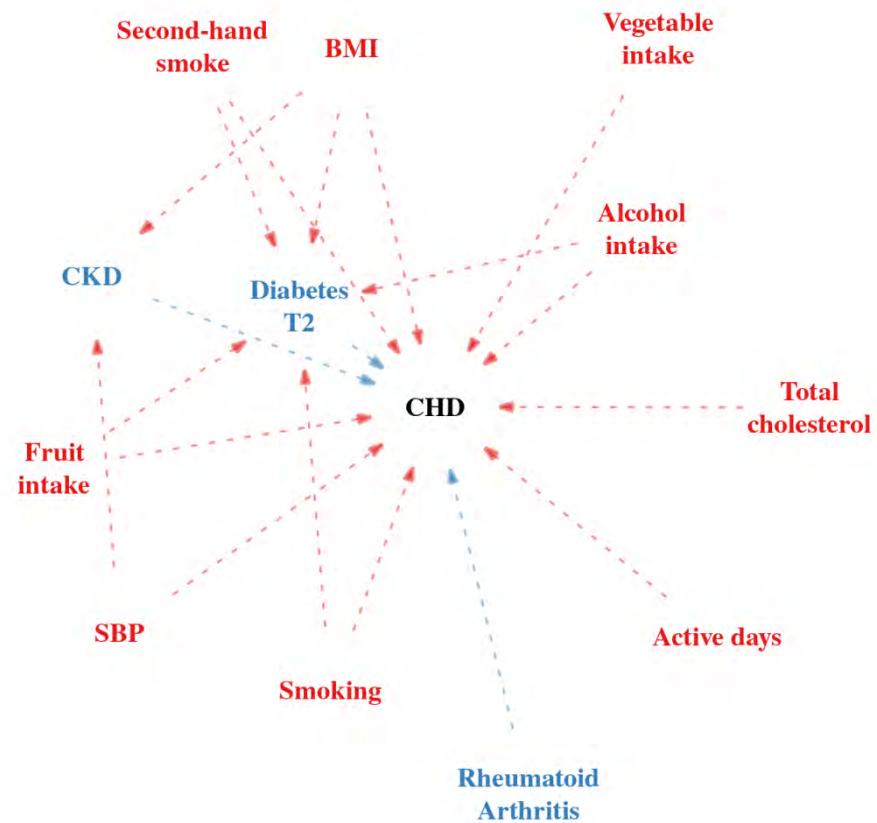


Table A-2 - Data sources for causal associations between risk factors and CHD incidence

| <b>Parameter</b>                                | <b>Details</b>                                      | <b>Comments</b>   | <b>Source</b>  |
|---|---|---|--|
| Relative risk for active smoking                | GBD meta-analysis                                   | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking                    | GBD meta-analysis                                   | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | Meta-analysis of 10 cohort and case-control studies | Adjusted for important CHD risk factors. The effect was applied to never regularly smokers. | He J, Vupputuri S, Allen K, Prerost MR, Hughes J, Whelton PK. Passive Smoking and the Risk of Coronary Heart Disease — A Meta-Analysis of Epidemiologic Studies. N Engl J Med 1999;340:920–6. (Table 3. Adjusted RR)   |

| <b>Parameter</b>                          | <b>Details</b>   | <b>Comments</b>  | <b>Source</b>  |
|---|--|--|--|
| Relative risk for systolic blood pressure | Meta-analysis of individual data from 61 prospective studies | Stratified by age and sex. Adjusted for regression dilution and total blood cholesterol and, where available, lipid fractions (HDL and non-HDL cholesterol), diabetes, weight, alcohol consumption, and smoking at baseline. | Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. <i>The Lancet</i> 2002;360:1903–13. (Figures 3 and 5)   |
| Relative risk for total cholesterol       | Meta-analysis of individual data from 61 prospective studies | Stratified by age and sex. Adjusted for regression dilution and age, sex, study, systolic blood pressure and smoking.  | Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55 000 vascular deaths. <i>The Lancet</i> 2007;370:1829–39. (Web-table 6 fully adjusted and Figure 3) |
| Relative risk for body mass index         | Meta-analysis of 58 prospective studies                      | Stratified by age. Adjusted for age, sex, smoking status, systolic blood pressure, history of diabetes, and total and HDL cholesterol.   | The Emerging Risk Factors Collaboration. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. <i>The Lancet</i> 2011;377:1085–95. (Table 1 and Figure 2)                       |

| <b>Parameter</b>                                  | <b>Details</b>   | <b>Comments</b>   | <b>Source</b>   |
|---|--|---|---|
| Relative risk for diabetes mellitus type 2        | Meta-analysis of 102 prospective studies   | Stratified by age. Adjusted for age, smoking status, body-mass index, and systolic blood pressure.            | The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. <i>The Lancet</i> 2010;375:2215–22. (Figure 2)                                     |
| Relative risk for physical activity               | Meta-analysis of 18 cohort studies for CHD and 8 cohort studies for ischaemic stroke | Stratified by age and sex. Adjusted for measurement error, age, sex, smoking, blood pressure and cholesterol. | Bull FC, Armstrong TP, Dixon T, Ham S, Neiman A, Pratt M. Comparative quantification of health risks. Chapter 10: physical inactivity. Geneva: World Health Organisation; 2004. (Tables 10.19 and 10.20)  |
| Relative risk for fruit and vegetable consumption | Meta-analysis of 9 cohort studies  | RR per portion of F&V. Multiply-adjusted.   | Dauchet L, Amouyel P, Hercberg S, Dallongeville J. Fruit and Vegetable Consumption and Risk of Coronary Heart Disease: A Meta-Analysis of Cohort Studies. <i>J Nutr</i> 2006;136:2588–93.   |
| Relative risk for alcohol intake                  | GBD meta-analysis  | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

| <b>Parameter</b>  | <b>Details</b>         | <b>Comments</b>   | <b>Source</b>  |
|---|------------------------|---|--|
| Exposure levels below which no excess risk for cardiometabolic disease is assumed for SBP, BMI, and total cholesterol | Pooling of 123 cohorts | Data on 1.4 million individuals and 52,000 CVD events. We assumed the levels are similar for other diseases beyond cardiometabolic. | Singh GM, Danaei G, Farzadfar F, Stevens GA, Woodward M, Wormser D, et al. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. PLOS ONE 2013;8:e65174. |

Validation plots for CHD incidence, case fatality, and prevalence

Figure A-3 - Validation plot for modelled CHD incidence (age-sex-dimd standardised)

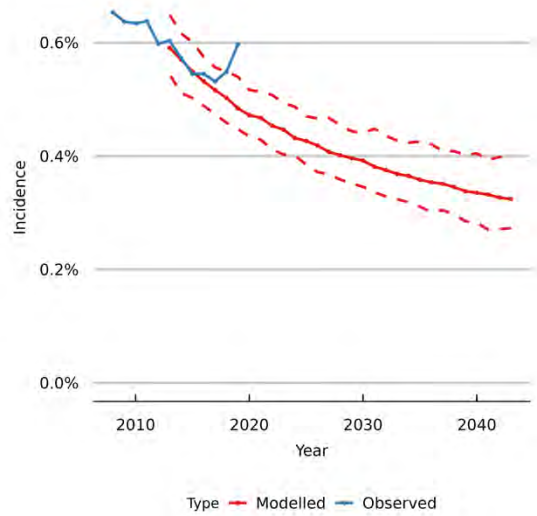


Figure A-4 - Validation plot for modelled CHD case fatality (age-sex-dimd standardised)

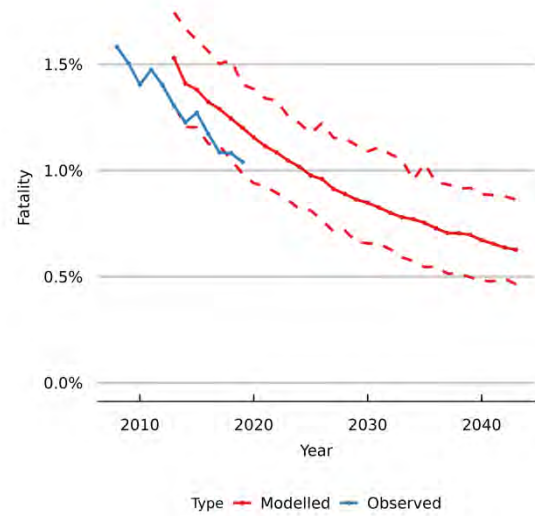
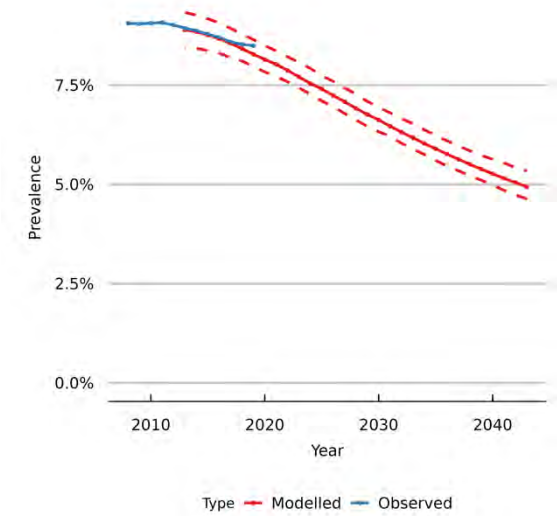


Figure A-5 - Validation plot for modelled CHD prevalence (age-sex-dimd standardised)





Stroke (including transient ischaemic attack (TIA))

Table A-3 - Modelling assumptions for incident stroke

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery  |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke, systolic blood pressure, total cholesterol, body mass index, physical activity, alcohol intake, fruit and vegetable intake |
| <b>Disease dependencies</b>     | Atrial fibrillation, diabetes mellitus type 2  |
| <b>Calibration factor</b>       | Intercept: 0.99<br>Trend: 1.005  |

Figure A-6 - Causal structure of risk factor associations and disease dependencies for incident stroke

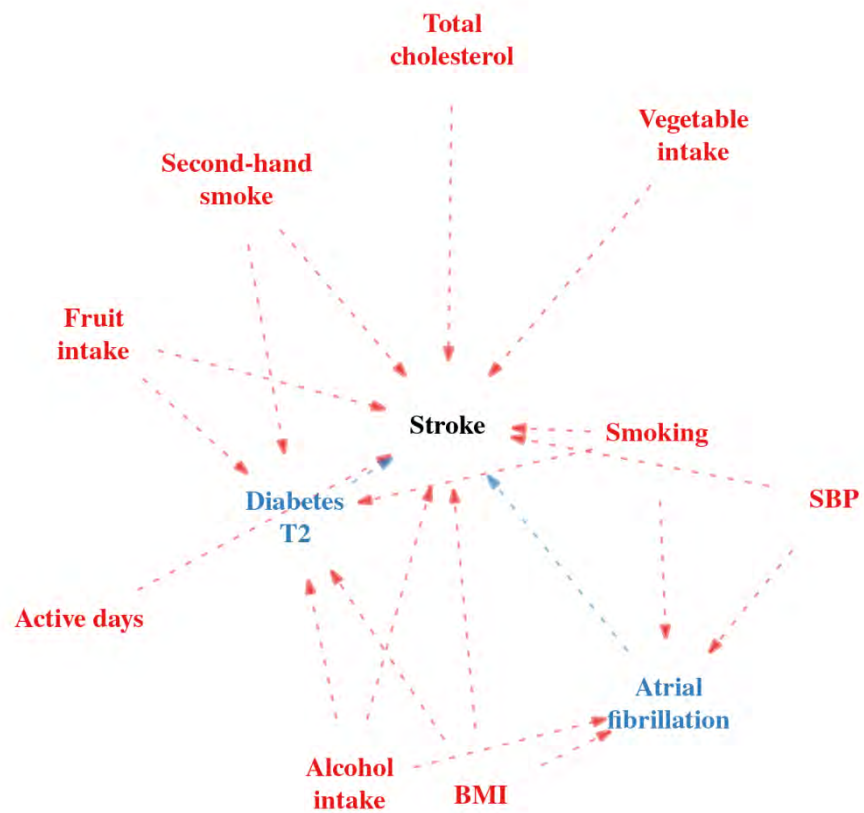


Table A-4 - Data sources for causal associations between risk factors and stroke incidence

| Parameter                                       | Details   | Comments  | Source  |
|---|---|---|---|
| Relative risk for active smoking                | GBD meta-analysis   | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking                    | GBD meta-analysis   | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | Meta-analysis of 20 prospective, case-control and cross-sectional studies | 13 studies adjusted for important CHD risk factors. The overall effect from all 20 studies was used. The effect was applied to never regularly smokers. | Oono IP, Mackay DF, Pell JP. Meta-analysis of the association between secondhand smoke exposure and stroke. J Public Health 2011;33:496–502. (Figure 1)   |

|  |  |  |  |
|--|--|--|--|
| Relative risk for systolic blood pressure  | Meta-analysis of 61 prospective studies  | Stratified by age and sex. Adjusted for regression dilution and total blood cholesterol and, where available, lipid fractions (HDL and non-HDL cholesterol), diabetes, weight, alcohol consumption, and smoking at baseline. | Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. <i>The Lancet</i> 2002;360:1903–13. (Figures 3 and 5)   |
| Relative risk for total cholesterol        | Meta-analysis of 61 prospective studies  | Stratified by age and sex. Adjusted for regression dilution and age, sex, study, systolic blood pressure and smoking.  | Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55 000 vascular deaths. <i>The Lancet</i> 2007;370:1829–39. (Web-table 6 fully adjusted and Figure 3) |
| Relative risk for body mass index          | Meta-analysis of 58 prospective studies  | Stratified by age. Adjusted for age, sex, smoking status, systolic blood pressure, history of diabetes, and total and HDL cholesterol.   | The Emerging Risk Factors Collaboration. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. <i>The Lancet</i> 2011;377:1085–95. (Table 1 and Figure 2)                       |
| Relative risk for diabetes mellitus type 2 | Meta-analysis of 102 prospective studies | Stratified by age. Adjusted for age, smoking status, body-mass index, and systolic blood pressure.   | The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. <i>The Lancet</i> 2010;375:2215–22. (Figure 2)  |

|   |  |   |   |
|---|--|---|---|
| Relative risk for physical activity               | Meta-analysis of 18 cohort studies for CHD and 8 cohort studies for ischaemic stroke | Stratified by age and sex. Adjusted for measurement error, age, sex, smoking, blood pressure and cholesterol. | Bull FC, Armstrong TP, Dixon T, Ham S, Neiman A, Pratt M. Comparative quantification of health risks. Chapter 10: physical inactivity. Geneva: World Health Organisation; 2004. (Tables 10.19 and 10.20)  |
| Relative risk for fruit and vegetable consumption | Meta-analysis of 7 cohort studies  | RR per portion of F&V. Multiply-adjusted.   | Dauchet L, Amouyel P, Dallongeville J. Fruit and vegetable consumption and risk of stroke A meta-analysis of cohort studies. Neurology 2005;65:1193–7.  |
| Relative risk for alcohol intake                  | GBD meta-analysis  | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for atrial fibrillation             | Cohort study   | Ages < 65 are an extrapolation  | Yuan Z, Bowlin S, Einstadter D, Cebul RD, Connors AR Jr, Rimm AA. Atrial fibrillation as a risk factor for stroke: a retrospective cohort study of hospitalized Medicare beneficiaries. Am J Public Health 1998 Mar;88(3):395-400   |

Validation plots for stroke incidence, case fatality, and prevalence

Figure A-7 - Validation plot for modelled stroke incidence (age-sex-dimd standardised)

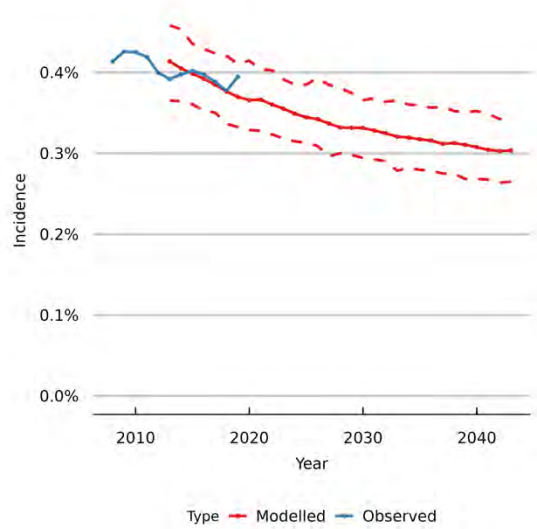


Figure A-8 - Validation plot for modelled stroke case fatality (age-sex-dimd standardised)

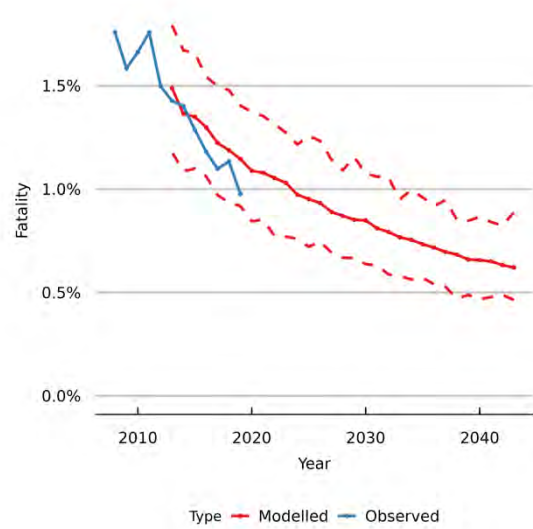
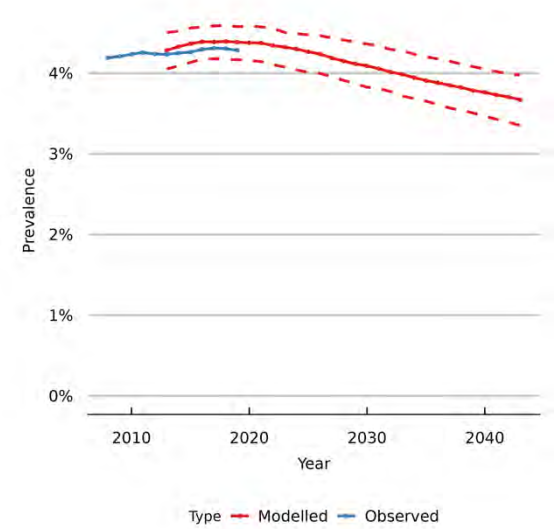


Figure A-9 - Validation plot for modelled stroke prevalence (age-sex-dimd standardised)



## Breast cancer

Table A-5 - Modelling assumptions for incident breast cancer

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Recovery after 10 years; no recurrence; women only                                       |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke, body mass index, physical activity, alcohol intake |
| <b>Disease dependencies</b>     | Diabetes mellitus type 2   |
| <b>Calibration factor</b>       | None   |

Figure A-10 - Causal structure of risk factor associations and disease dependencies for incident breast cancer

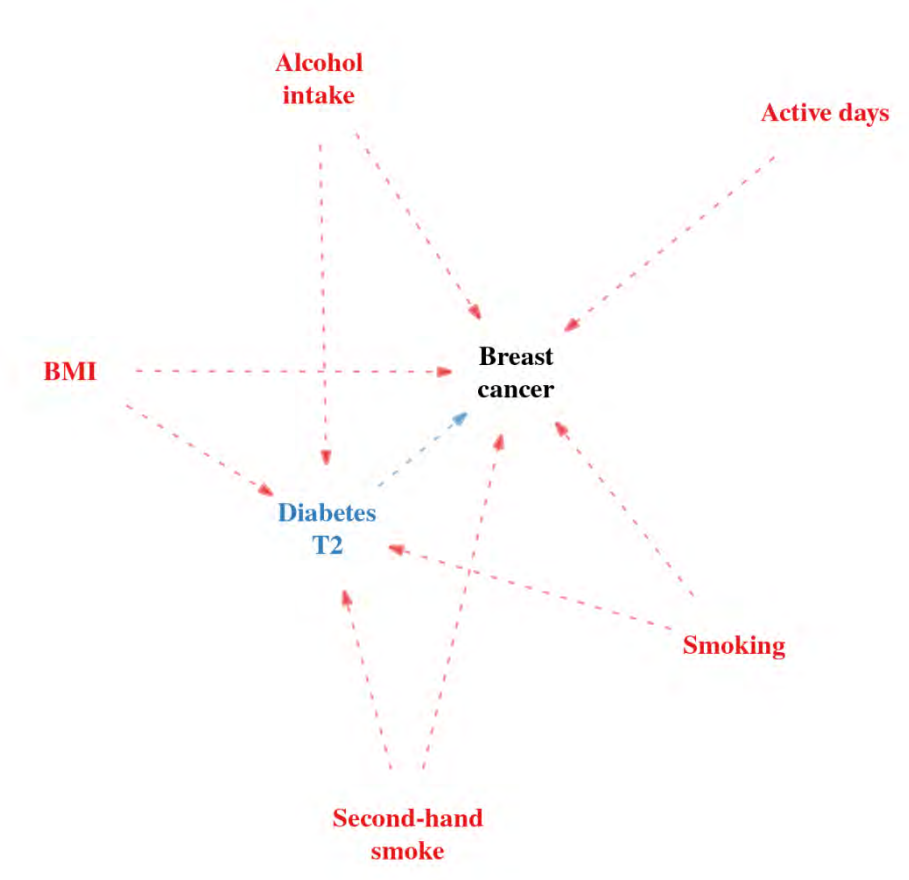




Table A-6 - Data sources for causal associations between risk factors and breast cancer incidence

| Parameter                                       | Details  | Comments  | Source   |
|---|--|---|--|
| Relative risk for active smoking                | Random effect meta-analysis of 27 prospective and 44 retrospective studies | The results were stable across different subgroup analyses, notably pre/post-menopause, alcohol consumption adjustments, including/excluding passive smokers from the referent group. | Macacu A, Autier P, Boniol M, Boyle P. Active and passive smoking and risk of breast cancer: a meta-analysis. Breast Cancer Res Treat 2015;154:213–24. (Table 1)   |
| Relative risk for ex-smoking                    | GBD meta-analysis  | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | GBD meta-analysis  | RR from the GBD 2019 study  | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

|  |                            |   |
|--|----------------------------|---|
| Relative risk for GBD meta-analysis<br>body mass index             | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from:<br><a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for GBD meta-analysis<br>diabetes mellitus<br>type 2 | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from:<br><a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for Meta-analysis<br>physical activity               |                            | Bull FC, Armstrong TP, Dixon T, Ham S, Neiman A, Pratt M. Comparative quantification of health risks. Chapter 10: physical inactivity. Geneva: World Health Organisation; 2004. (Tables 10.19 and 10.20)  |
| Relative risk for GBD meta-analysis<br>alcohol intake              | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from:<br><a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for breast cancer incidence, case fatality, and prevalence

Figure A-11 - Validation plot for modelled breast cancer incidence (age-sex-dimd standardised)

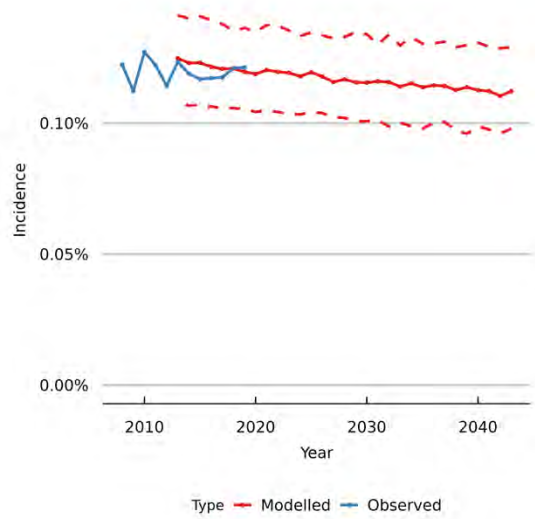


Figure A-12 - Validation plot for modelled breast cancer case fatality (age-sex-dimd standardised)

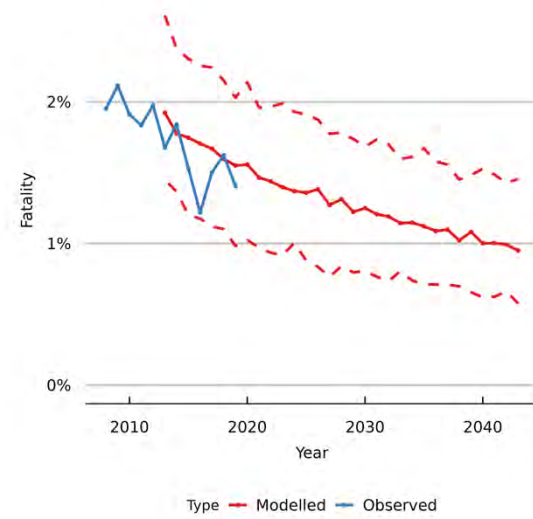
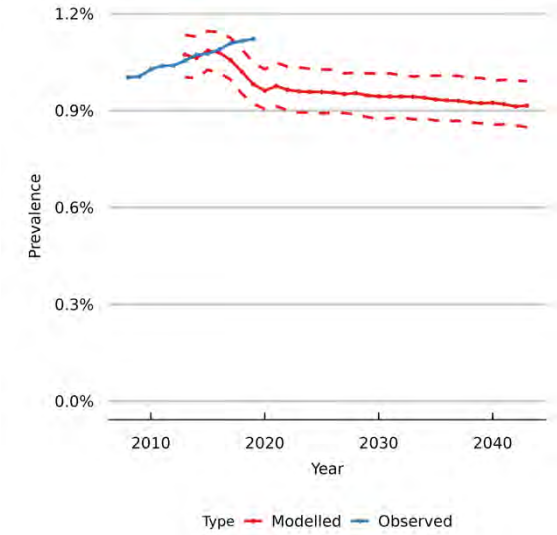


Figure A-13 - Validation plot for modelled breast cancer prevalence (age-sex-dimd standardised)



Colorectal cancer

Table A-7 - Modelling assumptions for incident colorectal cancer

| <b>Component</b>                | <b>Assumptions / Details</b>                                |
|---------------------------------|---|
| <b>Disease type</b>             | Recovery after 10 years; no recurrence                      |
| <b>Risk factor associations</b> | Smoking, body mass index, physical activity, alcohol intake |
| <b>Disease dependencies</b>     | Diabetes mellitus type 2                                    |
| <b>Calibration factor</b>       | None  |

Figure A-14 - Causal structure of risk factor associations and disease dependencies for incident colorectal cancer

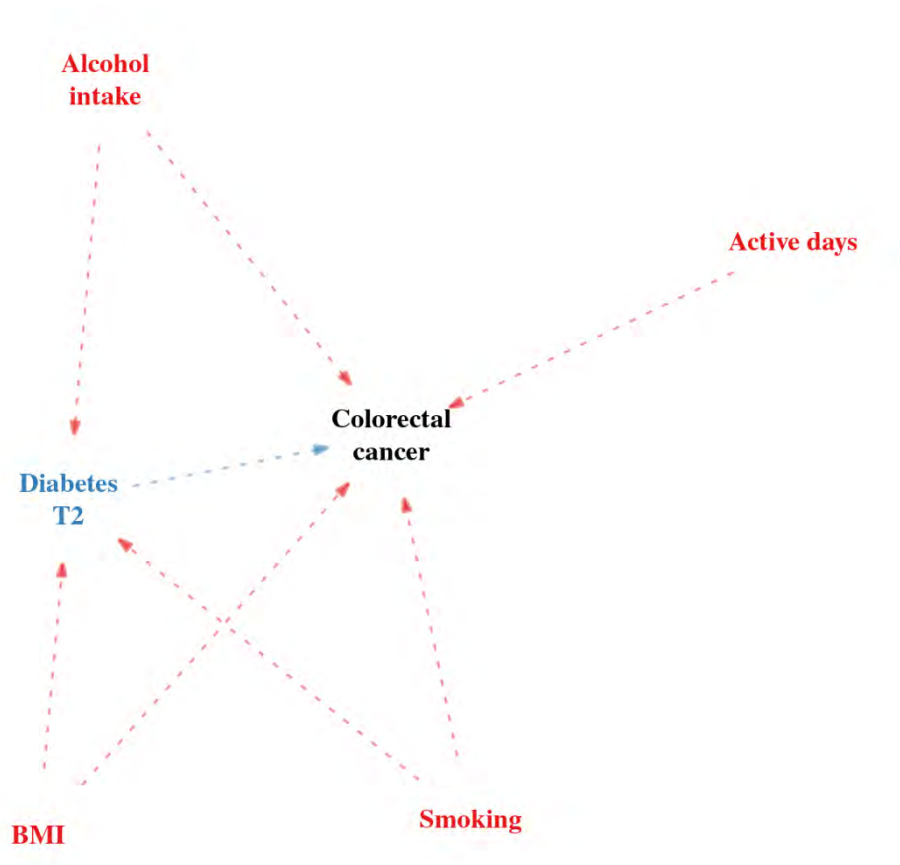


Table A-8 - Data sources for causal associations between risk factors and colorectal cancer incidence

| Parameter                                  | Details           | Comments                   | Source  |
|--|-------------------|----------------------------|---|
| Relative risk for pack years               | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking               | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for body mass index          | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for diabetes mellitus type 2 | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for physical activity        | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for alcohol intake           | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for colorectal cancer incidence, case fatality, and prevalence

Figure A-15 - Validation plot for modelled colorectal cancer incidence (age-sex-dim standardised)

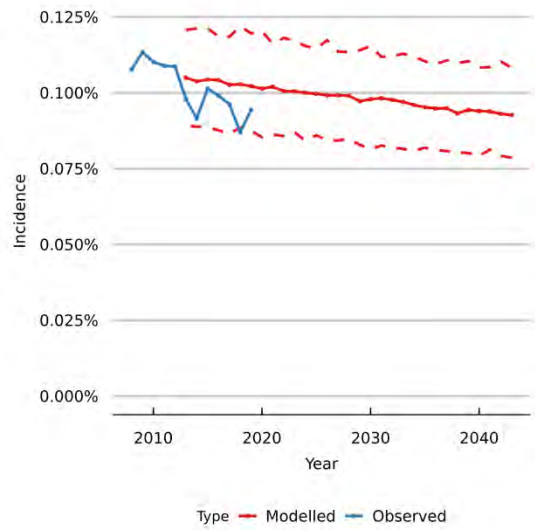


Figure A-16 - Validation plot for modelled colorectal cancer case fatality (age-sex-dim standardised)

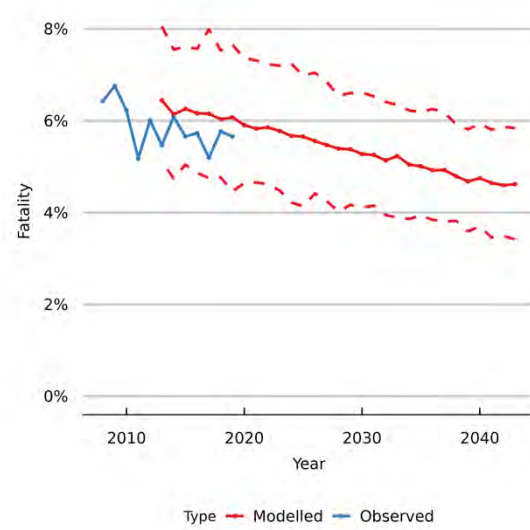
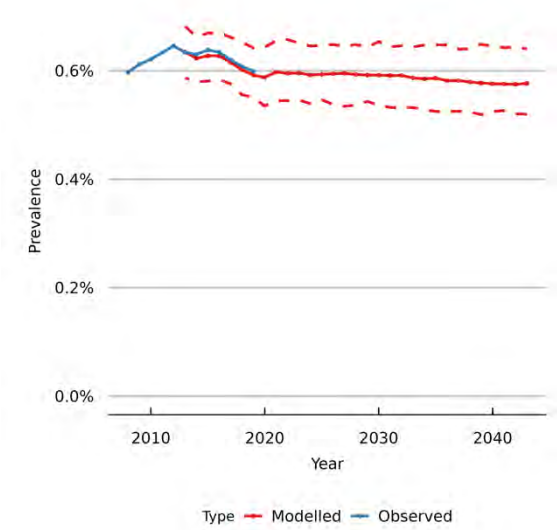


Figure A-17 - Validation plot for modelled colorectal cancer prevalence (age-sex-dim standardised)



Lung cancer

Table A-9 - Modelling assumptions for incident lung cancer

| <b>Component</b>                | <b>Assumptions / Details</b>                       |
|---------------------------------|--|
| <b>Disease type</b>             | Recovery after 10 years; no recurrence             |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke, fruit intake |
| <b>Disease dependencies</b>     | Diabetes mellitus type 2                           |
| <b>Calibration factor</b>       | Intercept: 1.005<br>Trend:1.1                      |



Figure A-18 - Causal structure of risk factor associations and disease dependencies for incident lung cancer

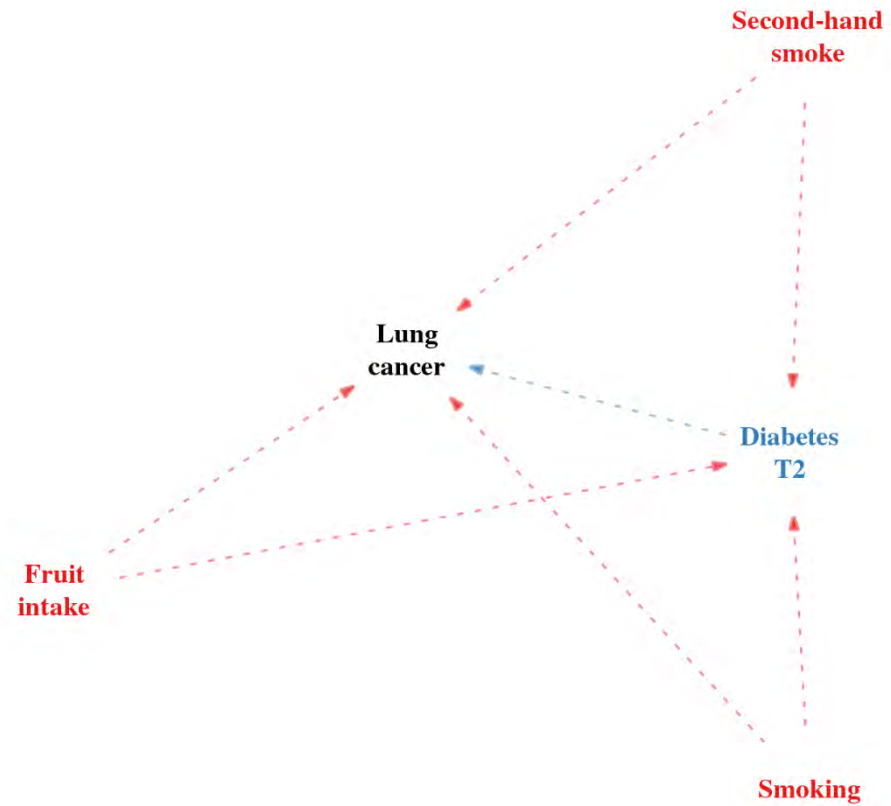


Table A-10 - Data sources for causal associations between risk factors and lung cancer incidence

| Parameter                                       | Details                                  | Comments   | Source  |
|---|--|--|---|
| Relative risk for pack years                    | RCT of 208,371 individuals               | We used the PLCO2014 model                         | Tammemägi MC, Church TR, Hocking WG, Silvestri GA, Kvale PA, Riley TL, et al. Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts. PLoS Med 2014;11:e1001764. (Table S1)                   |
| Relative risk for ex-smoking                    | GBD meta-analysis                        | RR from the GBD 2019 study                         | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | Meta-analysis of 18 case-control studies | The effect was applied to never regularly smokers. | Kim CH, Lee Y-CA, Hung RJ, McNallan SR, Cote ML, Lim W-Y, et al. Exposure to secondhand tobacco smoke and lung cancer by histological type: A pooled analysis of the International Lung Cancer Consortium (ILCCO). Int. J. Cancer 2014;135:1918–30.                         |

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|  |                             |  |  |
|--|-----------------------------|--|--|
| Relative risk for fruit consumption        | Dose response meta-analysis | The effect was like that estimated by Wang Y, et al. Fruit and vegetable consumption and risk of lung cancer: A dose-response meta-analysis of prospective cohort studies. Lung Cancer 2015;88:124-30. | Vieira AR, Abar L, Vingeliene S, Chan DSM, Aune D, Navarro-Rosenblatt D, et al. Fruits, vegetables and lung cancer risk: a systematic review and meta-analysis. Ann Oncol 2016;27:81–96  |
| Relative risk for diabetes mellitus type 2 | GBD meta-analysis           | RR from the GBD 2019 study   | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

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Validation plots for lung cancer incidence, case fatality, and prevalence

Figure A-19 - Validation plot for modelled lung cancer incidence (age-sex-dimd standardised)

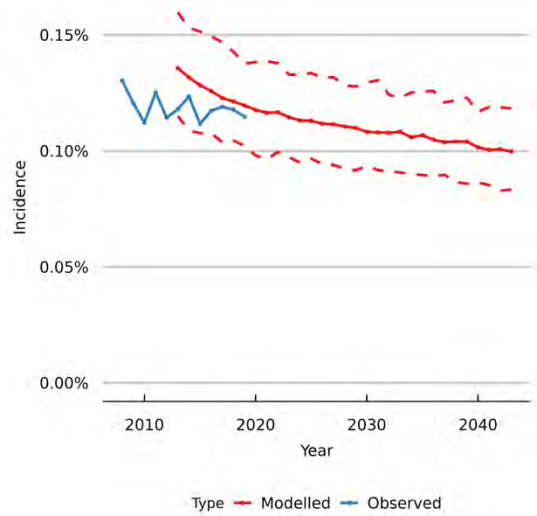


Figure A-20 - Validation plot for modelled lung cancer case fatality (age-sex-dimd standardised)

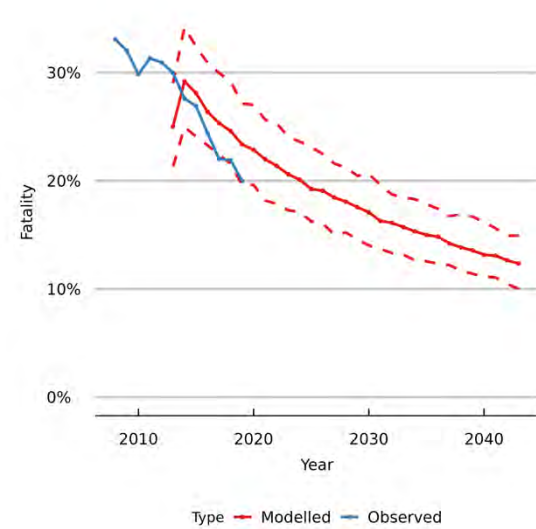
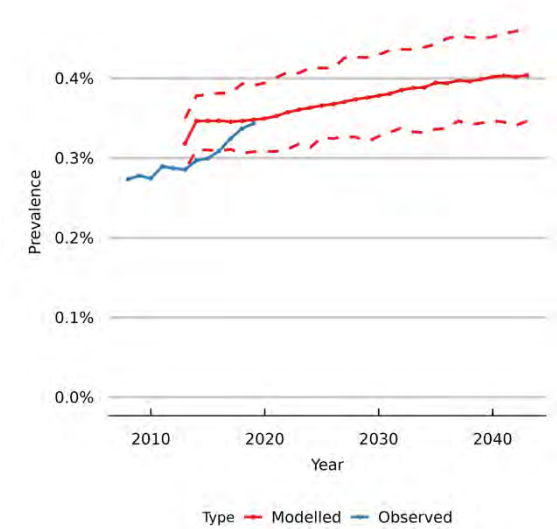


Figure A-21 - Validation plot for modelled lung cancer prevalence (age-sex-dimd standardised)



Prostate cancer

Table A-11 - Modelling assumptions for incident prostate cancer

| <b>Component</b>                | <b>Assumptions / Details</b>                     |
|---------------------------------|--|
| <b>Disease type</b>             | Recovery after 10 years; no recurrence; men only |
| <b>Risk factor associations</b> | Smoking  |
| <b>Disease dependencies</b>     | None   |
| <b>Calibration factor</b>       | Trend: 1.002                                     |

Figure A-22 - Causal structure of risk factor associations and disease dependencies for incident prostate cancer

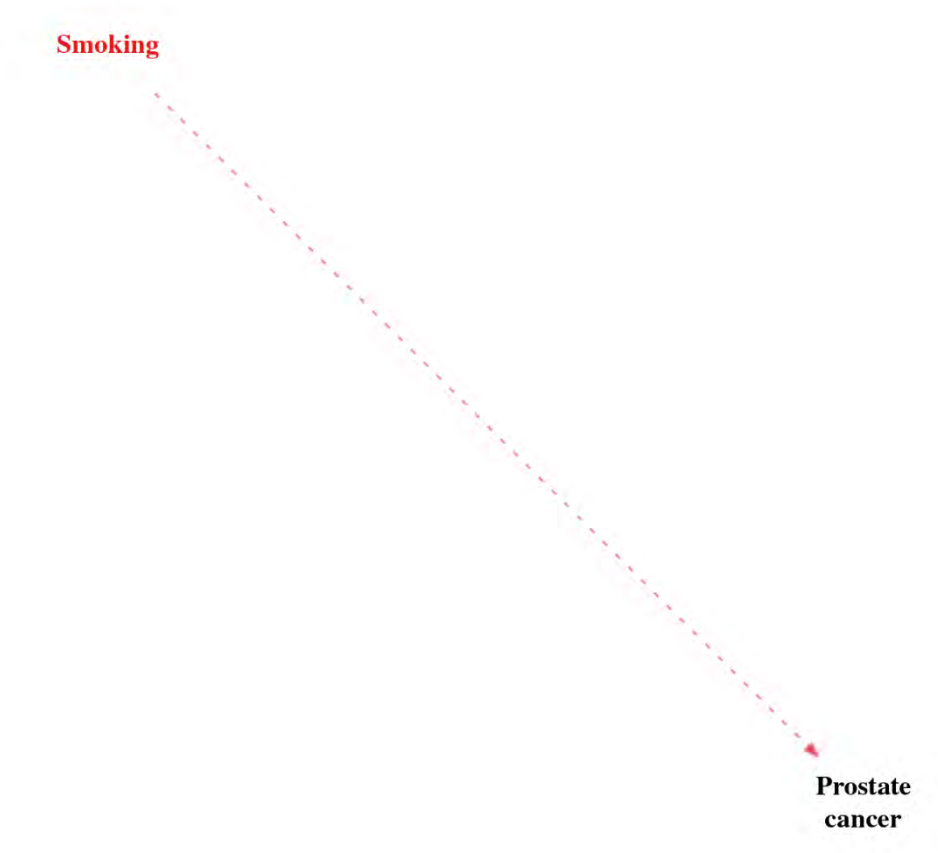


Table A-12 - Data sources for causal associations between risk factors and prostate cancer incidence

| <b>Parameter</b>                 | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>   |
|----------------------------------|-------------------|----------------------------|---|
| Relative risk for active smoking | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking     | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for prostate cancer incidence, case fatality, and prevalence

Figure A-23 - Validation plot for modelled prostate cancer incidence (age-sex-dimd standardised)

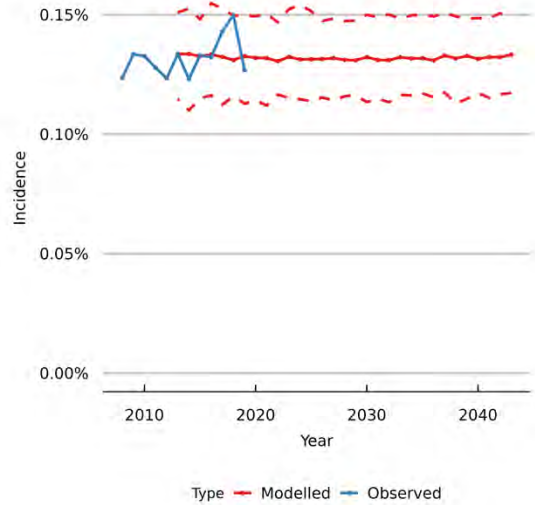


Figure A-24 - Validation plot for modelled prostate cancer case fatality (age-sex-dimd standardised)

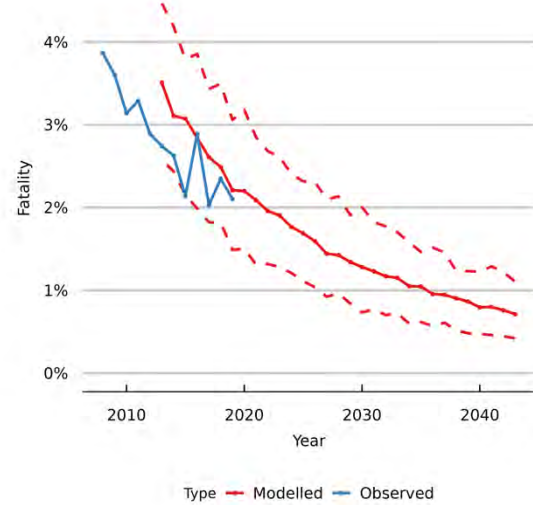
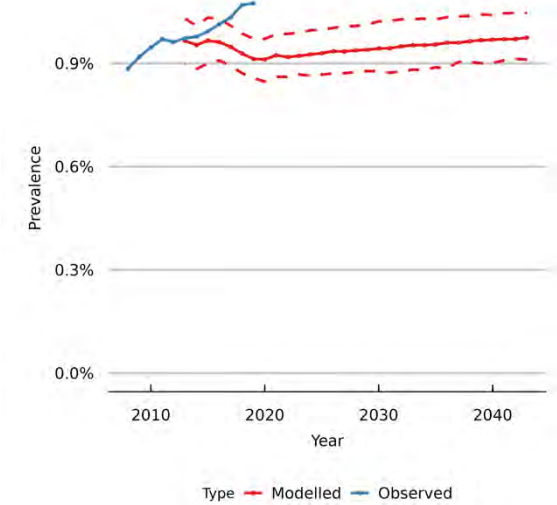


Figure A-25 - Validation plot for modelled prostate cancer prevalence (age-sex-dimd standardised)



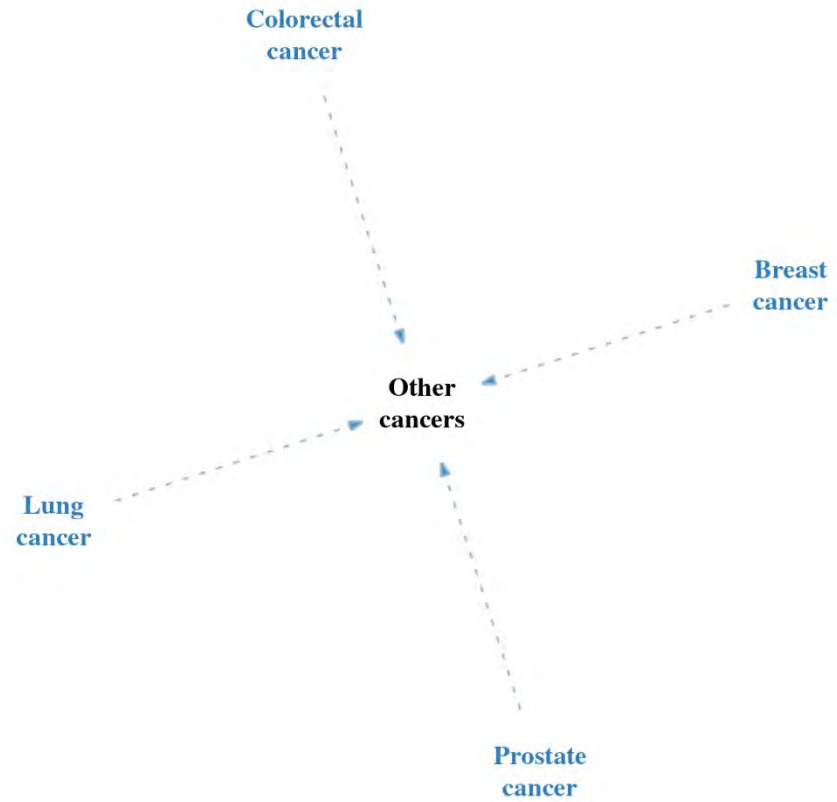


## Other cancers

Table A-13 - Modelling assumptions for incident other cancers

| <b>Component</b>                | <b>Assumptions / Details</b>  |
|---------------------------------|---|
| <b>Disease type</b>             | Recovery after 10 years; no recurrence; all primary malignancies aside from breast, colorectal, lung and prostate |
| <b>Risk factor associations</b> | None  |
| <b>Disease dependencies</b>     | Breast cancer, colorectal cancer, lung cancer, prostate cancer  |
| <b>Calibration factor</b>       | Intercept: 0.98<br>Trend: 0.999   |

Figure A-26 - Causal structure of risk factor associations and disease dependencies for incident other cancer



Validation plots for other cancer incidence, case fatality, and prevalence

Figure A-27 - Validation plot for modelled other cancer incidence (age-sex-dimd standardised)

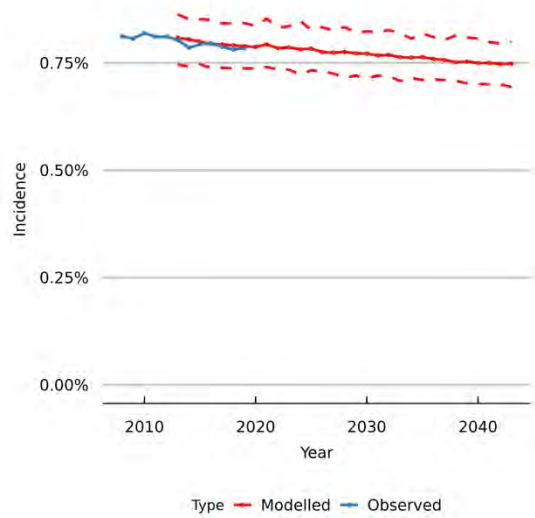


Figure A-28 - Validation plot for modelled other cancer case fatality (age-sex-dimd standardised)

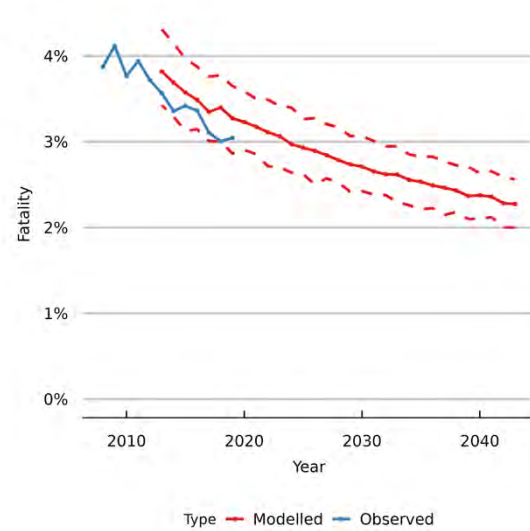
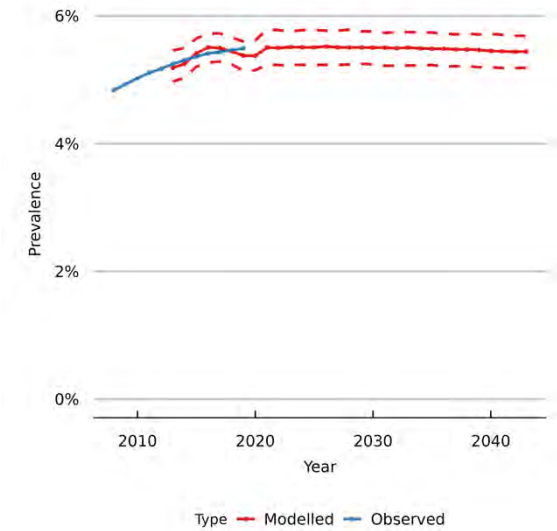


Figure A-29 - Validation plot for modelled other cancer prevalence (age-sex-dimd standardised)



Chronic obstructive pulmonary disease (COPD)

Table A-14 - Modelling assumptions for incident COPD

| <b>Component</b>                | <b>Assumptions / Details</b>         |
|---------------------------------|--------------------------------------|
| <b>Disease type</b>             | Chronic – no recovery                |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke |
| <b>Disease dependencies</b>     | None                                 |
| <b>Calibration factor</b>       | None                                 |

Figure A-30 - Causal structure of risk factor associations and disease dependencies for incident COPD

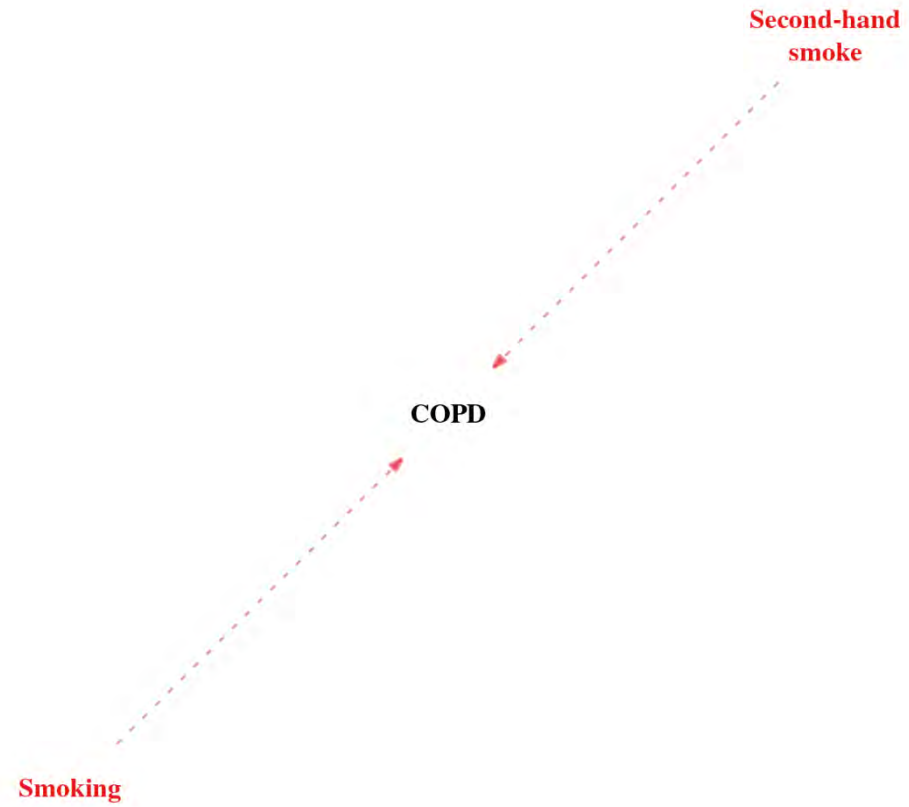


Table A-15 - Data sources for causal associations between risk factors and COPD incidence

| Parameter                                       | Details                                   | Comments   | Source  |
|---|---|--|---|
| Relative risk for pack years                    | Very detailed random effect meta-analysis | Smoking duration was not significant but intensity and pack years were. We used pack years because they indirectly capture age effect. Most studies for pack years were about incidence rather than mortality. There was no differentiation between current and ex-smokers. This may dilute the effect | Forey BA, Thornton AJ, Lee PN. Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. BMC Pulmonary Medicine. 2011 Jun 14;11(1):36.   |
| Relative risk for ex-smoking                    | GBD meta-analysis                         | RR from the GBD 2019 study   | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | Random effect meta-analysis of 24 studies | The effect was applied to never regularly smokers.   | Fischer F, Kraemer A. Meta-analysis of the association between second-hand smoke exposure and ischaemic heart diseases, COPD and stroke. BMC Public Health. 2015 Dec;15(1):1202.  |

Validation plots for COPD incidence, case fatality, and prevalence

Figure A-31 - Validation plot for modelled COPD incidence (age-sex-dimd standardised)

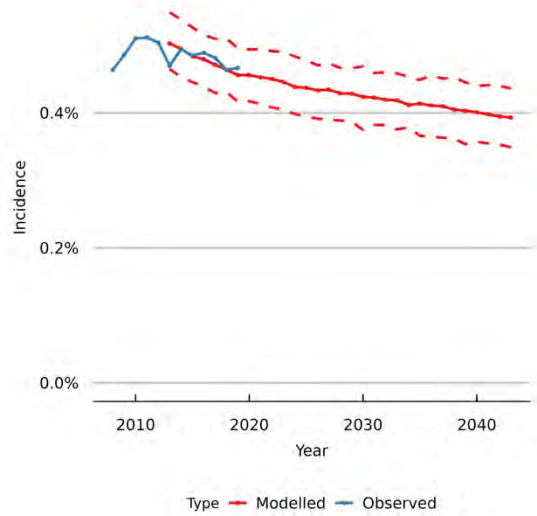


Figure A-32 - Validation plot for modelled COPD case fatality (age-sex-dimd standardised)

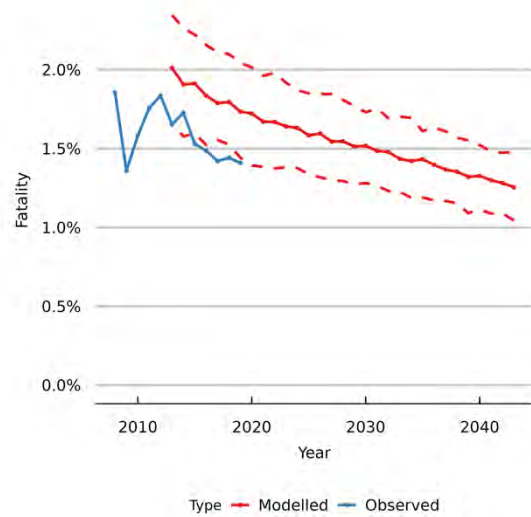
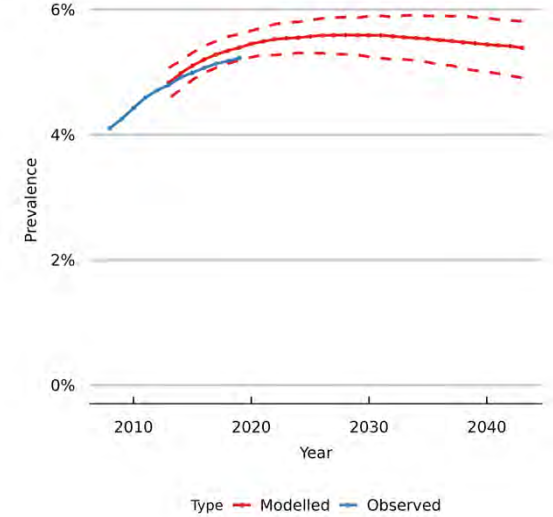


Figure A-33 - Validation plot for modelled COPD prevalence (age-sex-dimd standardised)



## Atrial fibrillation

Table A-16 - Modelling assumptions for incident atrial fibrillation

| <b>Component</b>                | <b>Assumptions / Details</b>                                      |
|---------------------------------|---|
| <b>Disease type</b>             | Chronic – no recovery   |
| <b>Risk factor associations</b> | Smoking, alcohol intake, systolic blood pressure, body mass index |
| <b>Disease dependencies</b>     | Coronary heart disease  |
| <b>Calibration factor</b>       | Trend: 1.002  |



Figure A-34 - Causal structure of risk factor associations and disease dependencies for incident atrial fibrillation

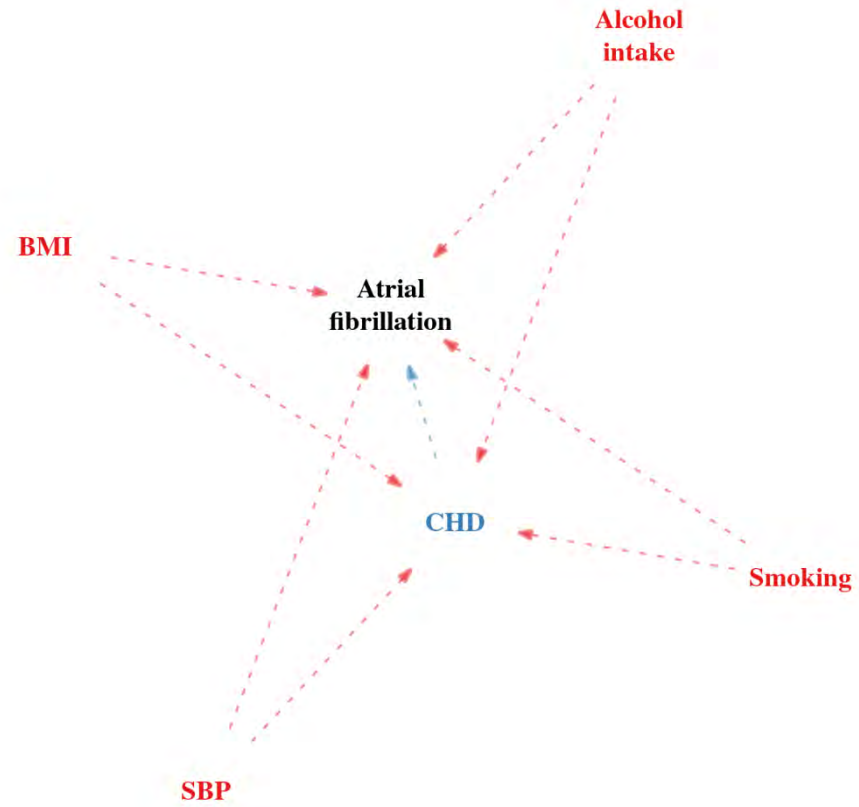


Table A-17 - Data sources for causal associations between risk factors and atrial fibrillation incidence

| <b>Parameter</b>                          | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>   |
|---|-------------------|----------------------------|---|
| Relative risk for active smoking          | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking              | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for systolic blood pressure | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for body mass index         | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for alcohol intake          | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for atrial fibrillation incidence, case fatality, and prevalence

Figure A-35 - Validation plot for modelled atrial fibrillation incidence (age-sex-dimd standardised)

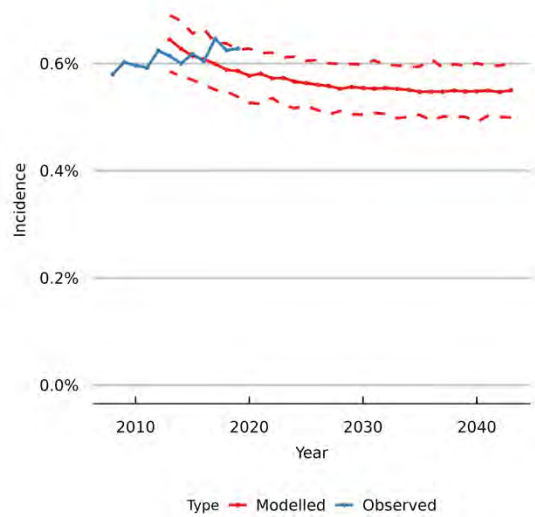


Figure A-36 - Validation plot for modelled atrial fibrillation case fatality (age-sex-dimd standardised)

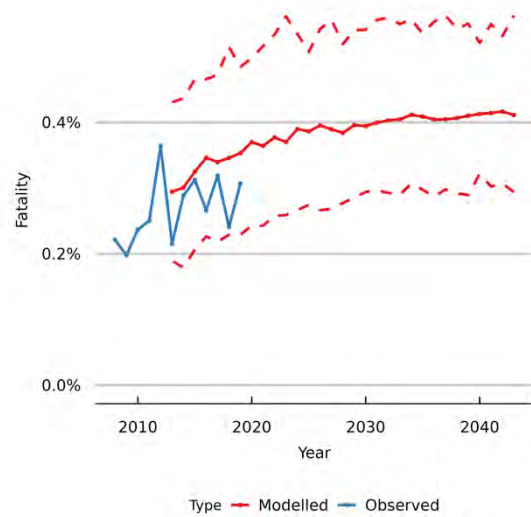
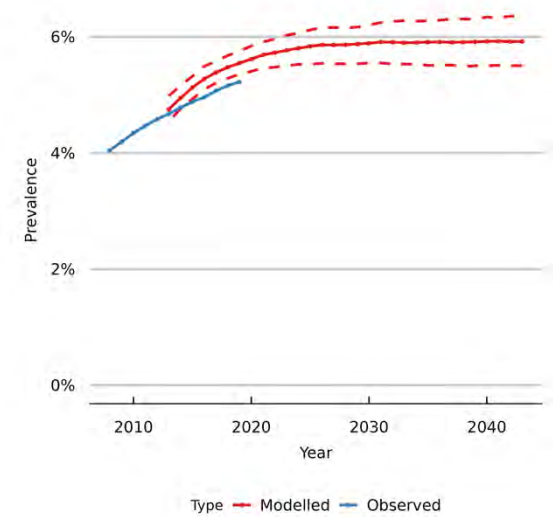


Figure A-37 - Validation plot for modelled atrial fibrillation prevalence (age-sex-dimd standardised)

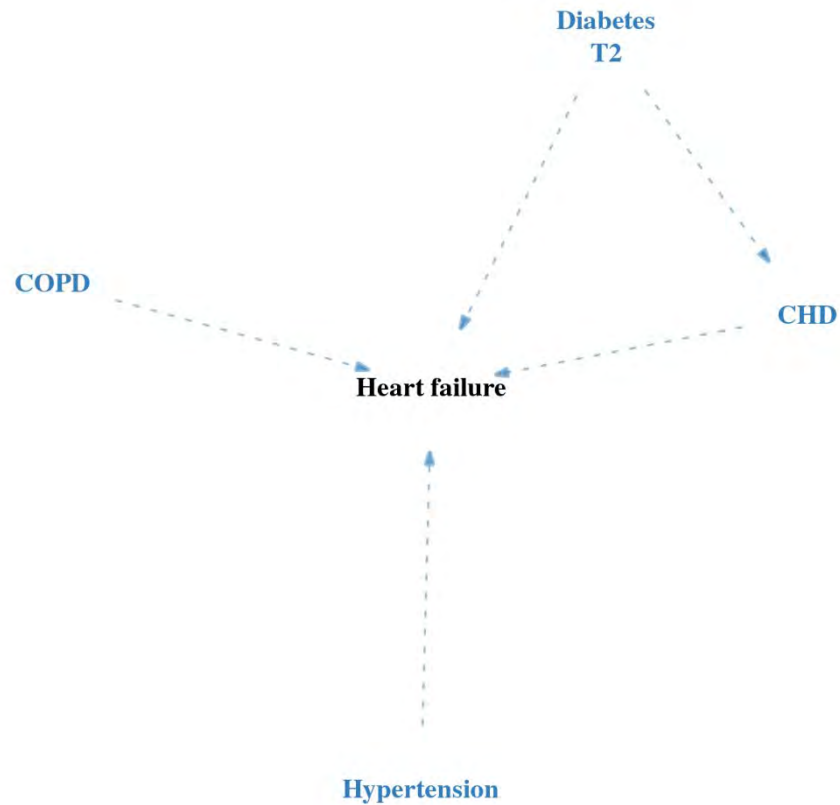


## Heart Failure

Table A-18 - Modelling assumptions for incident heart failure

| <b>Component</b>                | <b>Assumptions / Details</b>                      |
|---------------------------------|---|
| <b>Disease type</b>             | Chronic – no recovery                             |
| <b>Risk factor associations</b> | None  |
| <b>Disease dependencies</b>     | Diabetes mellitus type 2, CHD, COPD, hypertension |
| <b>Calibration factor</b>       | Trend: 1.01                                       |

Figure A-38 - Causal structure of risk factor associations and disease dependencies for incident heart failure



Validation plots for heart failure incidence, case fatality, and prevalence

Figure A-39 - Validation plot for modelled heart failure incidence (age-sex-dimd standardised)

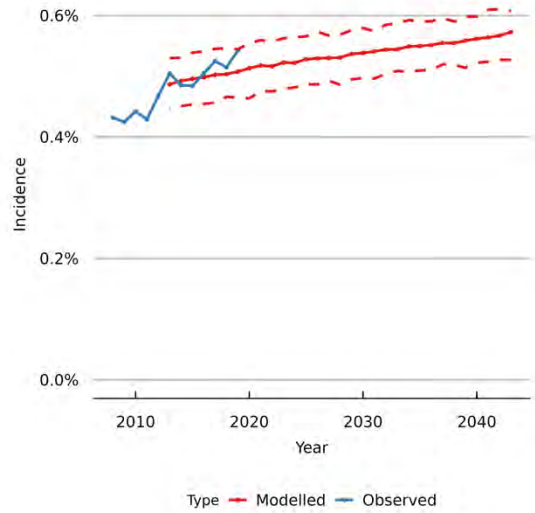


Figure A-40 - Validation plot for modelled heart failure case fatality (age-sex-dimd standardised)

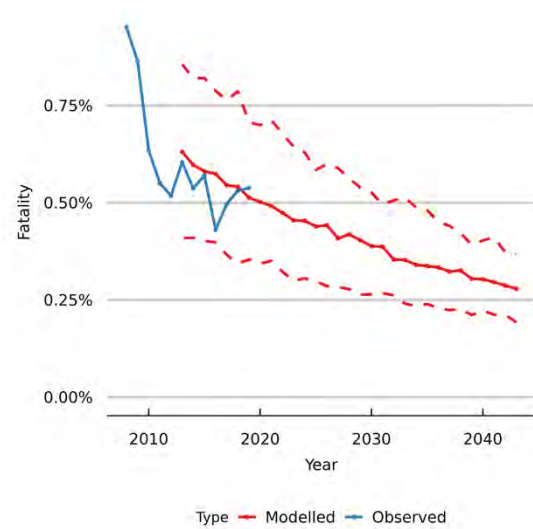
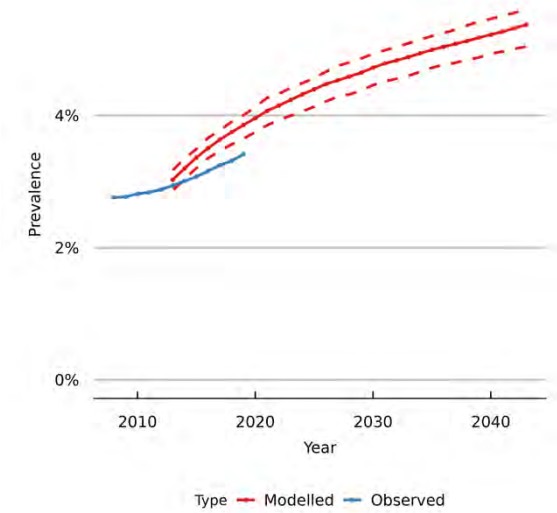


Figure A-41 - Validation plot for modelled heart failure prevalence (age-sex-dimd standardised)



## Type 2 diabetes mellitus

Table A-19 - Modelling assumptions for incident type 2 diabetes mellitus

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery  |
| <b>Risk factor associations</b> | Smoking, environmental tobacco smoke, alcohol intake, body mass index, fruit intake, metabolic equivalent task, statins prescription |
| <b>Disease dependencies</b>     | None   |
| <b>Calibration factor</b>       | Intercept: 1.05  |

Figure A-42 - Causal structure of risk factor associations and disease dependencies for incident type 2 diabetes mellitus

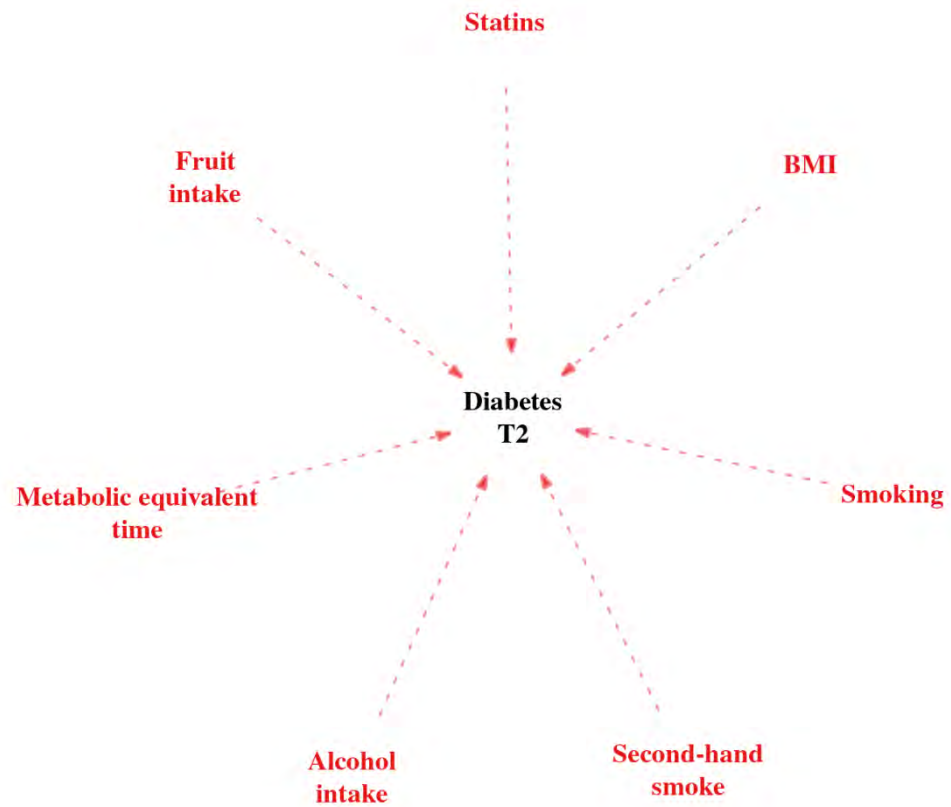




Table A-20 - Data sources for causal associations between risk factors and type 2 diabetes mellitus incidence

| <b>Parameter</b>                                | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>  |
|---|-------------------|----------------------------|--|
| Relative risk for active smoking                | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking                    | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for environmental tobacco smoking | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for body mass index               | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for alcohol intake                | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

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|  |                             |  |          |  |
|--|-----------------------------|--|----------|--|
| Relative risk for fruit consumption                  | GBD meta-analysis           | RR from the study  | GBD 2019 | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for Metabolic Equivalent of Task (MET) | GBD meta-analysis           | RR from the study. Metabolic Equivalent of Task (MET) minutes per week | GBD 2019 | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16];Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for statins prescription               | Random-effect meta-analysis | Assuming RR is approximately equal to Odds Ratio                       |          | Westendorp RG, Shepherd J, Davis BR, Pressel SL, Marchioli R, Marfisi RM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. <i>Lancet</i> . 2010 Feb 27;375(9716):735-42  |

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Validation plots for type 2 diabetes mellitus incidence, case fatality, and prevalence

Figure A-43 - Validation plot for modelled type 2 diabetes mellitus incidence (age-sex-dimd standardised)

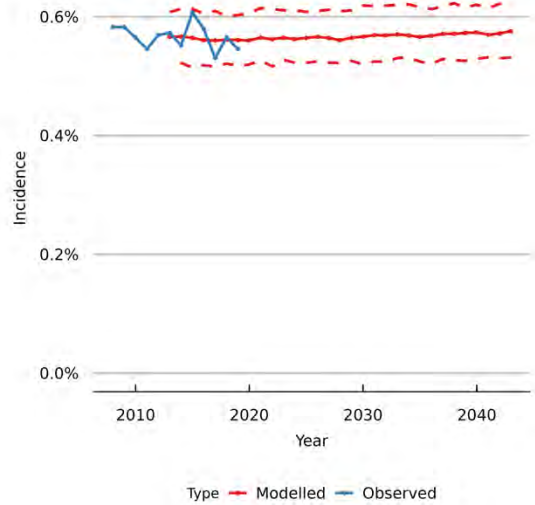


Figure A-44 - Validation plot for modelled type 2 diabetes mellitus case fatality (age-sex-dimd standardised)

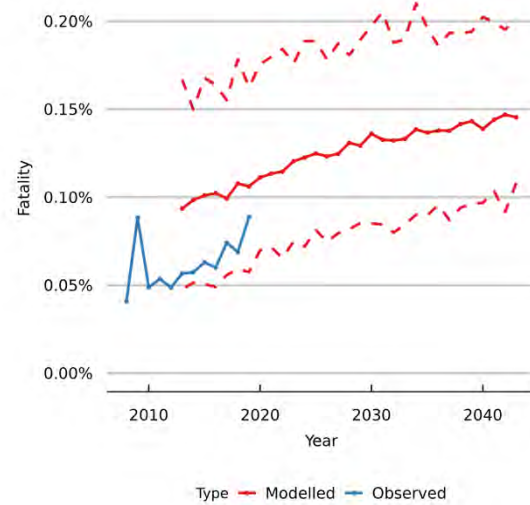
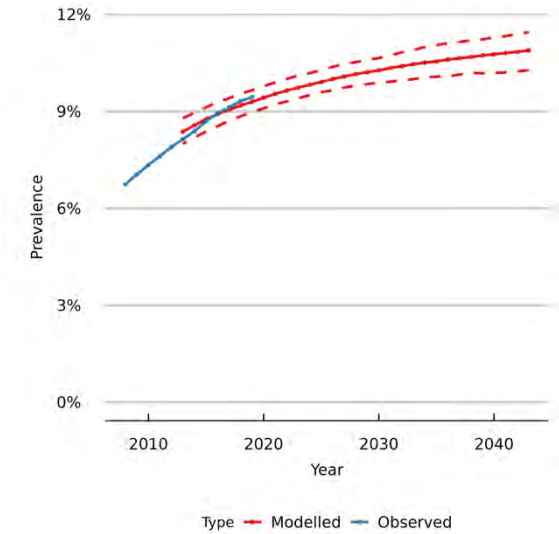


Figure A-45 - Validation plot for modelled type 2 diabetes mellitus prevalence (age-sex-dimd standardised)



## Chronic kidney disease (CKD)

Table A-21 - Modelling assumptions for incident chronic kidney disease

| <b>Component</b>                | <b>Assumptions / Details</b>             |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery                    |
| <b>Risk factor associations</b> | Body mass index, systolic blood pressure |
| <b>Disease dependencies</b>     | None                                     |
| <b>Calibration factor</b>       | Trend: 1.002                             |

Figure A-46 - Causal structure of risk factor associations and disease dependencies for incident chronic kidney disease

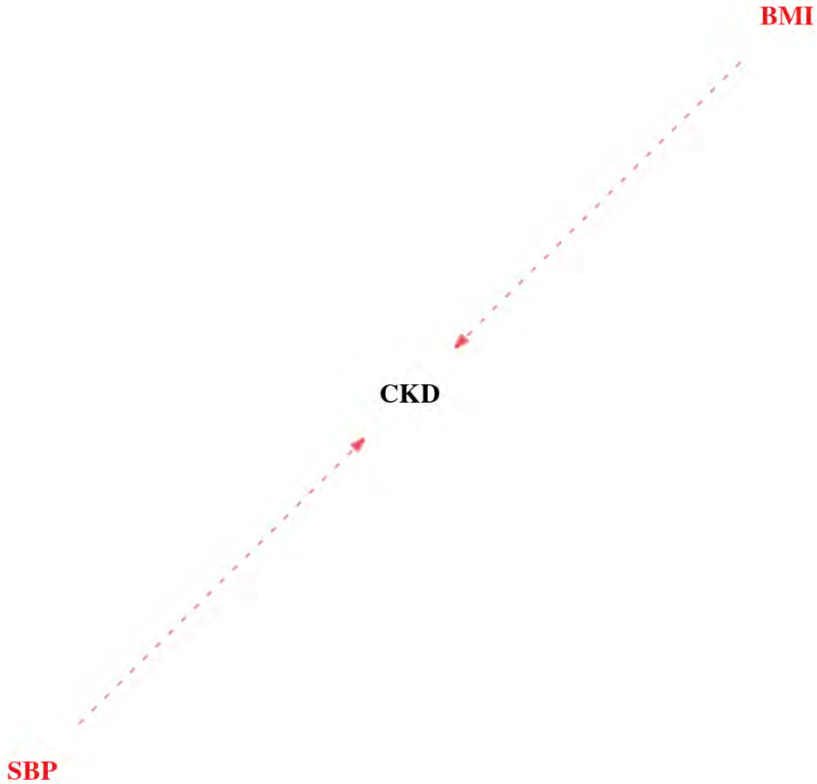


Table A-22 - Data sources for causal associations between risk factors and chronic kidney disease incidence

| <b>Parameter</b>                          | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>   |
|---|-------------------|----------------------------|---|
| Relative risk for body mass index         | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for systolic blood pressure | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for chronic kidney disease incidence and prevalence

Figure A-47 - Validation plot for modelled chronic kidney disease incidence (age-sex-dimnd standardised)

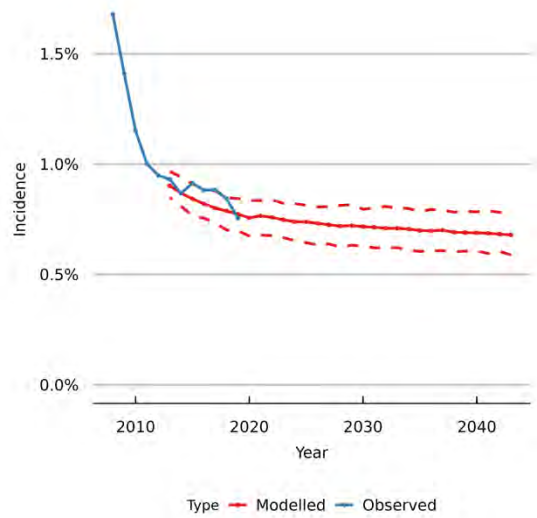
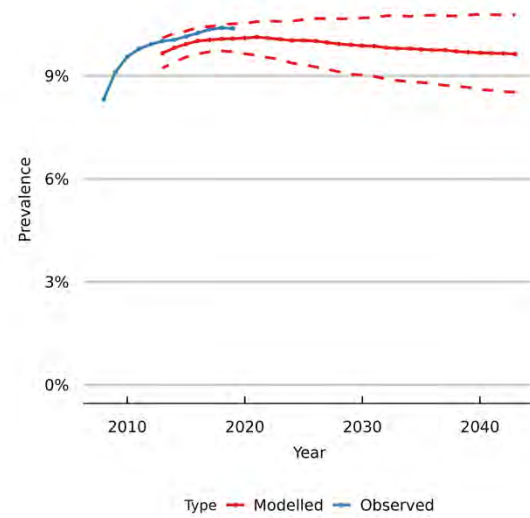


Figure A-48 - Validation plot for modelled chronic kidney disease prevalence (age-sex-dimnd standardised)



## Dementia

Table A-23 - Modelling assumptions for incident dementia

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | Smoking, body mass index     |
| <b>Disease dependencies</b>     | Diabetes mellitus type 2     |
| <b>Calibration factor</b>       | None                         |



Figure A-49 - Causal structure of risk factor associations and disease dependencies for incident dementia

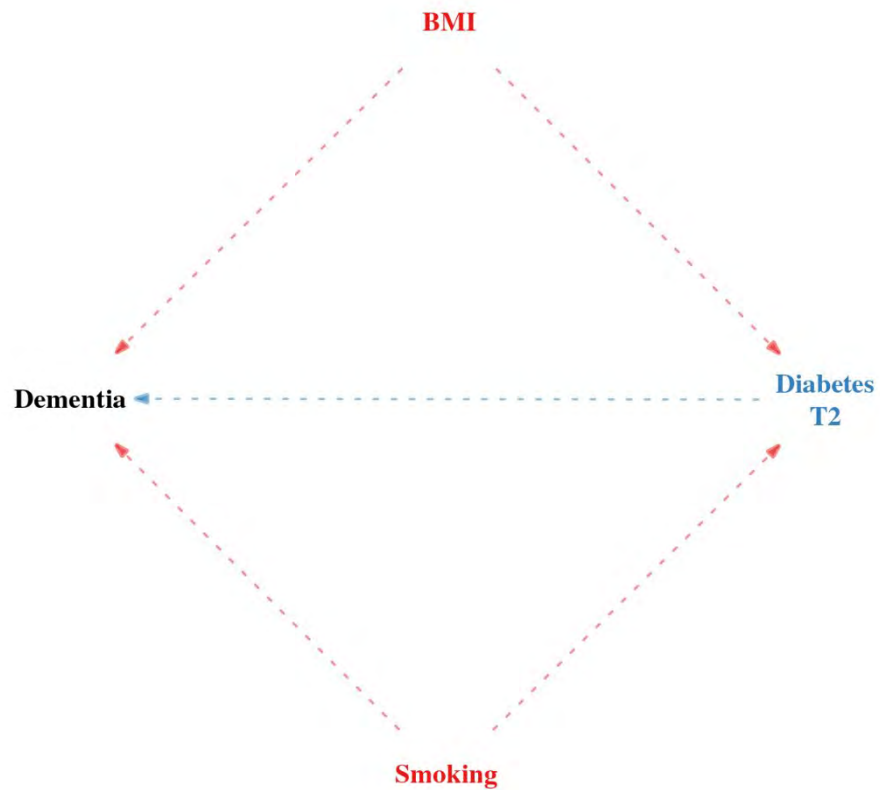


Table A-24 - Data sources for causal associations between risk factors and dementia incidence

| <b>Parameter</b>                           | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>   |
|--|-------------------|----------------------------|---|
| Relative risk for active smoking           | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking               | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for body mass index          | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for diabetes mellitus type 2 | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for dementia incidence, case fatality, and prevalence

Figure A-50 - Validation plot for modelled dementia incidence (age-sex-dimd standardised)

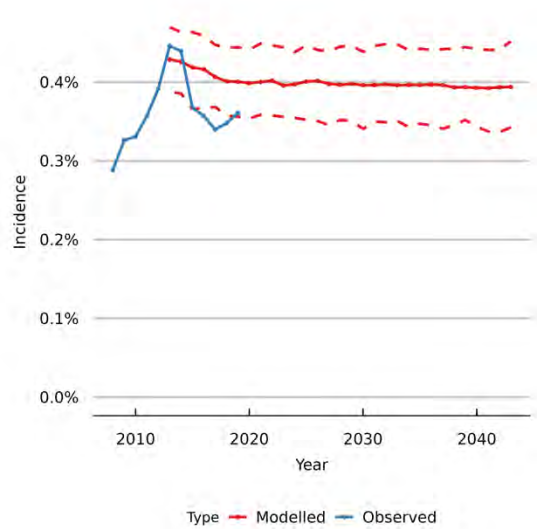


Figure A-51 - Validation plot for modelled dementia case fatality (age-sex-dimd standardised)

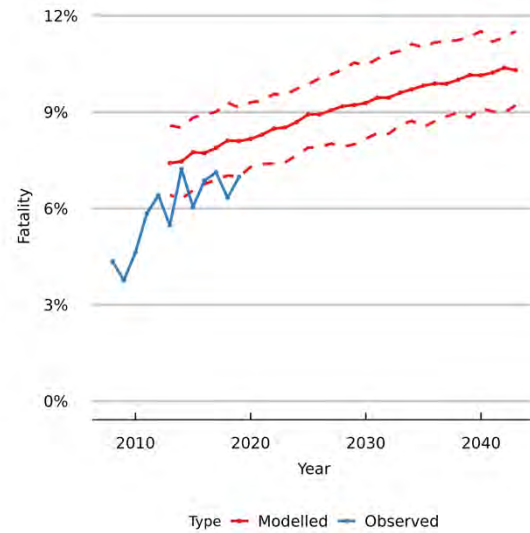
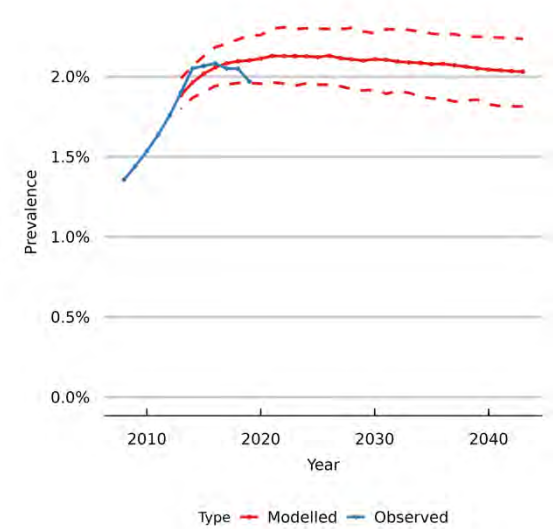


Figure A-52 - Validation plot for modelled dementia prevalence (age-sex-dimd standardised)



## Hypertension

Table A-25 - Modelling assumptions for incident hypertension

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | Systolic blood pressure      |
| <b>Disease dependencies</b>     | None                         |
| <b>Calibration factor</b>       | None                         |

Figure A-53 - Causal structure of risk factor associations and disease dependencies for incident hypertension

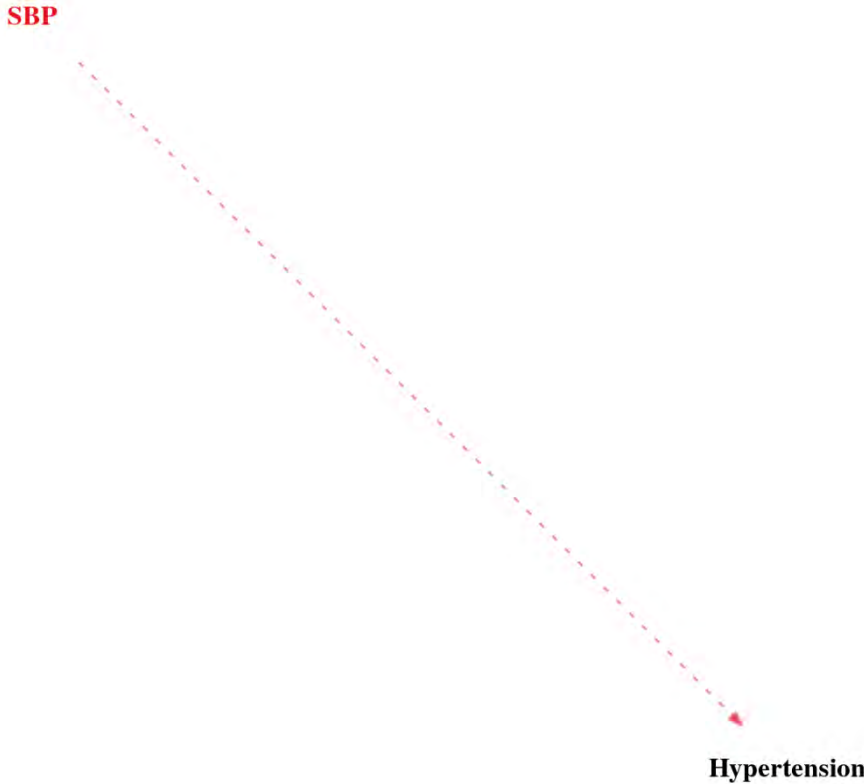


Table A-26 - Data sources for causal associations between risk factors and hypertension incidence

| Parameter                                 | Details                              | Comments | Source  |
|---|--------------------------------------|----------|---|
| Relative risk for systolic blood pressure | Own calculation of RRs from HSE data |          | Directly estimated from Health Survey for England 2003-2014 |

Validation plots for hypertension incidence and prevalence

Figure A-54 - Validation plot for modelled hypertension incidence (age-sex-dimd standardised)

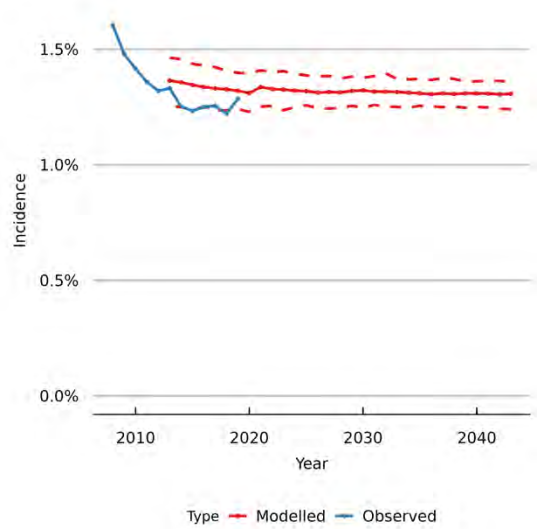
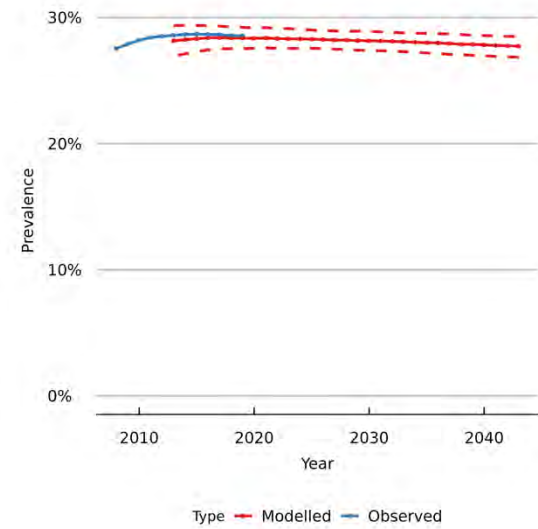


Figure A-55 - Validation plot for modelled hypertension prevalence (age-sex-dimd standardised)



## Asthma

Table A-27 - Modelling assumptions for incident asthma

| <b>Component</b>                | <b>Assumptions / Details</b>              |
|---------------------------------|---|
| <b>Disease type</b>             | Spell – duration is stochastic; can recur |
| <b>Risk factor associations</b> | Smoking, body mass index                  |
| <b>Disease dependencies</b>     | Past asthma                               |
| <b>Calibration factor</b>       | Trend: 1.01                               |



Figure A-56 - Causal structure of risk factor associations and disease dependencies for incident asthma

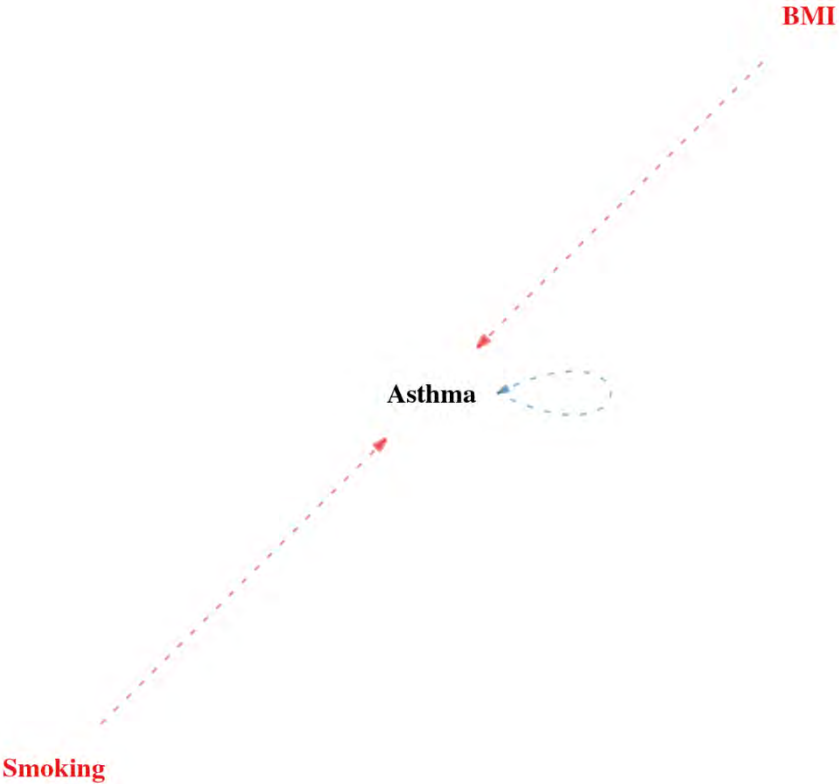


Table A-28 - Data sources for causal associations between risk factors and asthma incidence

| <b>Parameter</b>                  | <b>Details</b>    | <b>Comments</b>            | <b>Source</b>   |
|-----------------------------------|-------------------|----------------------------|---|
| Relative risk for active smoking  | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for ex-smoking      | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |
| Relative risk for body mass index | GBD meta-analysis | RR from the GBD 2019 study | Global Burden of Disease Study 2019 (GBD 2019) Data Resources   GHDx [Internet]. [cited 2022 Mar 16]; Available from: <a href="http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks">http://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks</a> |

Validation plots for asthma incidence and prevalence

Figure A-57 - Validation plot for modelled asthma incidence (age-sex-dimd standardised)

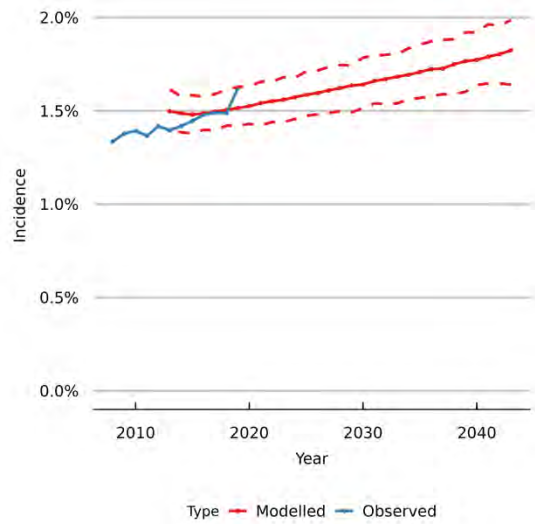
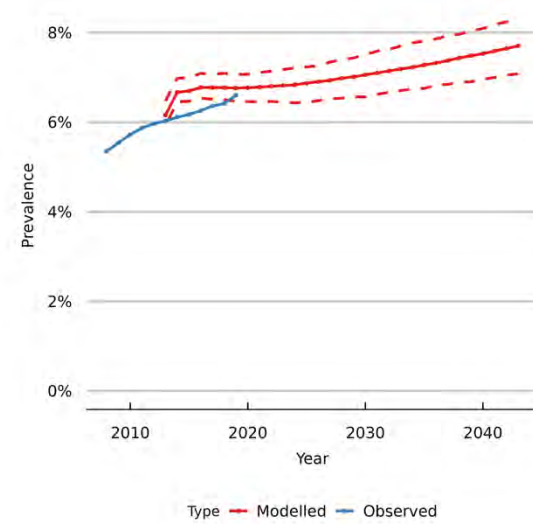


Figure A-58 - Validation plot for modelled asthma prevalence (age-sex-dimd standardised)



Alcohol problems

Table A-29 - Modelling assumptions for incident alcohol problems

| <b>Component</b>                | <b>Assumptions / Details</b>              |
|---------------------------------|---|
| <b>Disease type</b>             | Spell – duration is stochastic; can recur |
| <b>Risk factor associations</b> | None                                      |
| <b>Disease dependencies</b>     | Past alcohol problems                     |
| <b>Calibration factor</b>       | None                                      |

Figure A-59 - Causal structure of risk factor associations and disease dependencies for incident alcohol problems

**Alcohol  
problems**



Validation plots for alcohol problems incidence and prevalence

Figure A-60 - Validation plot for modelled alcohol problems incidence (age-sex-dimd standardised)

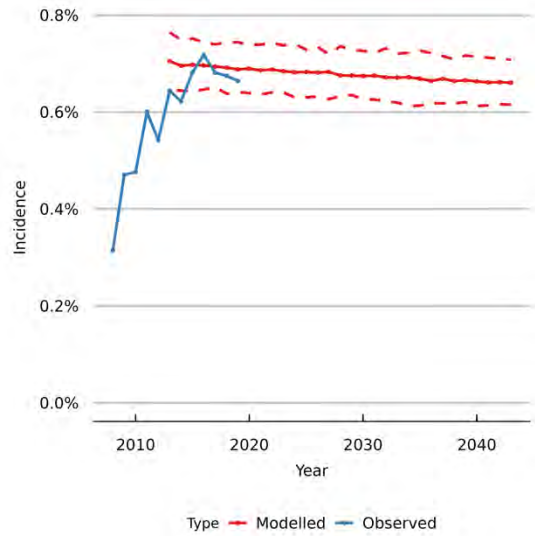
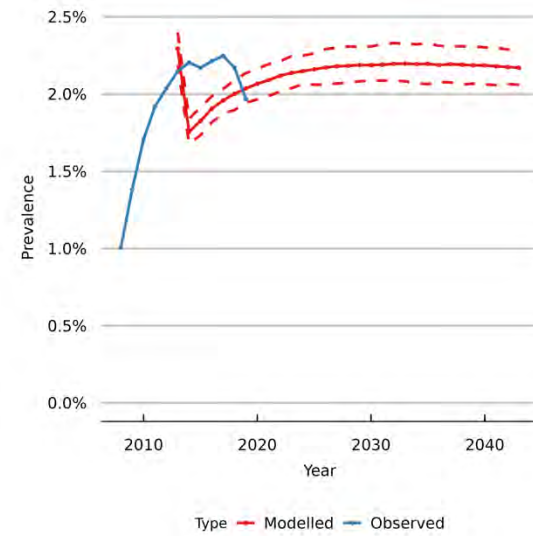


Figure A-61 - Validation plot for modelled alcohol problems prevalence (age-sex-dimd standardised)

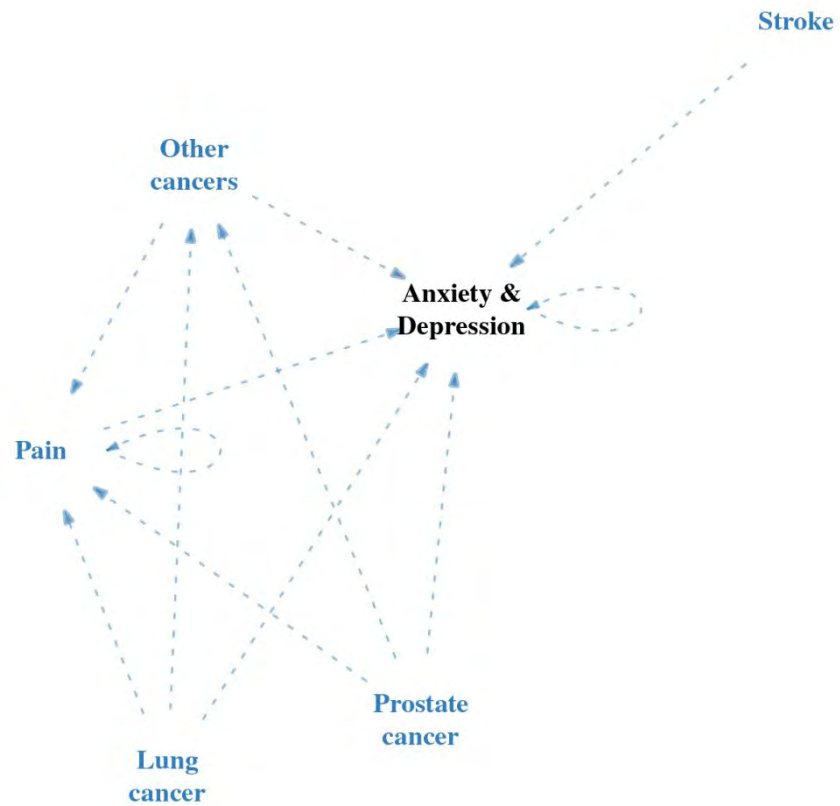


## Anxiety and depression

Table A-30 - Modelling assumptions for incident anxiety and depression

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Spell – duration is stochastic; can recur  |
| <b>Risk factor associations</b> | None   |
| <b>Disease dependencies</b>     | Past anxiety and depression, lung cancer, prostate cancer, other cancers, stroke, pain   |
| <b>Calibration factor</b>       | Intercept: 1.2<br><br>We did not calibrate to the observed incidence rate trends because their projections led to implausible rates. |

Figure A-62 - Causal structure of risk factor associations and disease dependencies for incident anxiety and depression





Validation plots for anxiety and depression incidence and prevalence

Figure A-63 - Validation plot for modelled anxiety and depression incidence (age-sex-dimd standardised)

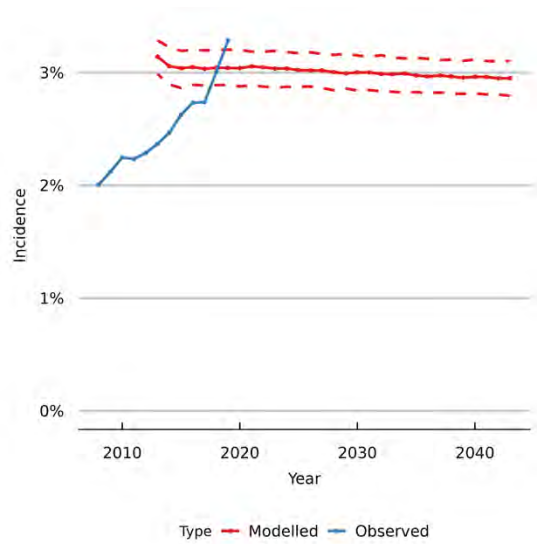
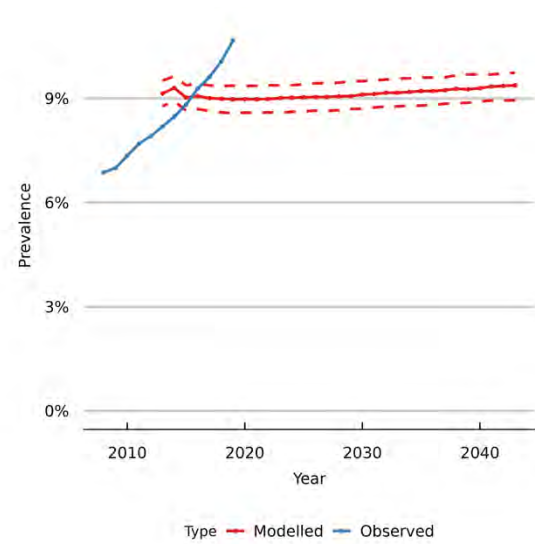


Figure A-64 - Validation plot for modelled anxiety and depression prevalence (age-sex-dimd standardised)

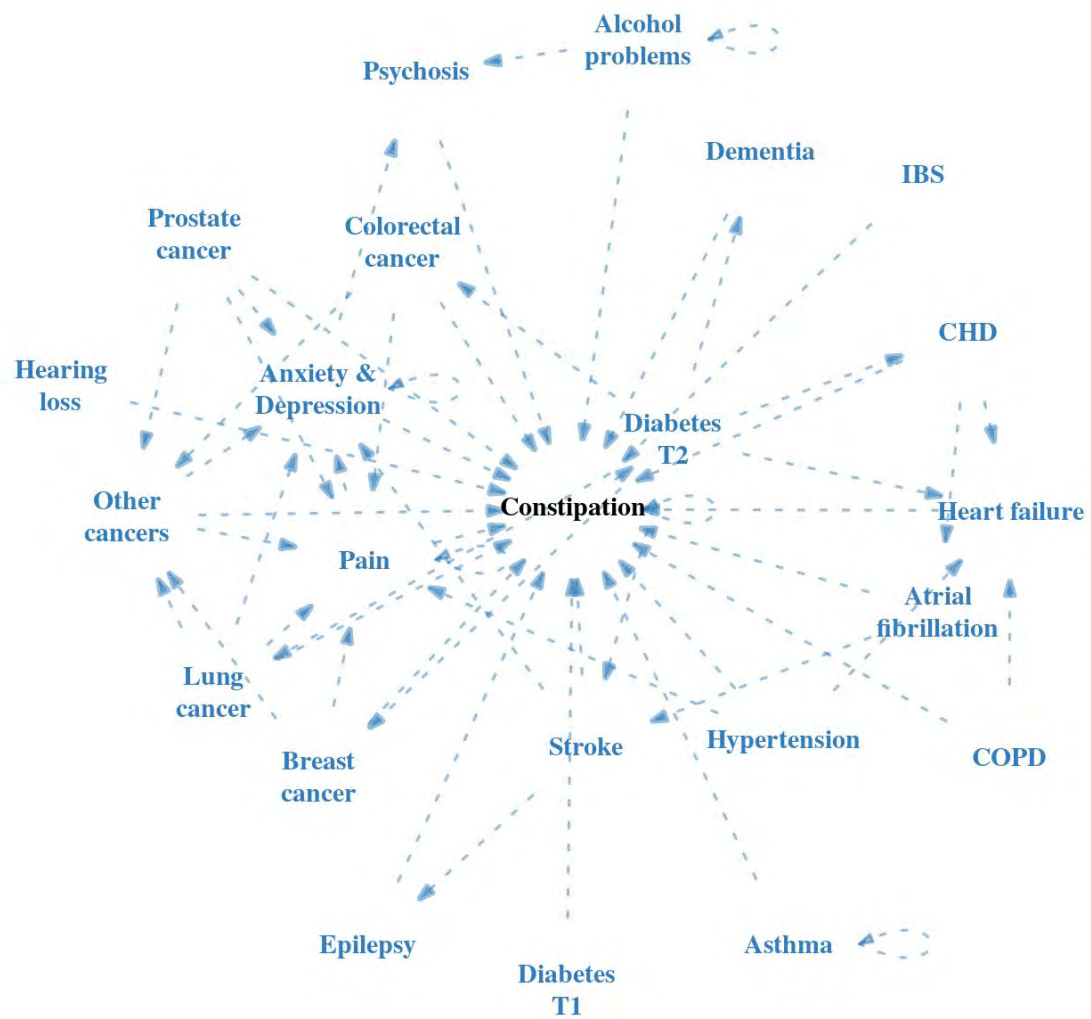


## Constipation

Table A-31 - Modelling assumptions for incident constipation

| <b>Component</b>                | <b>Assumptions / Details</b>  |
|---------------------------------|---|
| <b>Disease type</b>             | Spell – duration is stochastic; can recur   |
| <b>Risk factor associations</b> | None  |
| <b>Disease dependencies</b>     | Past constipation, anxiety and depression, breast cancer, colorectal cancer, lung cancer, prostate cancer, other cancers, stroke, pain, alcohol problems, IBS, epilepsy, dementia, type 1 diabetes mellitus, type 2 diabetes mellitus, hypertension, psychosis, heart failure, CHD, COPD, atrial fibrillation, asthma, hearing loss |
| <b>Calibration factor</b>       | None.<br><br>We did not calibrate to the observed incidence rate trends because their projections led to implausible rates.   |

Figure A-65 - Causal structure of risk factor associations and disease dependencies for incident constipation



Validation plots for constipation incidence and prevalence

Figure A-66 - Validation plot for modelled constipation incidence (age-sex-dim standardised)

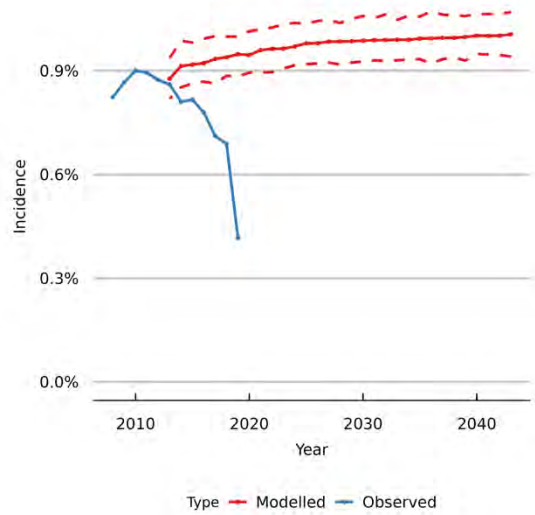
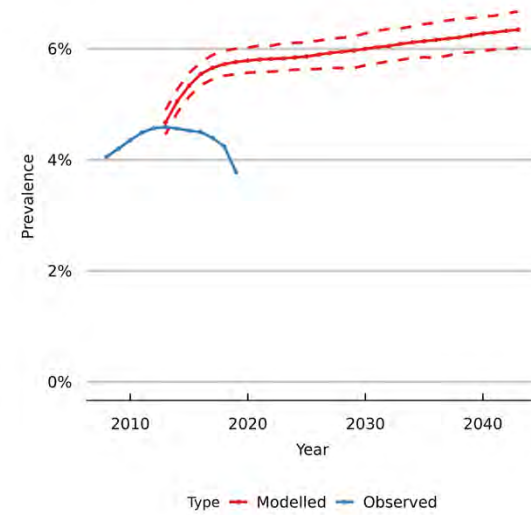


Figure A-67 - Validation plot for modelled constipation prevalence (age-sex-dim standardised)

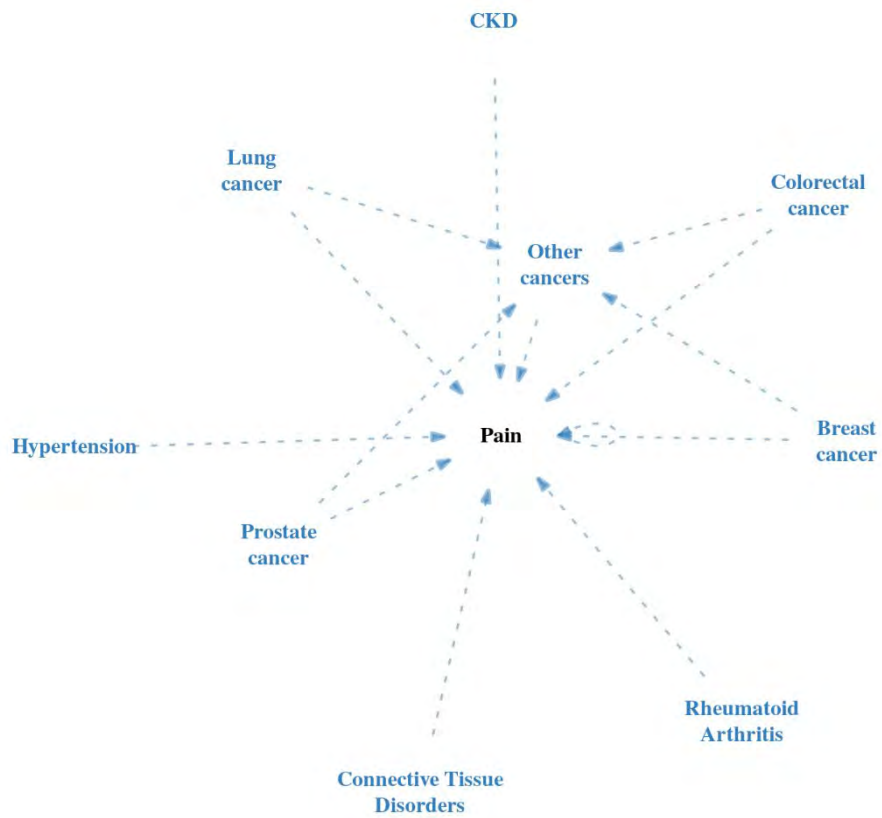


## Pain

Table A-32 - Modelling assumptions for incident pain

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Spell – duration is stochastic; can recur  |
| <b>Risk factor associations</b> | None   |
| <b>Disease dependencies</b>     | Past pain, connective tissue disorders, rheumatoid arthritis, breast cancer, colorectal cancer, prostate cancer, other cancers, CKD, hypertension, lung cancer |
| <b>Calibration factor</b>       | Intercept: 0.9   |
| <b>Other details</b>            | Due to data quality issues over time with the prescription data, we modelled the incidence of pain based on the incidence in 2013                              |

Figure A-68 - Causal structure of risk factor associations and disease dependencies for incident pain



Validation plots for pain incidence and prevalence

Figure A-69 - Validation plot for modelled pain incidence (age-sex-dimd standardised)

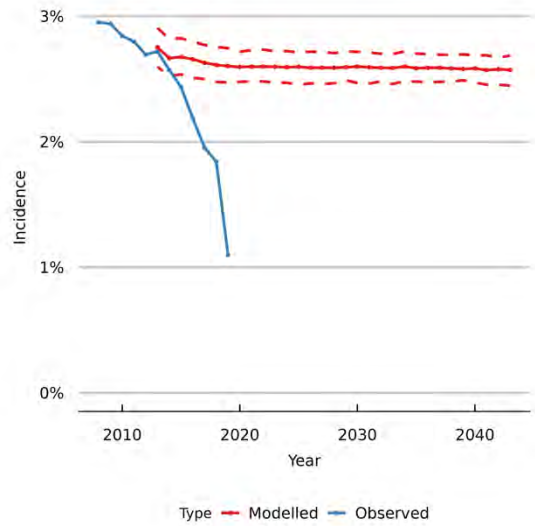
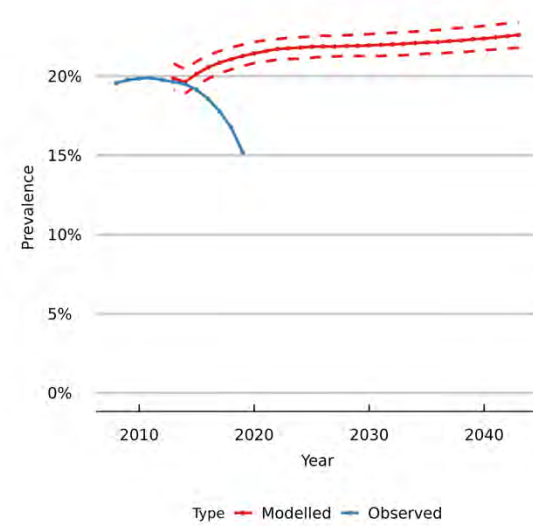


Figure A-70 - Validation plot for modelled pain prevalence (age-sex-dimd standardised)



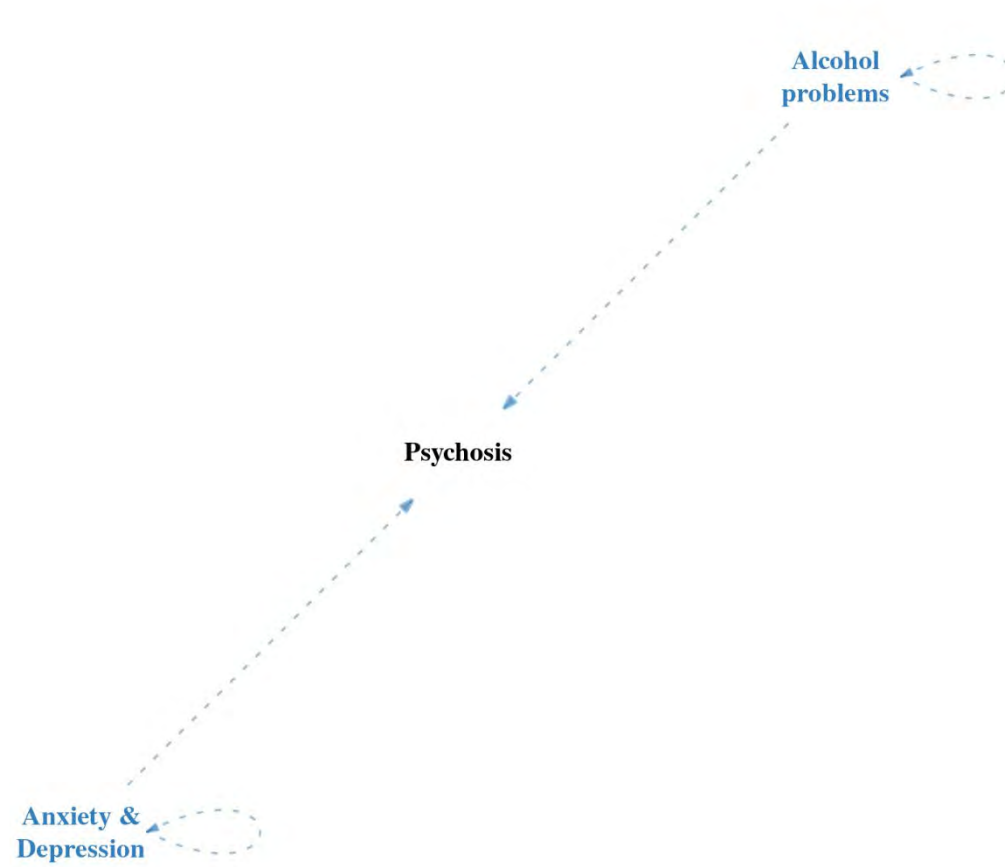
## Psychosis

Table A-33 - Modelling assumptions for incident psychosiss

| <b>Component</b>                | <b>Assumptions / Details</b>             |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery                    |
| <b>Risk factor associations</b> | None                                     |
| <b>Disease dependencies</b>     | Alcohol problems, anxiety and depression |
| <b>Calibration factor</b>       | Intercept = 0.92                         |



Figure A-71 - Causal structure of risk factor associations and disease dependencies for incident psychosis



### Validation plots for psychosis incidence and prevalence

Figure A-72 - Validation plot for modelled psychosis incidence (age-sex-dim standardised)

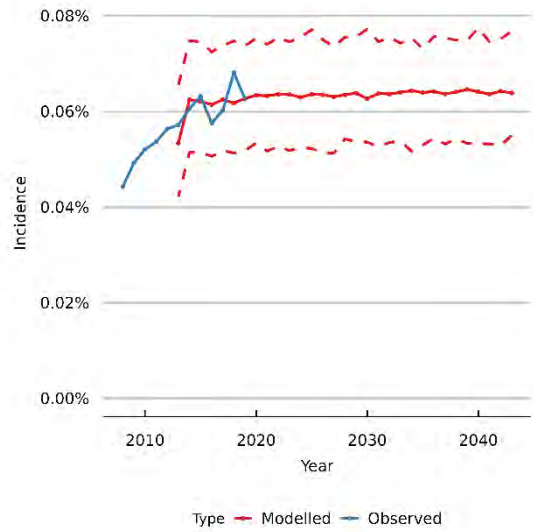
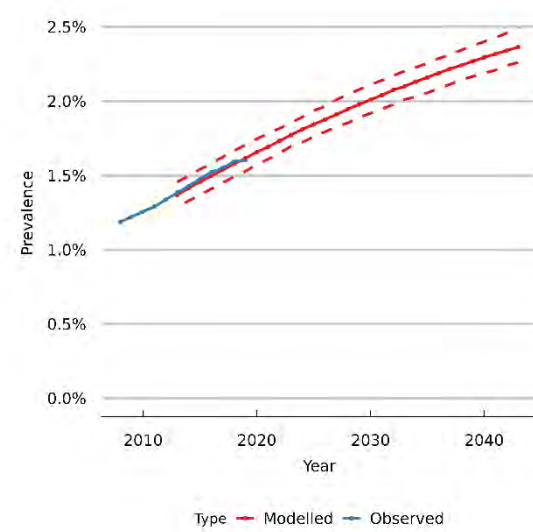


Figure A-73 - Validation plot for modelled psychosis prevalence (age-sex-dim standardised)

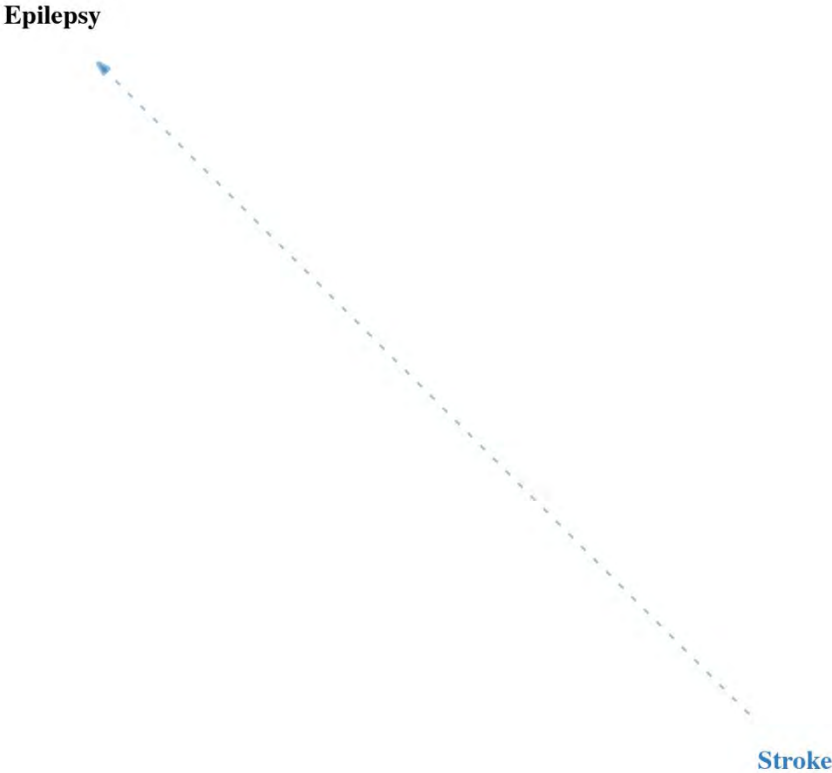


## Epilepsy

Table A-34 - Modelling assumptions for incident epilepsy

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | None                         |
| <b>Disease dependencies</b>     | Stroke                       |
| <b>Calibration factor</b>       | None                         |

Figure A-74 - Causal structure of risk factor associations and disease dependencies for incident epilepsy



Validation plots for epilepsy incidence, case fatality, and prevalence

Figure A-75 - Validation plot for modelled epilepsy incidence (age-sex-dimd standardised)

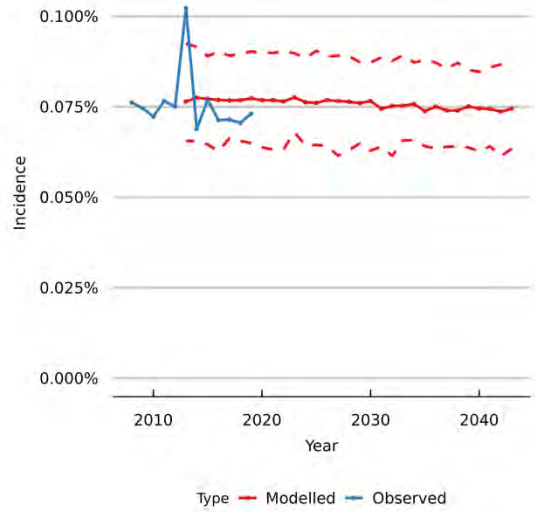


Figure A-76 - Validation plot for modelled epilepsy case fatality (age-sex-dimd standardised)

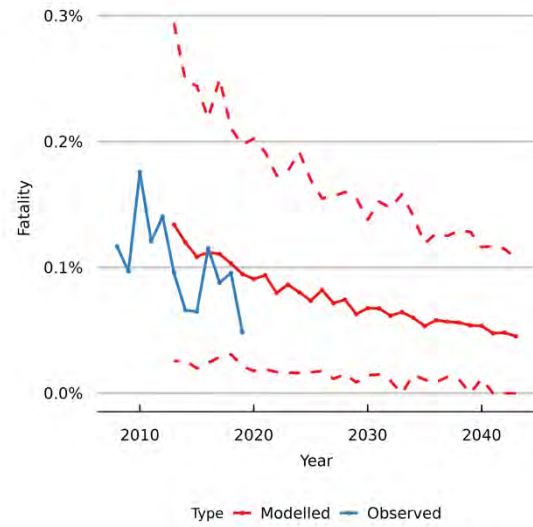
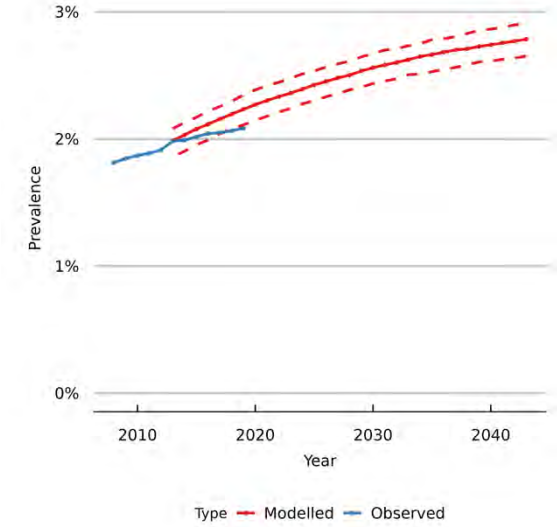


Figure A-77 - Validation plot for modelled epilepsy prevalence (age-sex-dimd standardised)



## Rheumatoid arthritis

Table A-35 - Modelling assumptions for incident rheumatoid arthritis

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | None                         |
| <b>Disease dependencies</b>     | None                         |
| <b>Calibration factor</b>       | Intercept: 0.95              |

Validation plots for rheumatoid arthritis incidence, case fatality, and prevalence

Figure A-78 - Validation plot for modelled rheumatoid arthritis incidence (age-sex-dimd standardised)

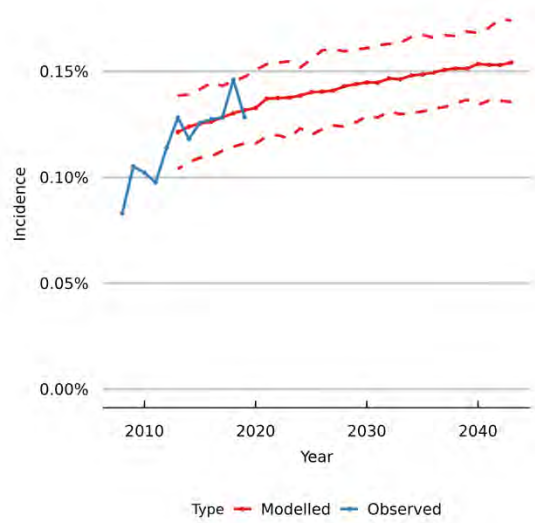


Figure A-79 - Validation plot for modelled rheumatoid arthritis case fatality (age-sex-dimd standardised)

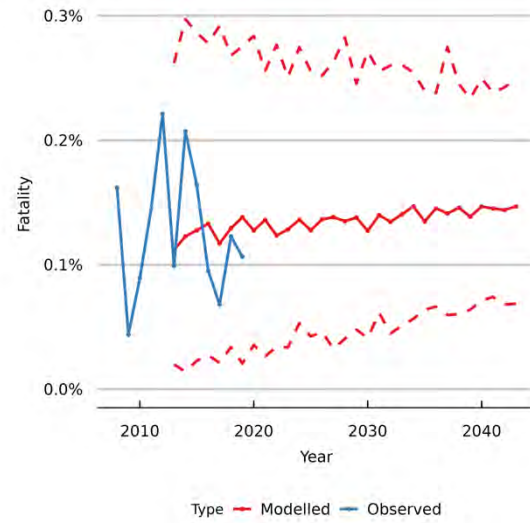
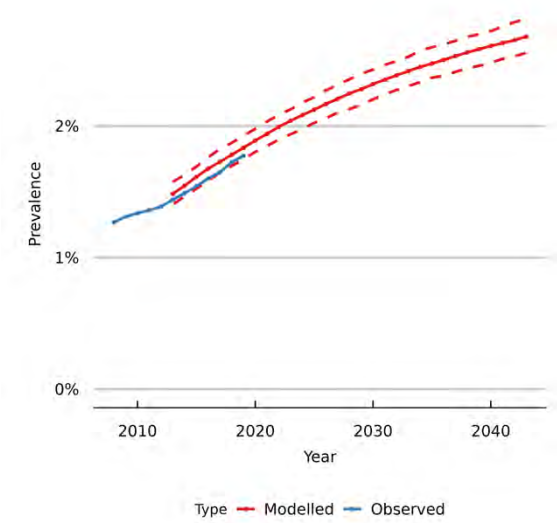


Figure A-80 - Validation plot for modelled rheumatoid arthritis prevalence (age-sex-dimd standardised)



## Connective tissue disorders

Table A-36 - Modelling assumptions for incident connective tissue disorders

| <b>Component</b>                | <b>Assumptions / Details</b>   |
|---------------------------------|--|
| <b>Disease type</b>             | Chronic – no recovery; all connective tissue disorders, excluding rheumatoid arthritis |
| <b>Risk factor associations</b> | None   |
| <b>Disease dependencies</b>     | None   |
| <b>Calibration factor</b>       | Trend: 0.999   |



Validation plots for connective tissue disorders incidence, case fatality, and prevalence

Figure A-81 - Validation plot for modelled connective tissue disorders incidence (age-sex-dimd standardised)

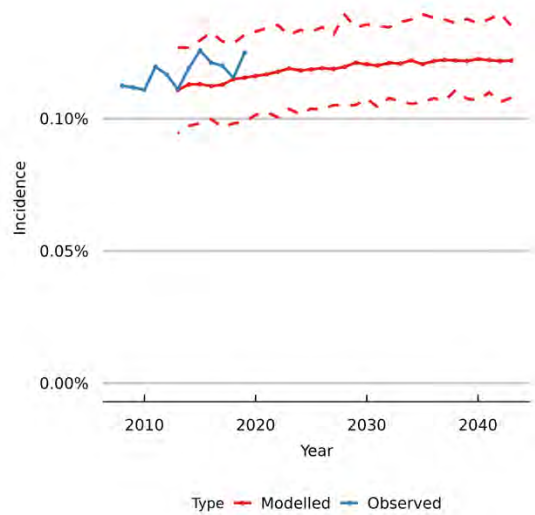


Figure A-82 - Validation plot for modelled connective tissue disorders case fatality (age-sex-dimd standardised)

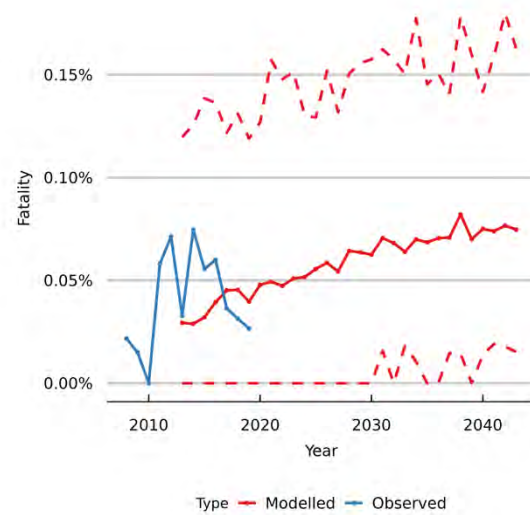
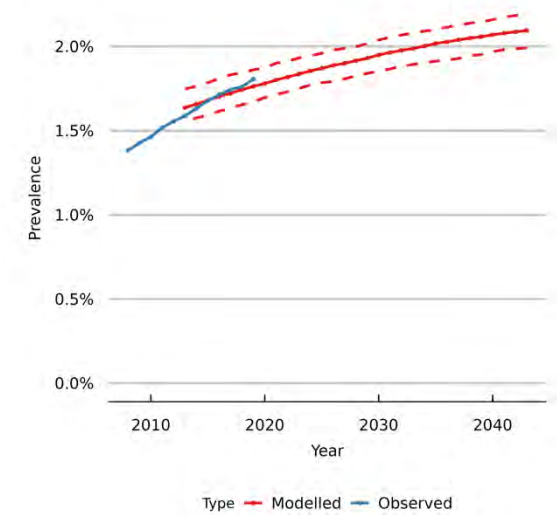


Figure A-83 - Validation plot for modelled connective tissue disorders prevalence (age-sex-dimd standardised)



Type 1 Diabetes Mellitus

Table A-37 - Modelling assumptions for incident type 1 diabetes mellitus

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | None                         |
| <b>Disease dependencies</b>     | None                         |
| <b>Calibration factor</b>       | None                         |

Validation plots for type 1 diabetes mellitus incidence, case fatality, and prevalence

Figure A-84 - Validation plot for modelled type 1 diabetes mellitus incidence (age-sex-dimd standardised)

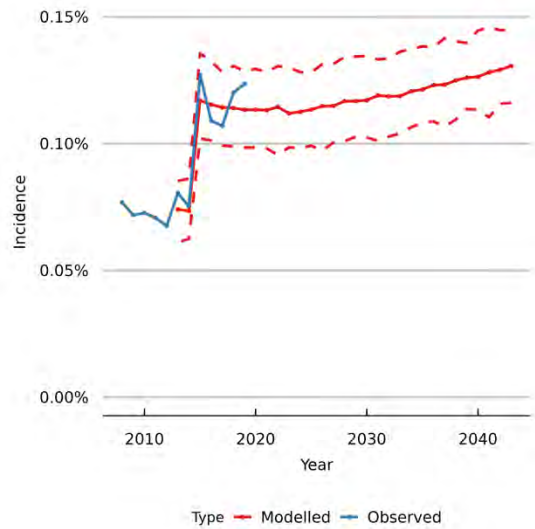


Figure A-85 - Validation plot for modelled type 1 diabetes mellitus case fatality (age-sex-dimd standardised)

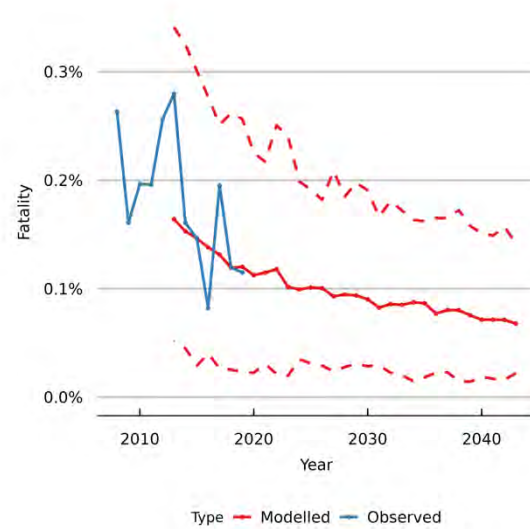
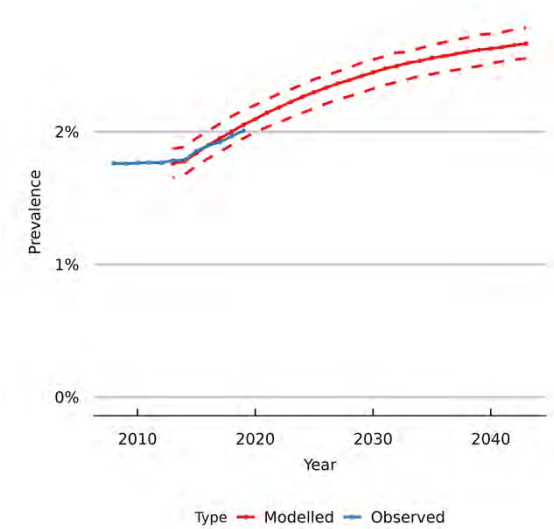


Figure A-86 - Validation plot for modelled type 1 diabetes mellitus prevalence (age-sex-dimd standardised)



## Hearing loss

Table A-38 - Modelling assumptions for incident hearing loss

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | None                         |
| <b>Disease dependencies</b>     | None                         |
| <b>Calibration factor</b>       | Intercept: 0.95              |

Validation plots for hearing loss incidence and prevalence

Figure A-87 - Validation plot for modelled hearing loss incidence (age-sex-dimd standardised)

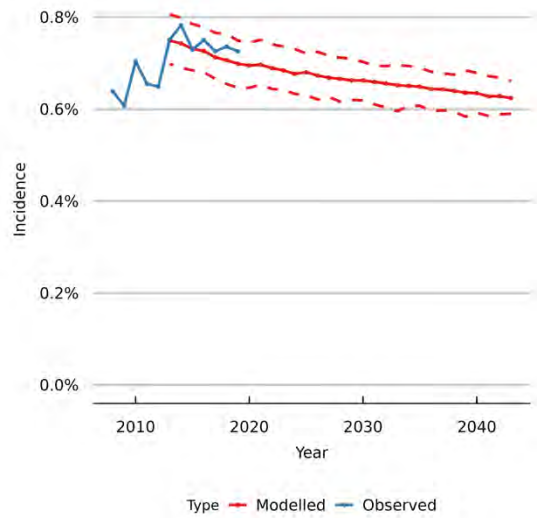
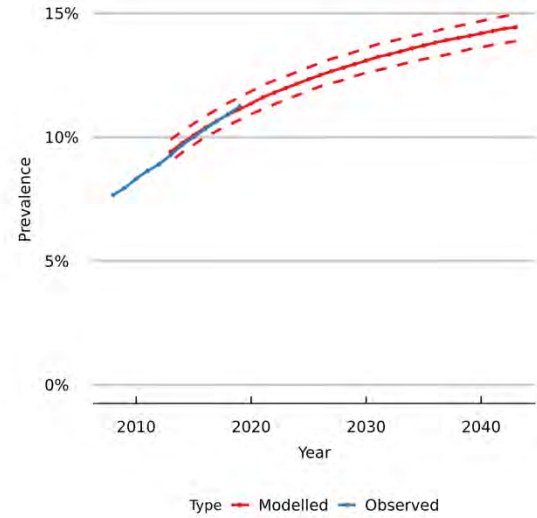


Figure A-88 - Validation plot for modelled hearing loss prevalence (age-sex-dimd standardised)



Irritable bowel syndrome (IBS)

Table A-39 - Modelling assumptions for incident IBS

| <b>Component</b>                | <b>Assumptions / Details</b> |
|---------------------------------|------------------------------|
| <b>Disease type</b>             | Chronic – no recovery        |
| <b>Risk factor associations</b> | None                         |
| <b>Disease dependencies</b>     | None                         |
| <b>Calibration factor</b>       | Trend: 0.99                  |

Validation plots for IBS incidence and prevalence

Figure A-89 - Validation plot for modelled IBS incidence (age-sex-dimd standardised)

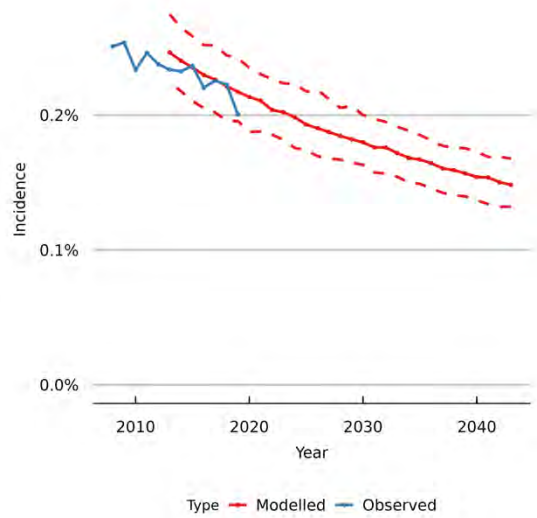
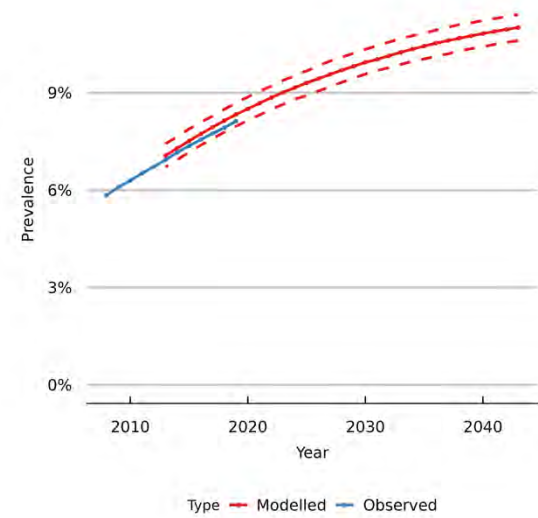


Figure A-90 - Validation plot for modelled IBS prevalence (age-sex-dimd standardised)



## Non-modelled mortality

Table A-40 - Modelling assumptions for mortality for causes other than the case fatalities described above

| <b>Component</b>                | <b>Assumptions / Details</b>  |
|---------------------------------|---|
| <b>Outcome type</b>             | Mortality from any cause other than the specifically modelled case fatality relationships described above |
| <b>Risk factor associations</b> | Smoking, systolic blood pressure, alcohol intake, physical activity                                       |
| <b>Disease dependencies</b>     | All 20 CMS conditions   |
| <b>Calibration factor</b>       | None  |



Figure A-91 - Causal structure of risk factor associations and disease dependencies for incident non-modelled mortality

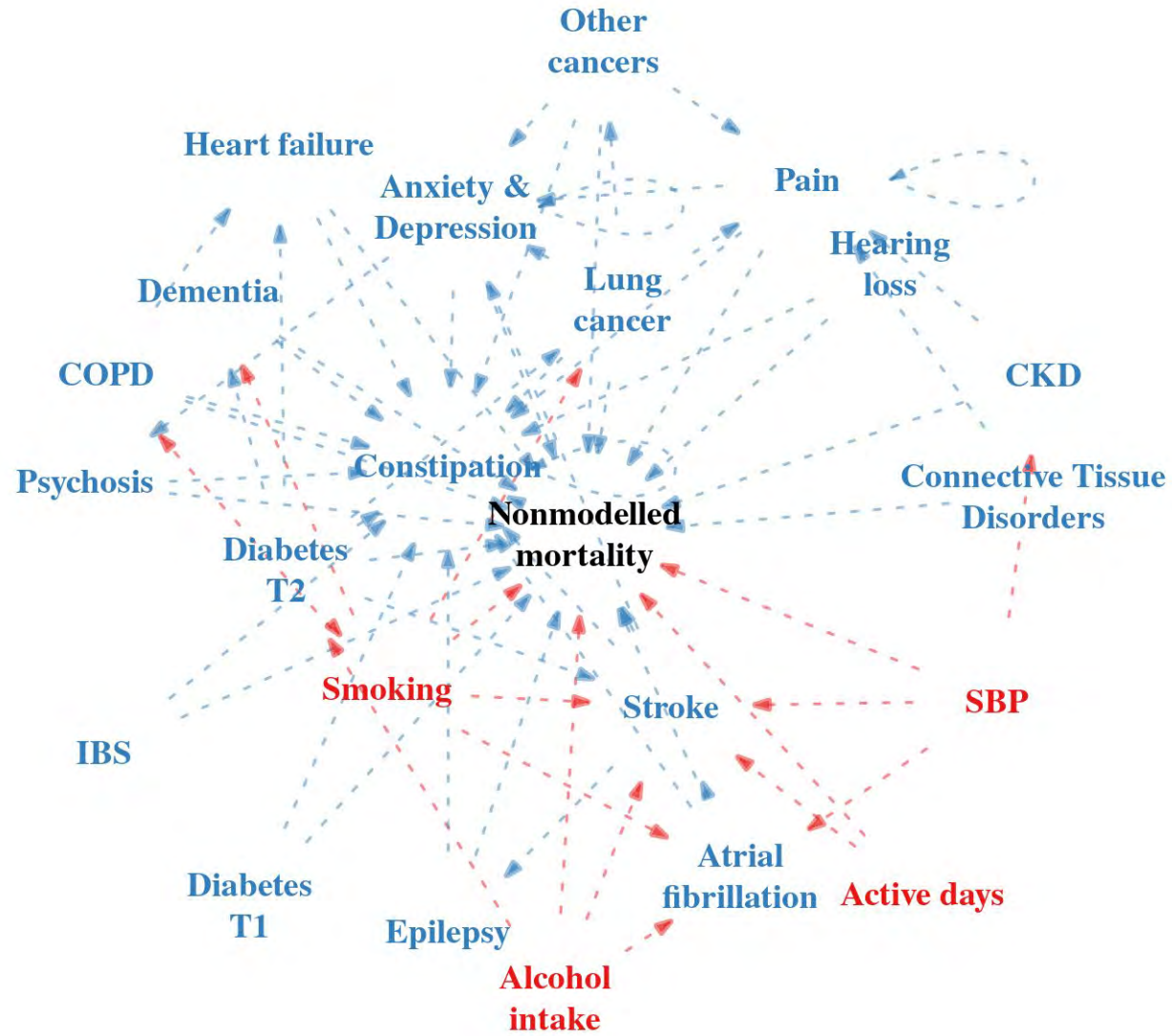
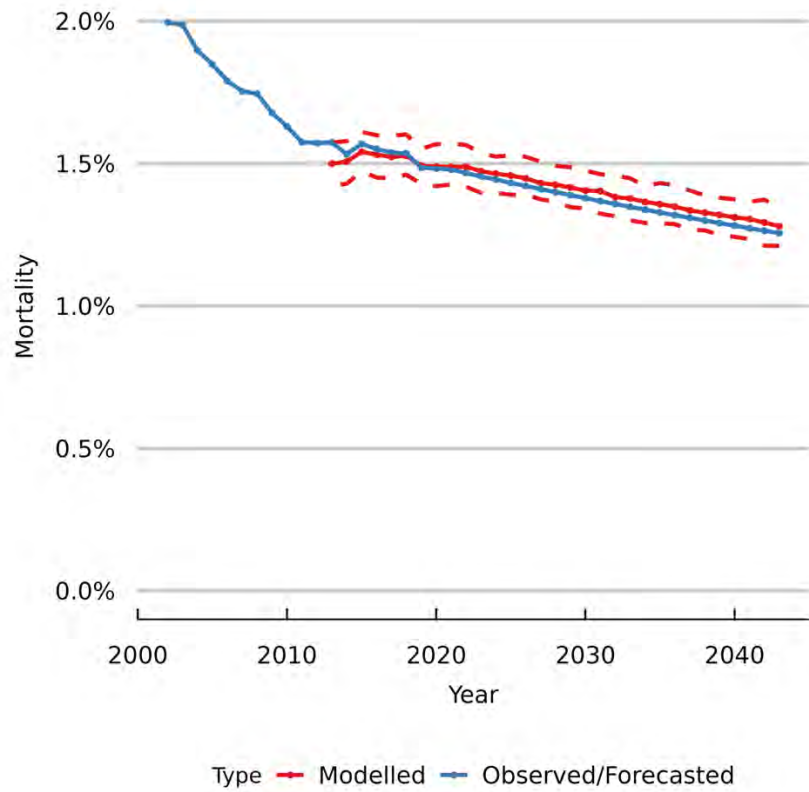


Table A-41 - Data sources for causal associations between risk factors and non-modelled mortality

| Parameter                                 | Details                                    | Comments   | Source   |
|---|--|--|--|
| Relative risk for smoking status          | Meta-analysis of 1.7 million men and women | Multiply adjusted. We used the Non-CVD, non-cancer mortality effects.  | Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. <i>The Lancet</i> 2017;389:1229–37. (Figure 4) |
| Relative risk for systolic blood pressure | Meta-analysis of 1.7 million men and women | Multiply adjusted. We used the Non-CVD, non-cancer mortality effects. We applied the effect to those with SBP > 140 mmHg                         | Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. <i>The Lancet</i> 2017;389:1229–37. (Figure 4) |
| Relative risk for physical activity       | Meta-analysis of 1.7 million men and women | Multiply adjusted. We used the Non-CVD, non-cancer mortality effects. We applied the effect only to those with one or less active days per week. | Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1.7 million men and women. <i>The Lancet</i> 2017;389:1229–37. (Figure 4) |
| Relative risk for alcohol intake          | Meta-analysis of 1.7 million men and women | Multiply adjusted. We used the Non-CVD, non-cancer mortality effects.  | Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-  |

Figure A-92- Validation plot for non-modelled mortality (age-sex-dimnd standardised)



## Cambridge Multimorbidity Score (CMS) Validation

Figure A-93 - Validation plot for prevalence of CMS > 0 (age-sex-dimd standardised)

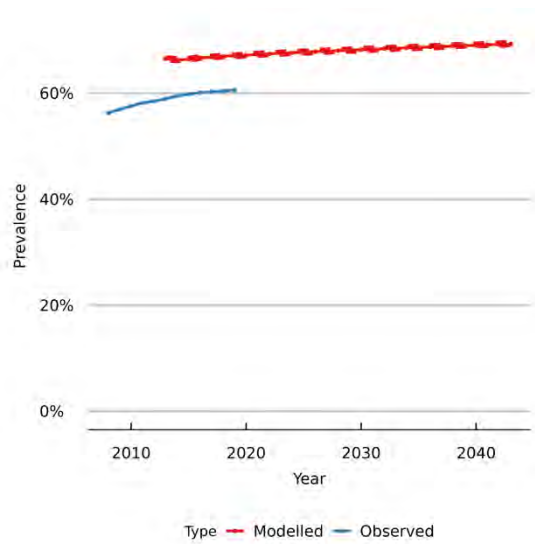
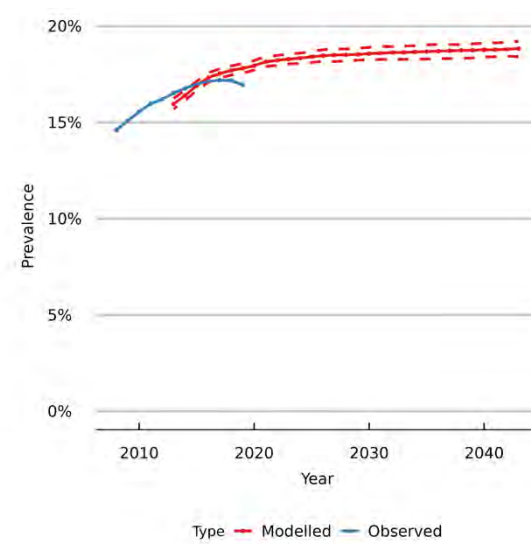


Figure A-94 - Validation plot for prevalence of CMS  $\geq 2$  (age-sex-dimd standardised)



## B) Supplementary materials B: exposure modelling details and validation

### Exposure modelling details

Table B-1 - Exposure modelling in IMPACT<sub>NCD</sub>

| <b>Exposure</b>                                | <b>Statistical Modelling (distribution)</b> | <b>Independent Variables</b>         | <b>Comment</b>  |
|--|---|--------------------------------------|---|
| Active days per week                           | Logit ordinal regression                    | Year, age, sex, QIMD, SHA, ethnicity |   |
| Daily fruit consumption in grams               | GAMLSS (Zero Inflated SICHEL)               | Year, age, sex, QIMD, SHA, ethnicity | 1 portion = 80g   |
| Daily vegetable consumption in grams           | GAMLSS (Delaporte)                          | Year, age, sex, QIMD, SHA, ethnicity | 1 portion = 80g   |
| Smoking status (never/ occasionally/ /current) | GAMLSS (Multinomial with four categories)   | Year, age, sex, QIMD, SHA, ethnicity | All the smoking-related variables are used in a smoking microsimulation subroutine that simulates smoking histories             |
| Years of abstinence for ex-smokers             | GAMLSS (double Poisson)                     | Year, age, sex, QIMD, SHA, ethnicity | Applies only to the first year that a synthetic individual enters the simulation. Then is estimated from the smoking subroutine |

| <b>Exposure</b>                        | <b>Statistical Modelling (distribution)</b> | <b>Independent Variables</b>         | <b>Comment</b>  |
|--|---|--------------------------------------|---|
| Smoking duration for ex-smokers        | GAMLSS (double Poisson)                     | Year, age, sex, QIMD, SHA, ethnicity | Applies only to the first year that a synthetic individual enters the simulation. Then is estimated from the smoking subroutine |
| Smoking duration for current smokers   | GAMLSS (negative binomial)                  | Year, age, sex, QIMD, SHA, ethnicity | Applies only to the first year that a synthetic individual enters the simulation. Then is estimated from the smoking subroutine |
| Smoking initiation probability         | GAMLSS (binomial)                           | Year, age, sex, QIMD, SHA, ethnicity |   |
| Smoking cessation probability          | GAMLSS (binomial)                           | Year, age, sex, QIMD, SHA, ethnicity |   |
| Smoking relapse probability            | Exponential decay                           | Sex, QIMD, years since cessation     |   |
| Cigarettes per day for ex-smokers      | GAMLSS (negative binomial)                  | Year, age, sex, QIMD, SHA, ethnicity |   |
| Cigarettes per day for current smokers | GAMLSS (negative binomial)                  | Year, age, sex, QIMD, SHA, ethnicity |   |

| <b>Exposure</b>  | <b>Statistical Modelling (distribution)</b> | <b>Independent Variables</b>                         | <b>Comment</b>  |
|--|---|--|---|
| Environmental tobacco smoking                                    | GAMLSS (binomial)                           | Year, age, sex, QIMD, SHA, ethnicity                 | Currently, this is independent of smoking prevalence in an area |
| Ethanol consumption per day, based on average weekly consumption | GAMLSS (negative binomial)                  | Year, age, sex, QIMD, SHA, ethnicity, smoking status | Since HSE 2011  |
| BMI  | GAMLSS (Box-Cox Power Exponential)          | Year, age, sex, QIMD, SHA, ethnicity, smoking status |   |
| SBP  | GAMLSS (Box-Cox Power Exponential)          | Year, age, sex, QIMD, SHA, ethnicity, smoking status |   |
| BP medication  | GAMLSS (binomial)                           | Year, age, sex, QIMD, SHA, ethnicity, SBP            | Since 2012  |
| Total cholesterol  | GAMLSS (Box-Cox t)                          | Year, age, sex, QIMD, SHA, ethnicity                 |   |
| HDL to total cholesterol ratio                                   | GAMLSS (generalized beta type 1)            | Year, age, sex, QIMD, SHA, ethnicity                 |   |

| Exposure | Statistical Modelling<br>(distribution) | Independent Variables   | Comment    |
|----------|---|---|------------|
| Statins  | GAMLSS (binomial)                       | Year, age, sex, QIMD,<br>SHA, ethnicity, total<br>cholesterol | Since 2012 |



### Exposure validation plots

The following figures are the cumulative probability validation plots for the modelled exposures in the simulation compared to the observed Health Survey for England data. Plots are presented by 1) year and 10-year age-group, 2) year and quintiles of IMD.

For the main exposures modelled (alcohol, active days, BMI, fruit and vegetable intake, smoking prevalence, second-hand smoke exposure, SBP, total cholesterol), we also present trends in exposures by quintiles of IMD (unstandardised).

Active days

Figure B-1 - Validation: Active days – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

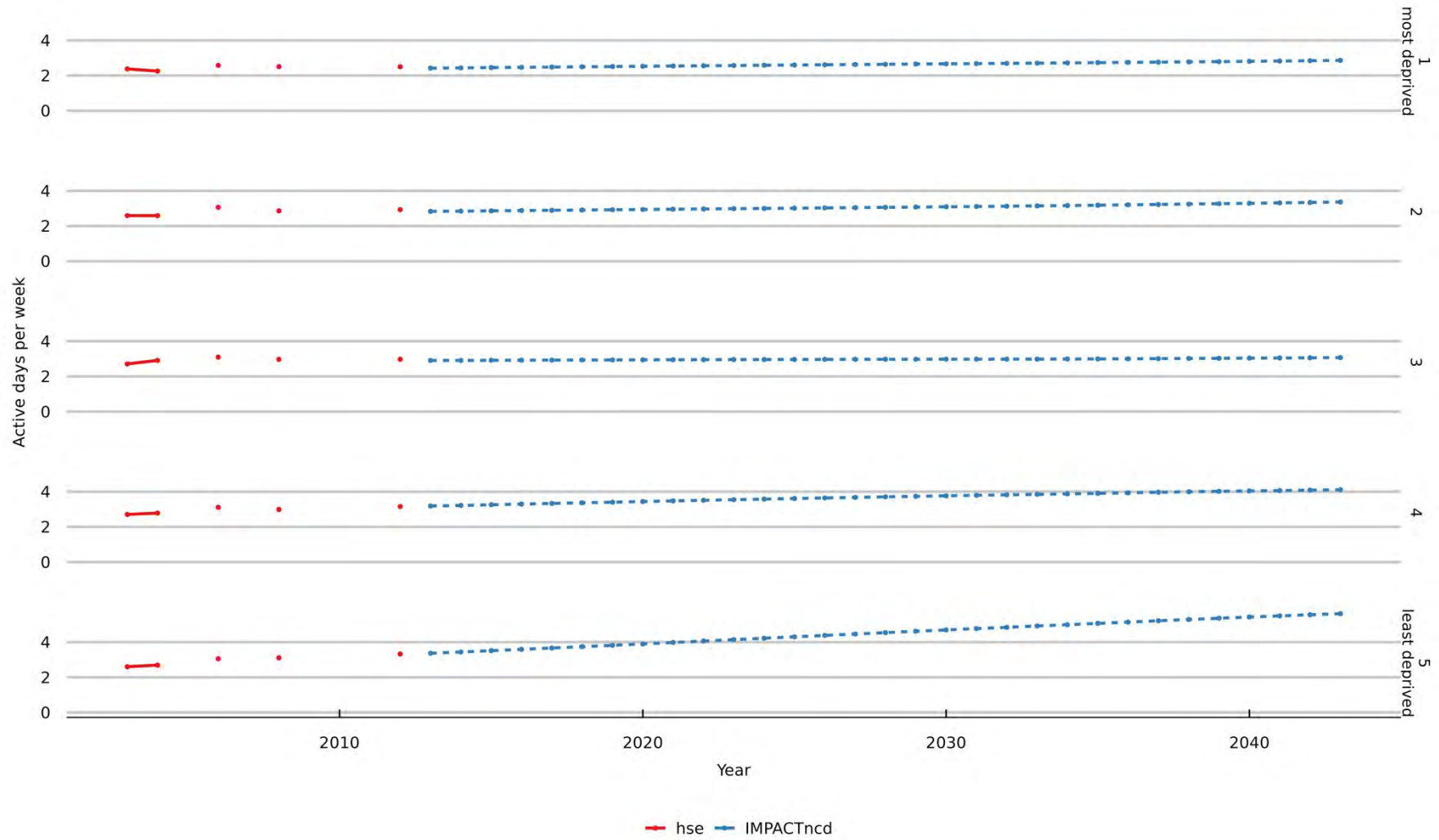


Figure B-2. Validation: Active days by year and age

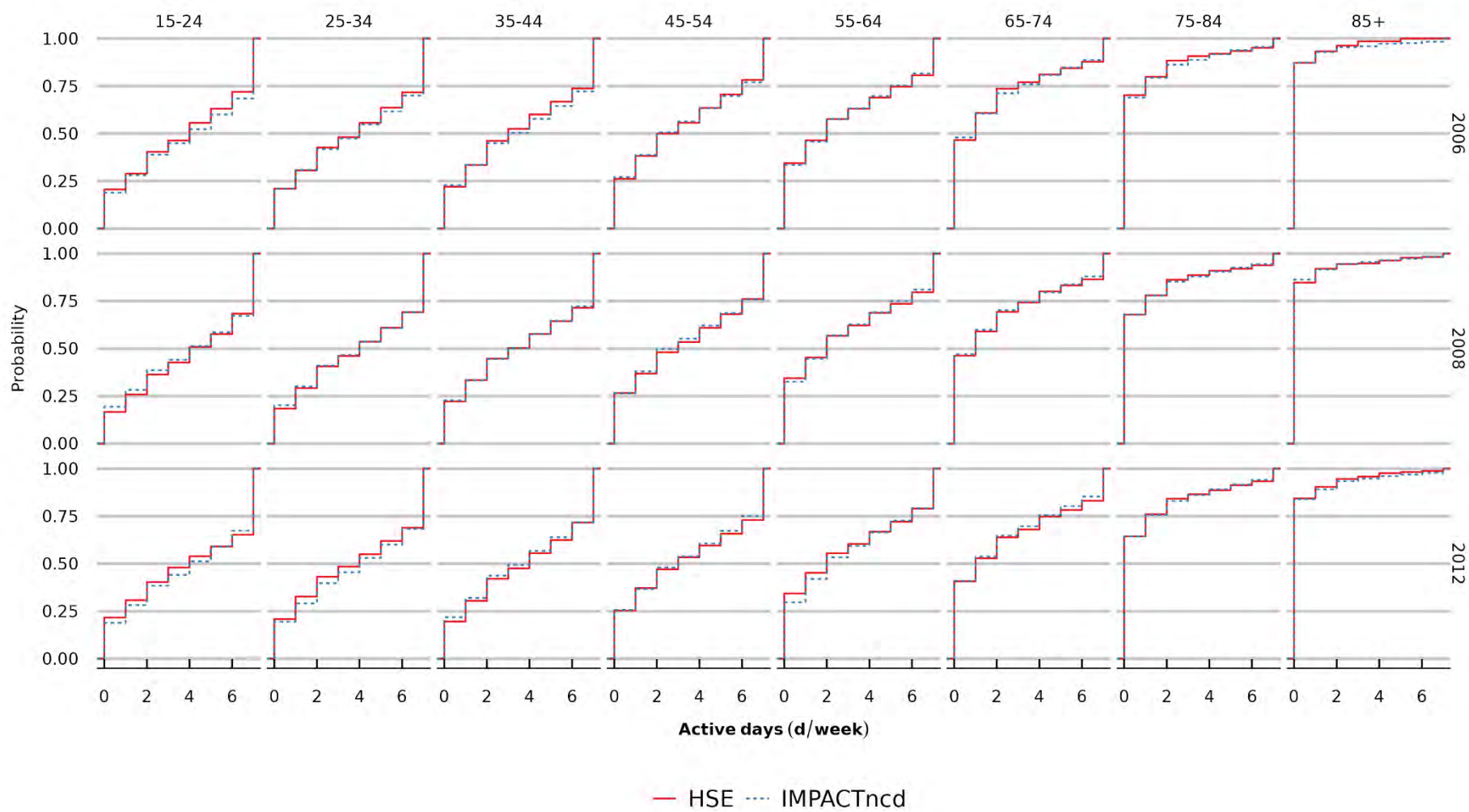
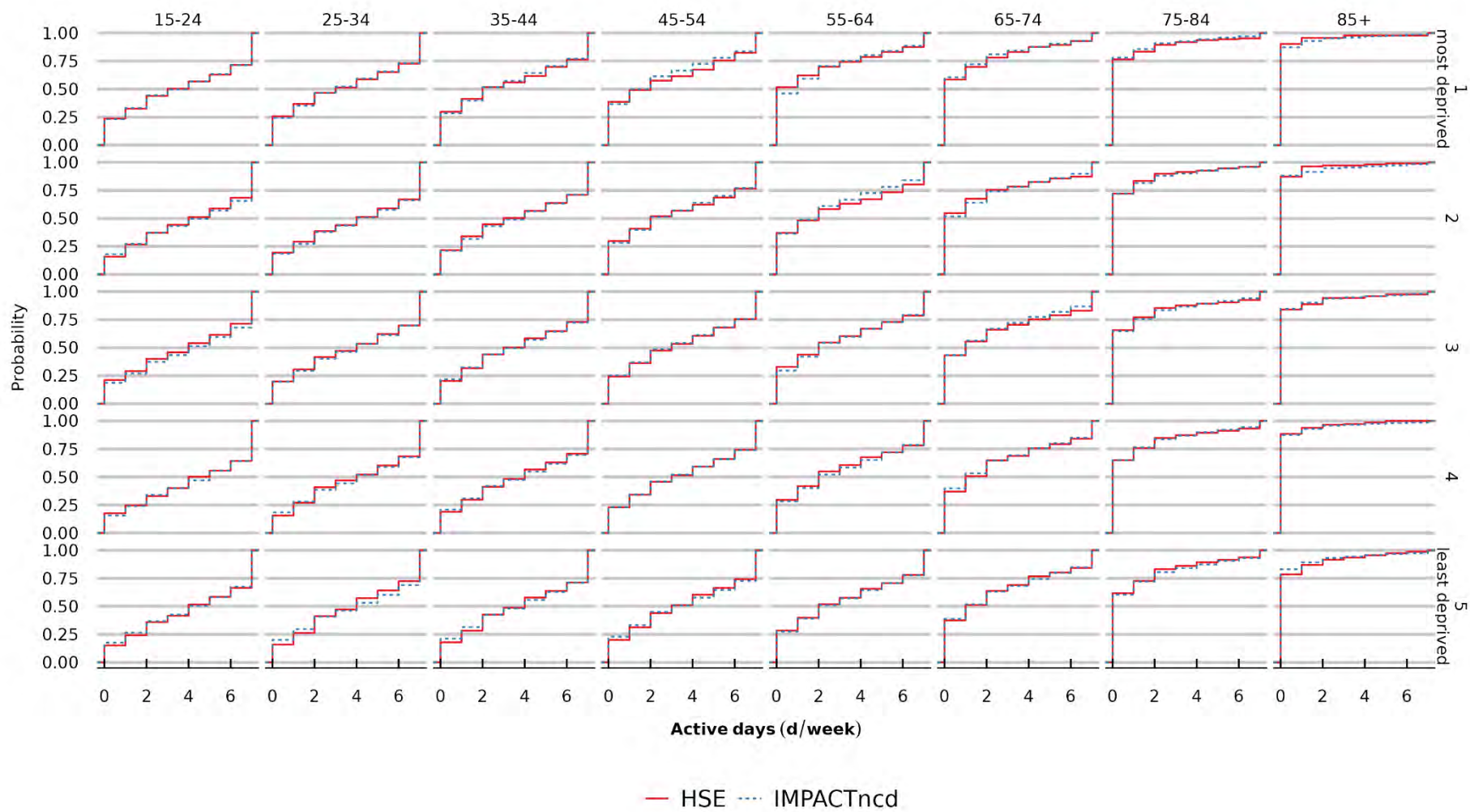


Figure B-3. Validation: Active days by quintiles of IMD and age



# Alcohol intake

Figure B-4 - Validation: Alcohol intake – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

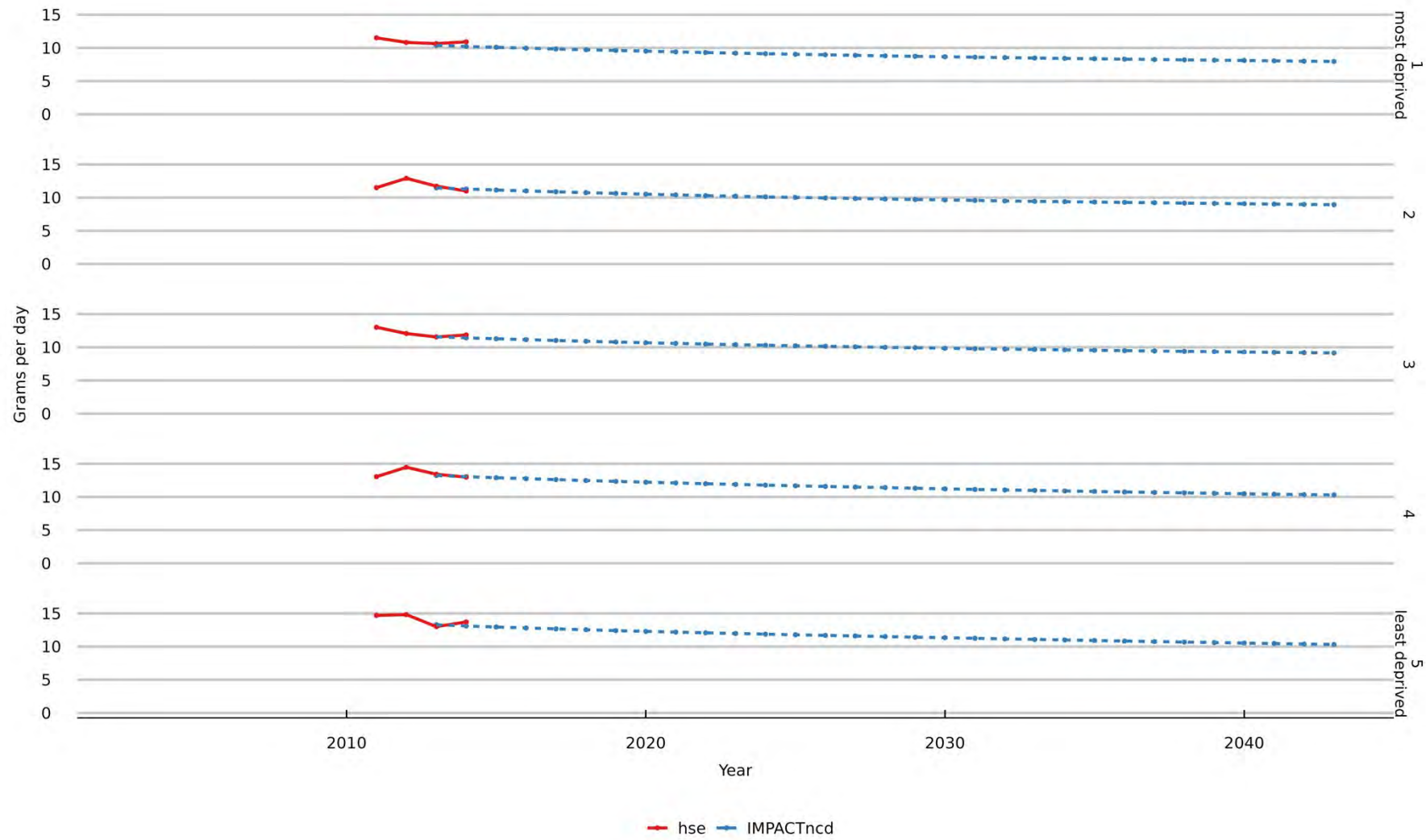




Figure B-5 - Validation: Alcohol intake (grams per day) by year and age

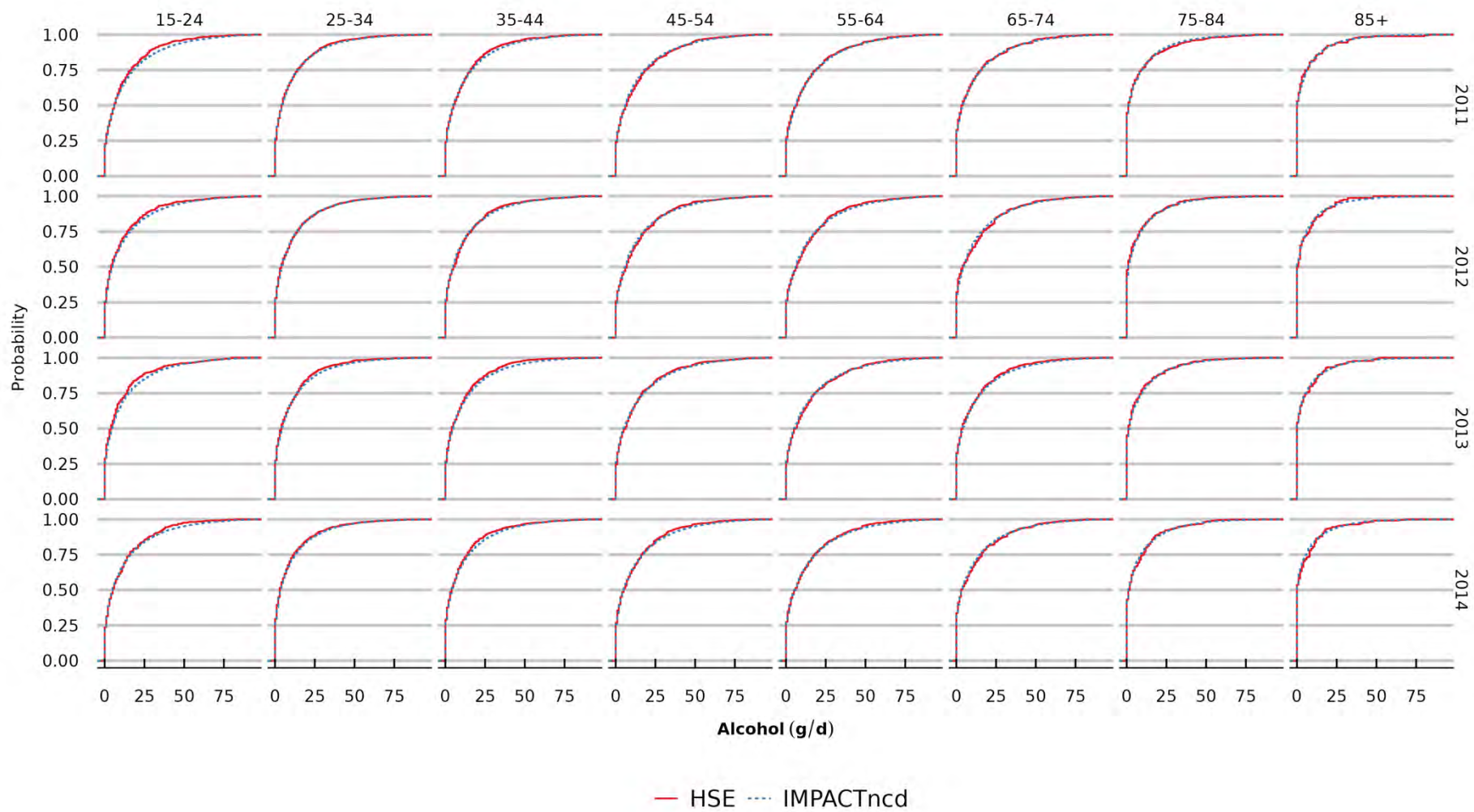
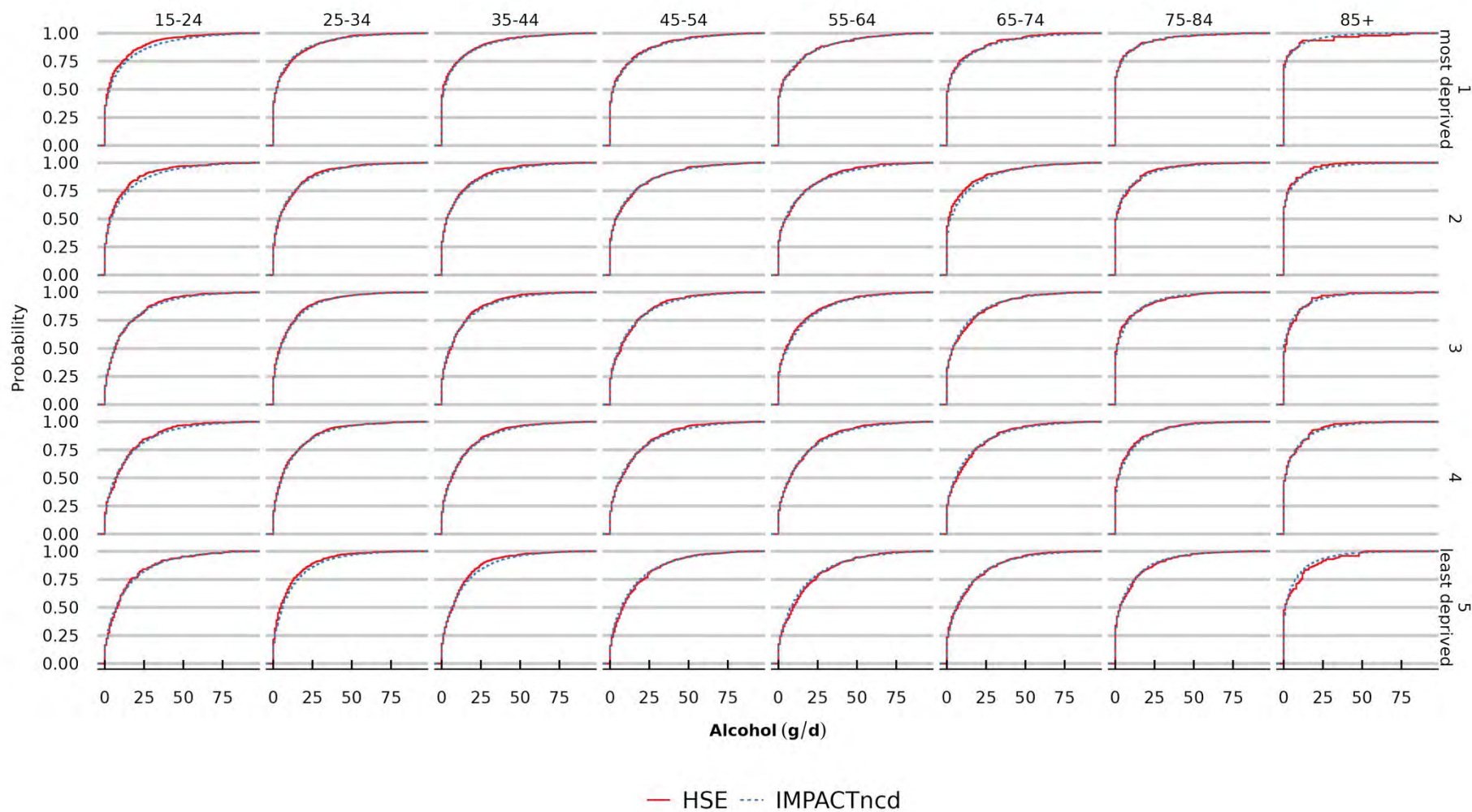


Figure B-6 - Validation: Alcohol intake (grams per day) by quintiles of IMD and age



# Body mass index

Figure B-7 - Validation: BMI – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

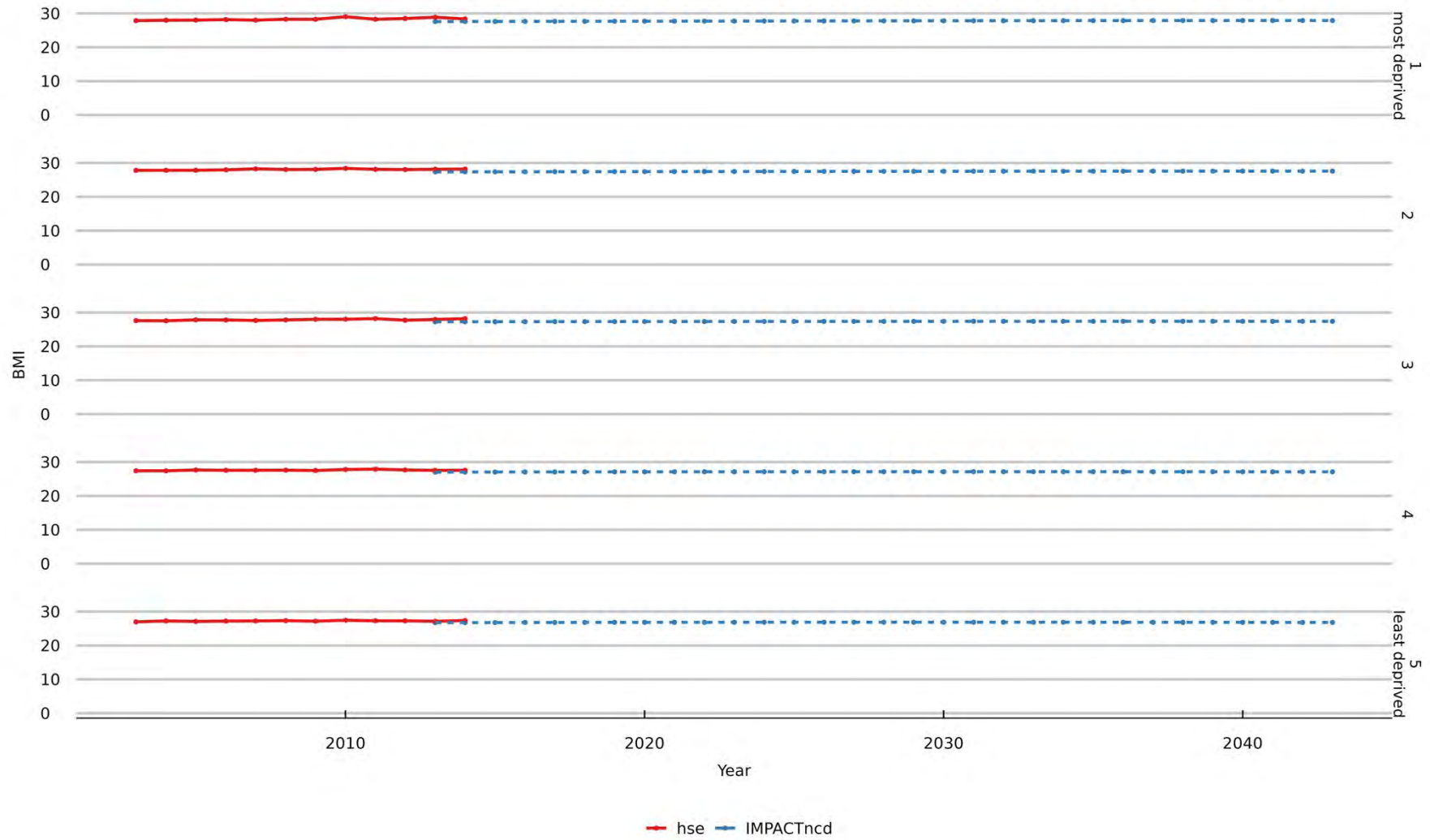




Figure B-8 Validation: Body mass index by year and age

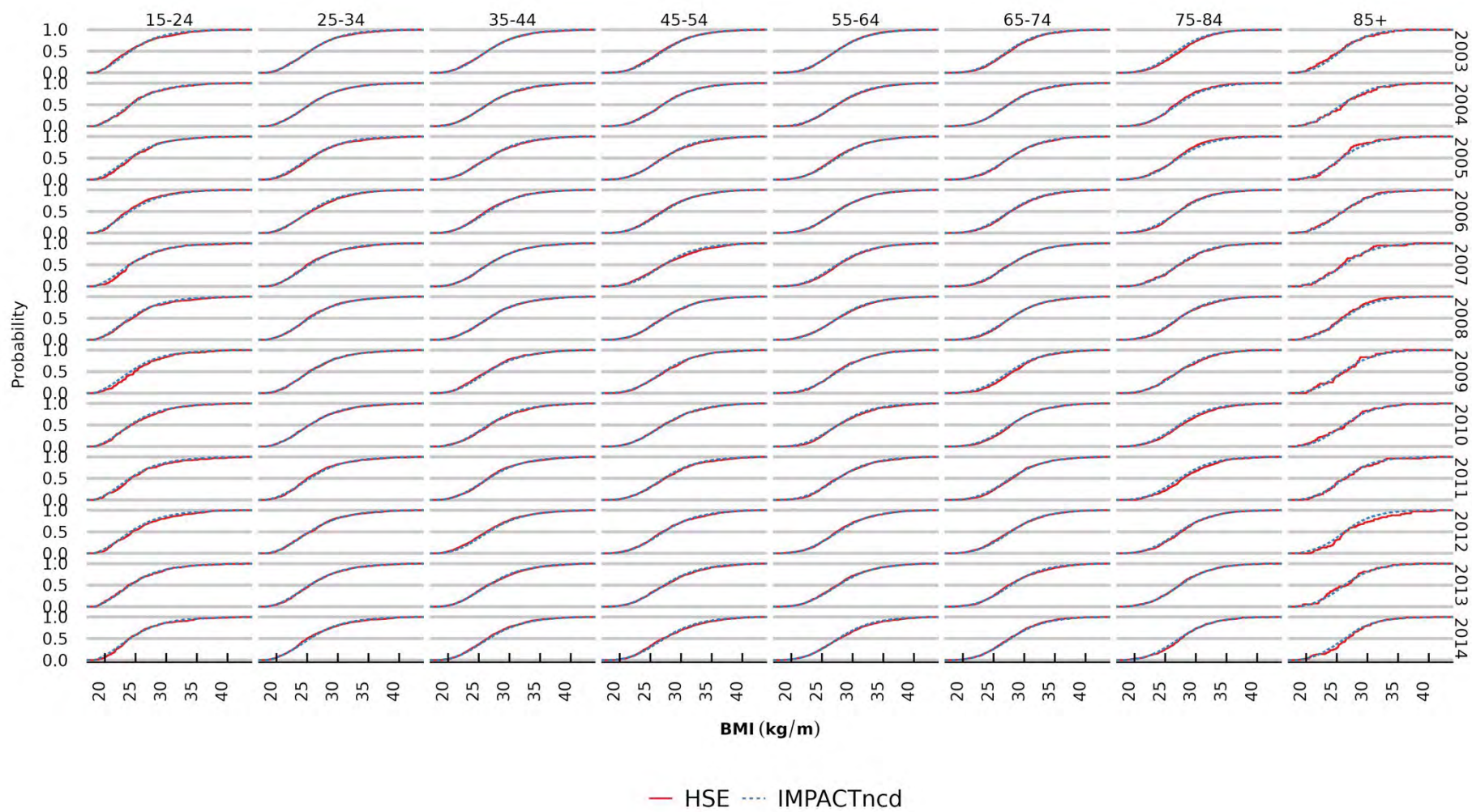
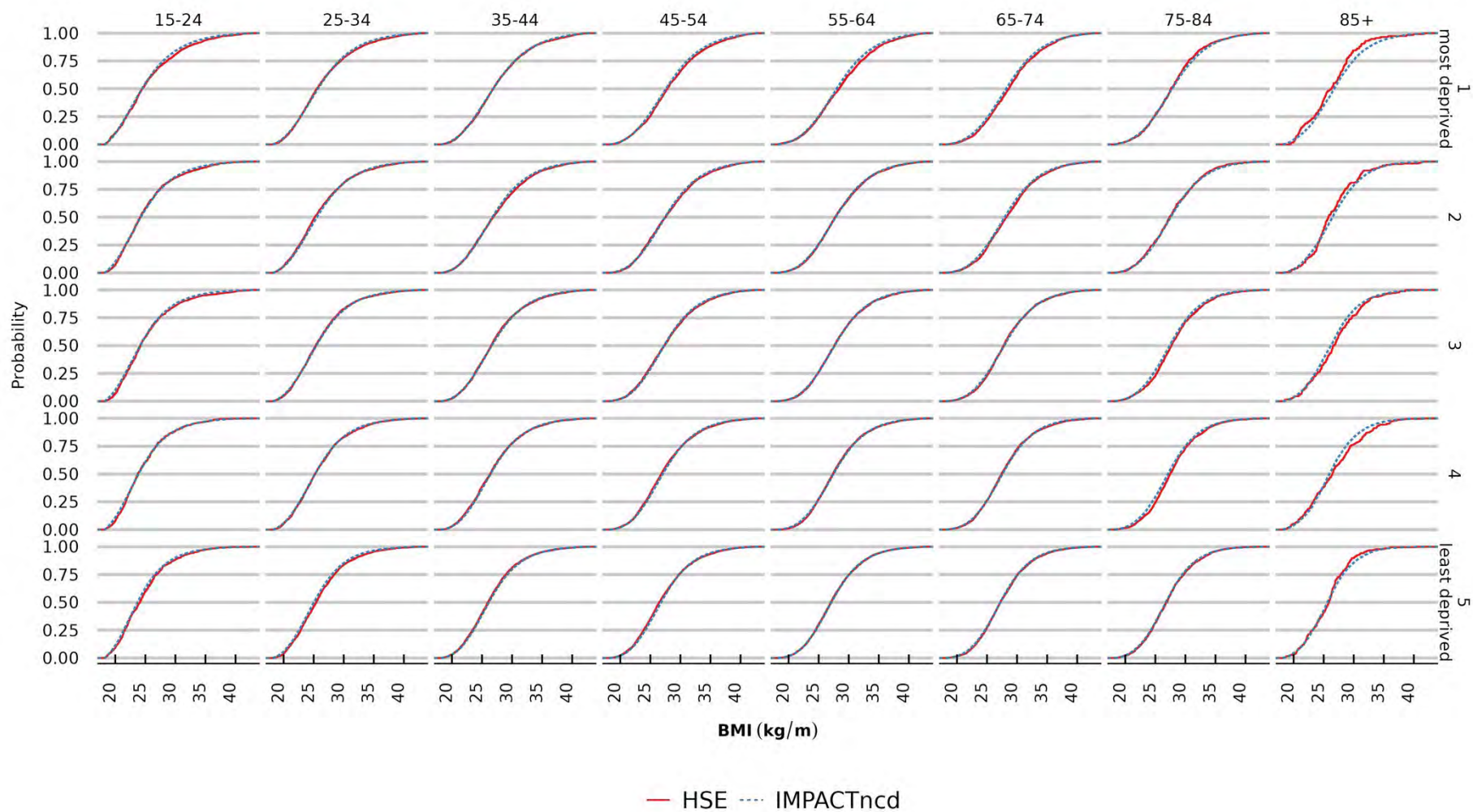


Figure B-9 - Validation: Body mass index by quintiles of IMD and age



# Systolic blood pressure

Figure B-10 - Validation: Systolic blood pressure – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

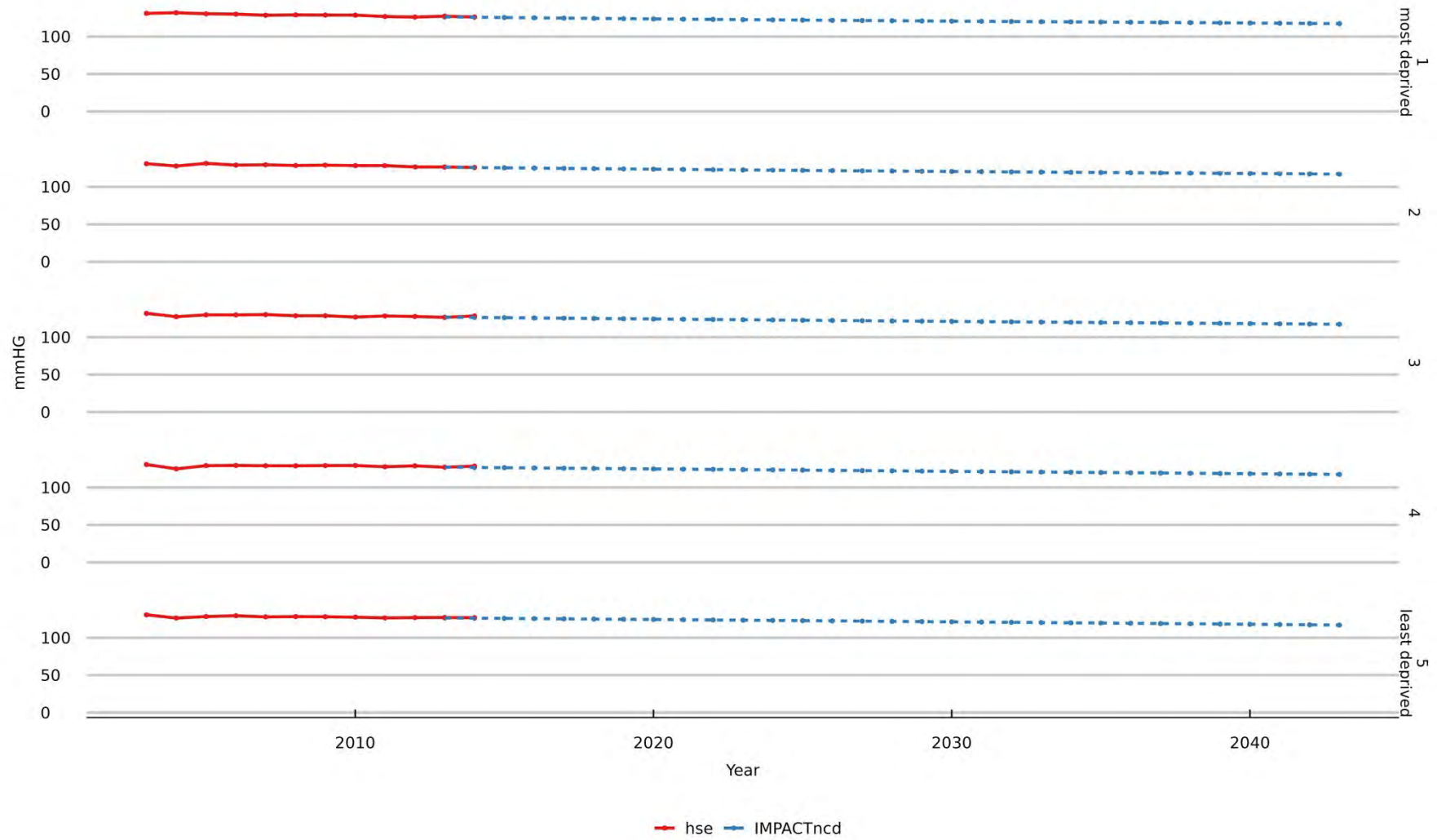




Figure B-11 - Validation: Systolic blood pressure by year and age group

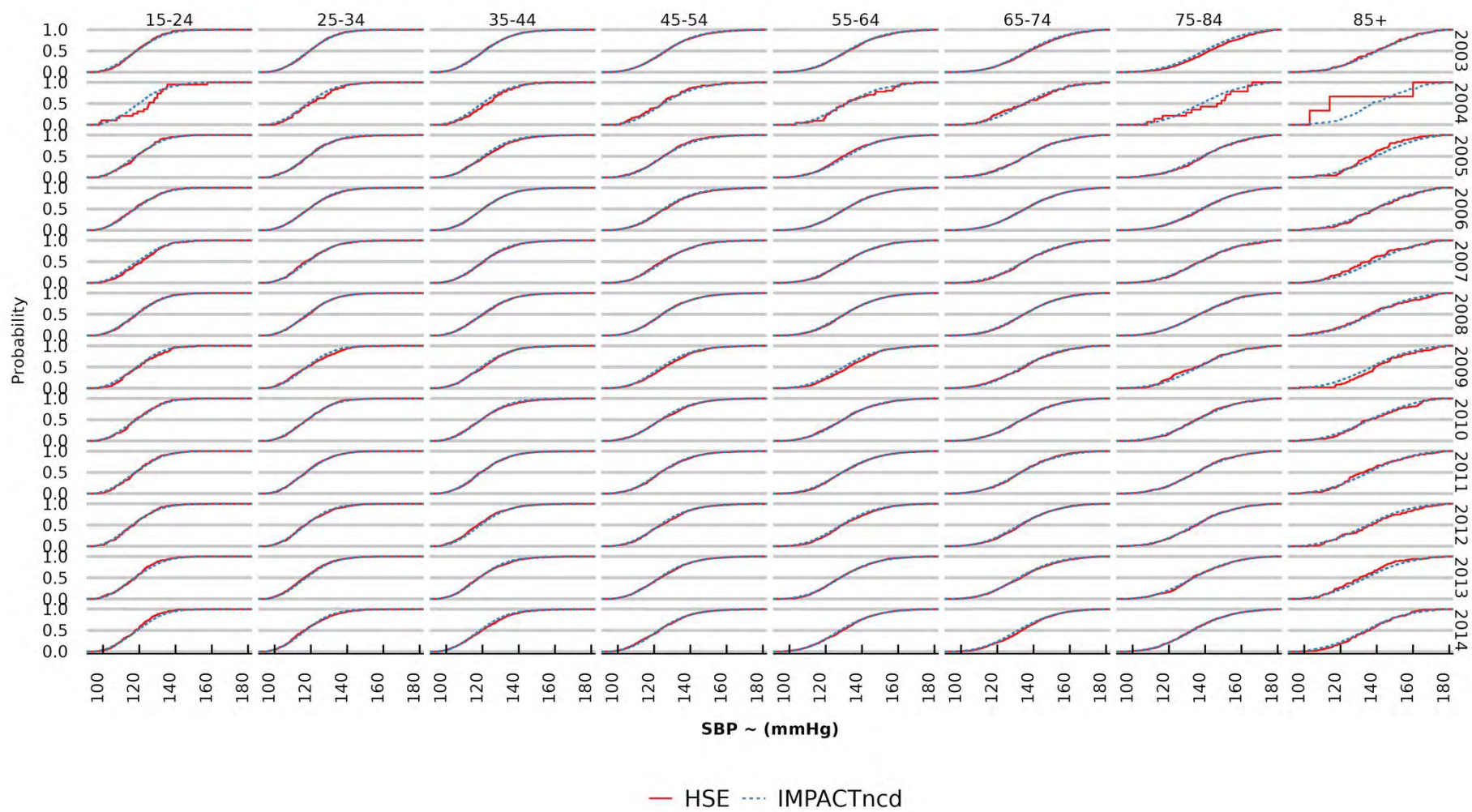
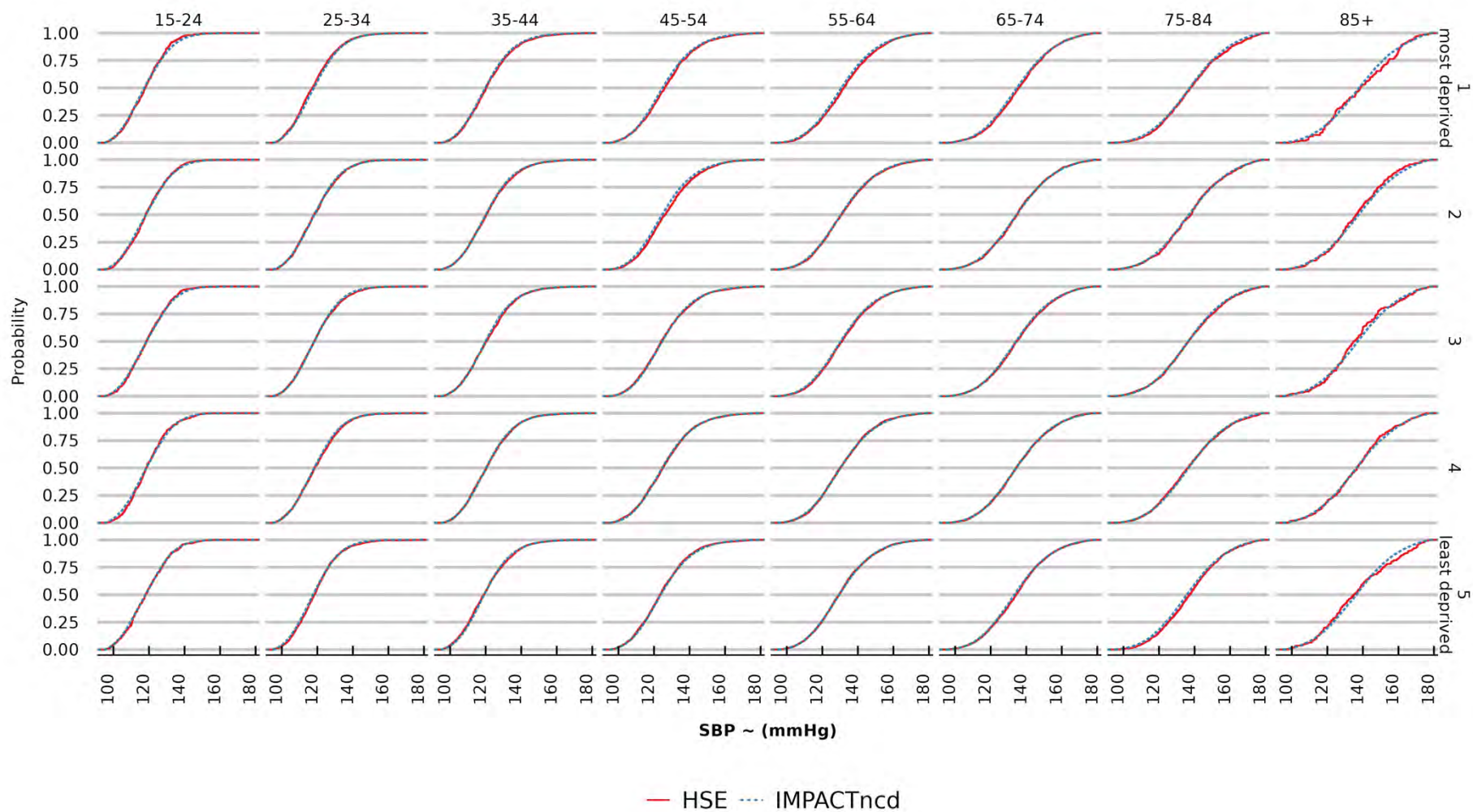


Figure B-12 - Validation: Systolic blood pressure by quintiles of IMD and age group



# Total cholesterol

Figure B-13 - Validation: Total cholesterol – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

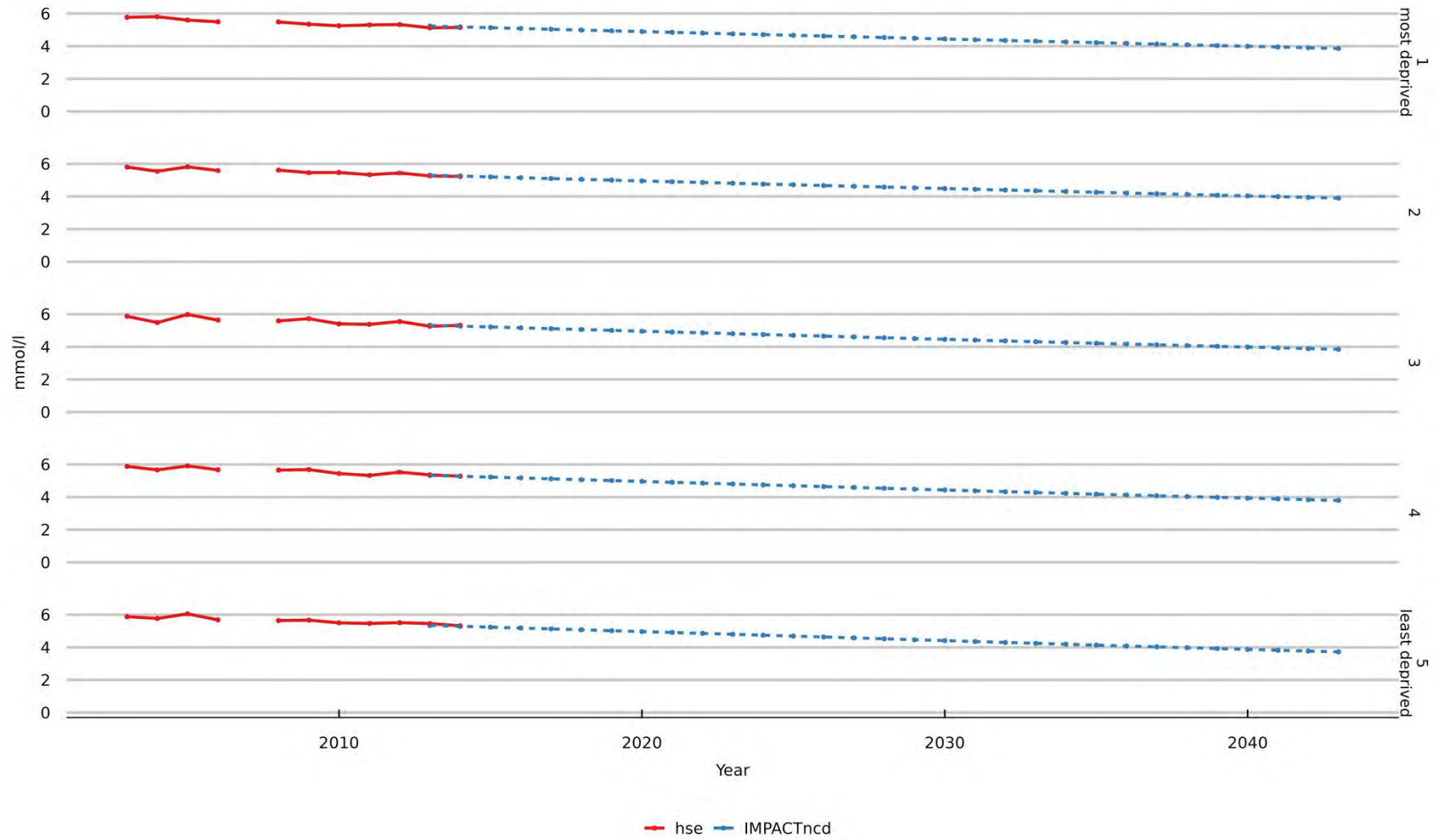




Figure B-14 - Validation: total cholesterol by year and age

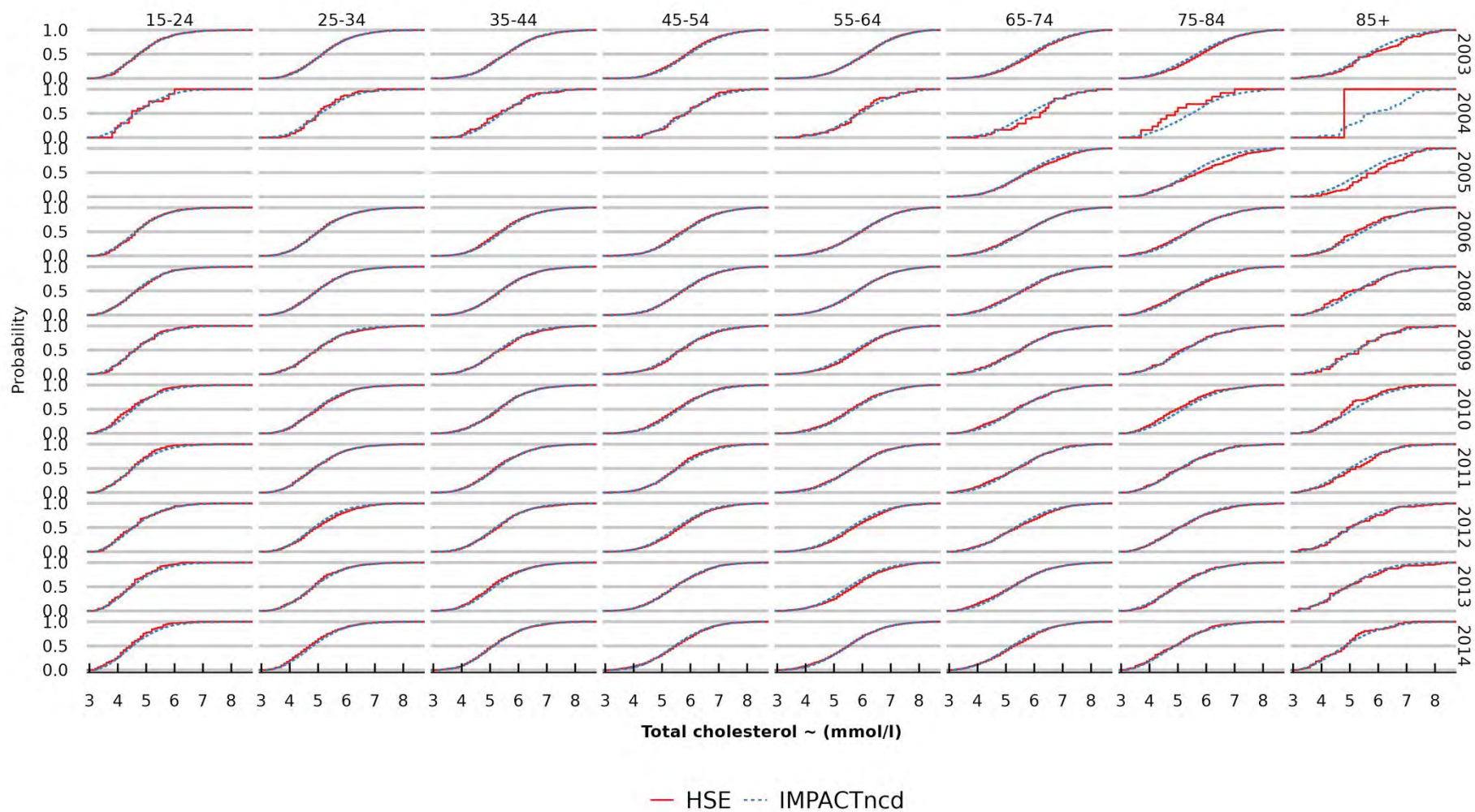
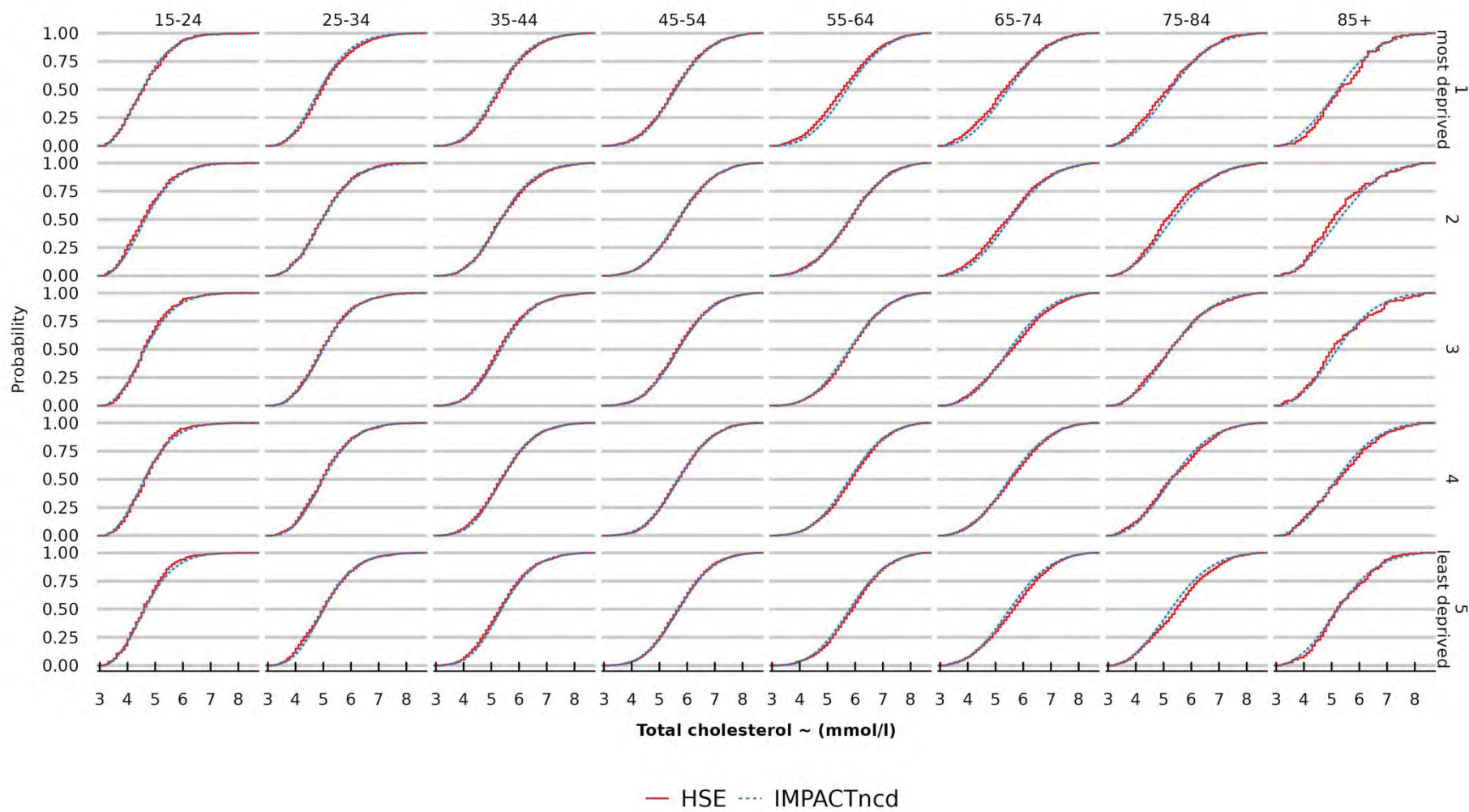


Figure B-15 - Validation: total cholesterol by quintiles of IMD and age





# Fruit intake

Figure B-16 - Validation: fruit intake (portions per day) by year and age

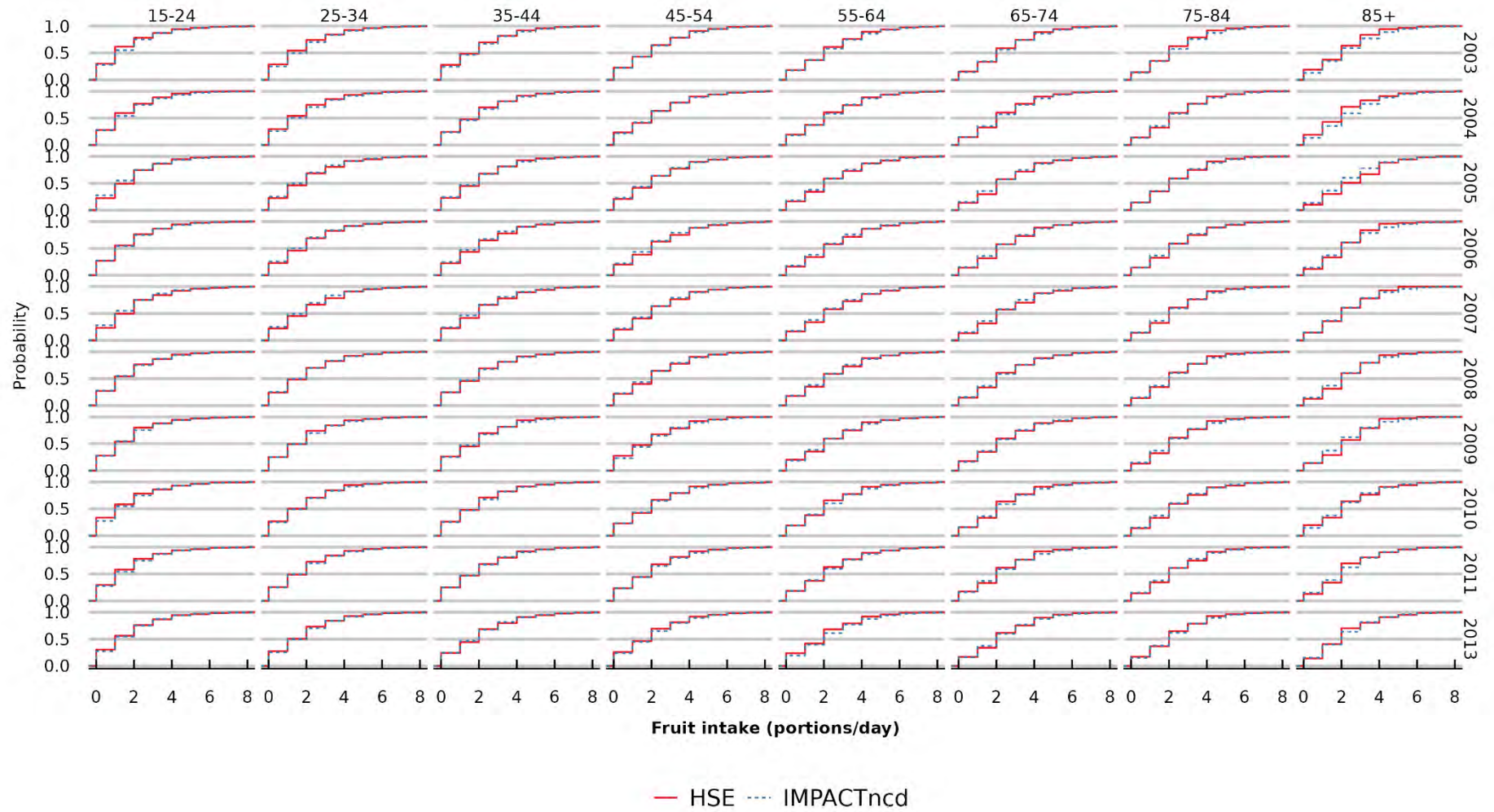
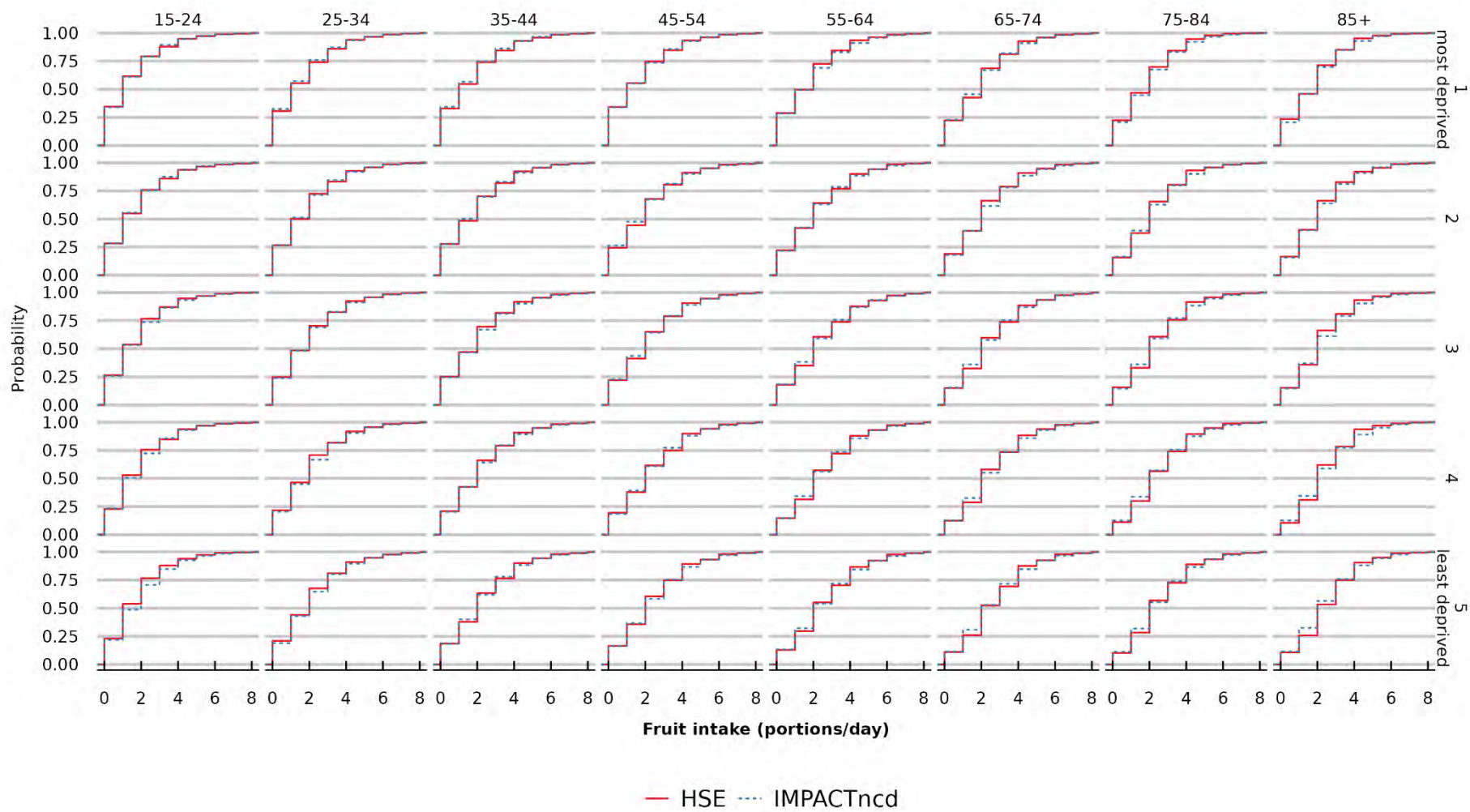


Figure B-17 - Validation: fruit intake (portions per day) by quintiles of IMD and age



# Vegetable intake

Figure B-18 - Validation: vegetable intake (portions per day) by year and age

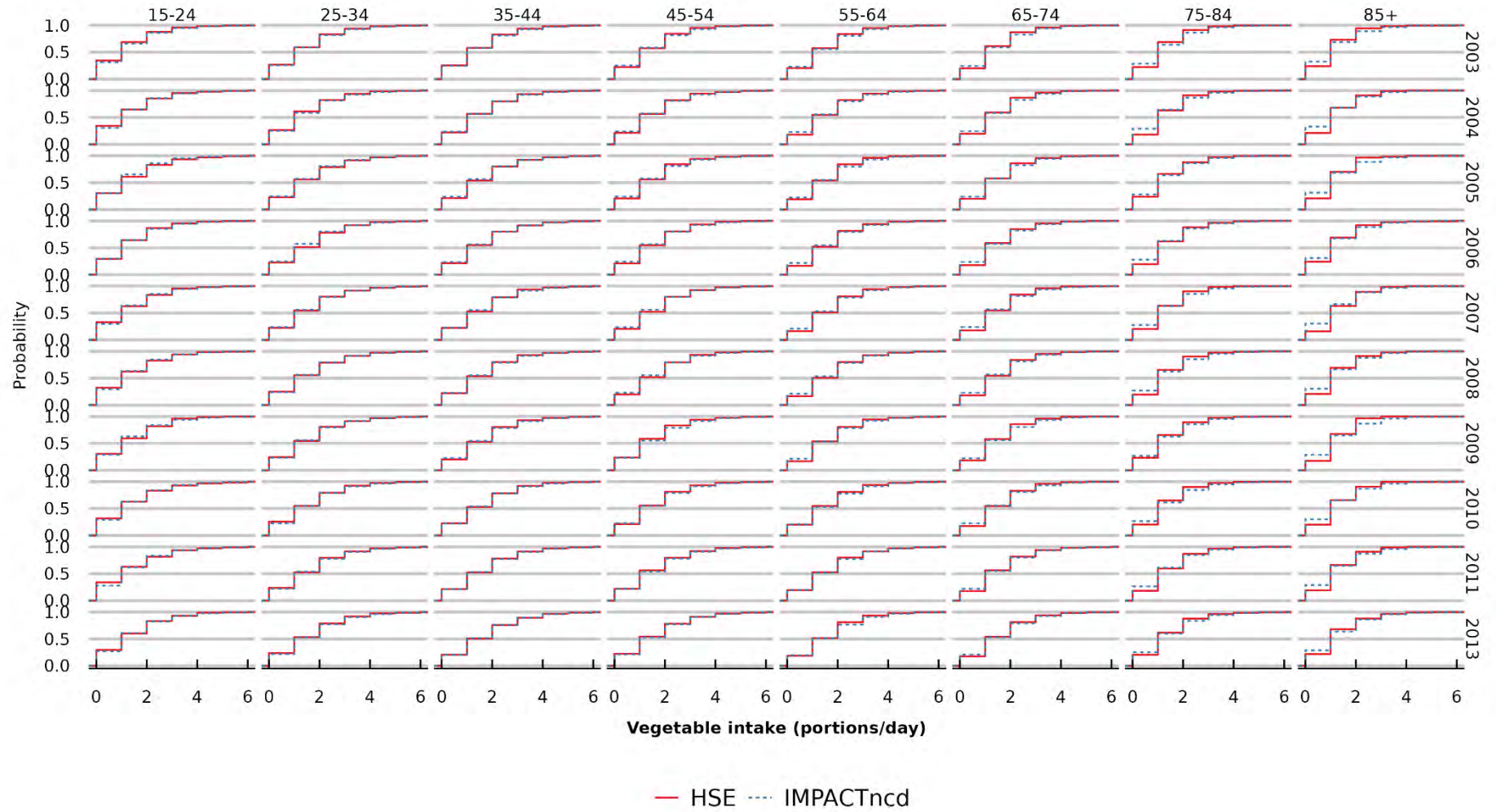
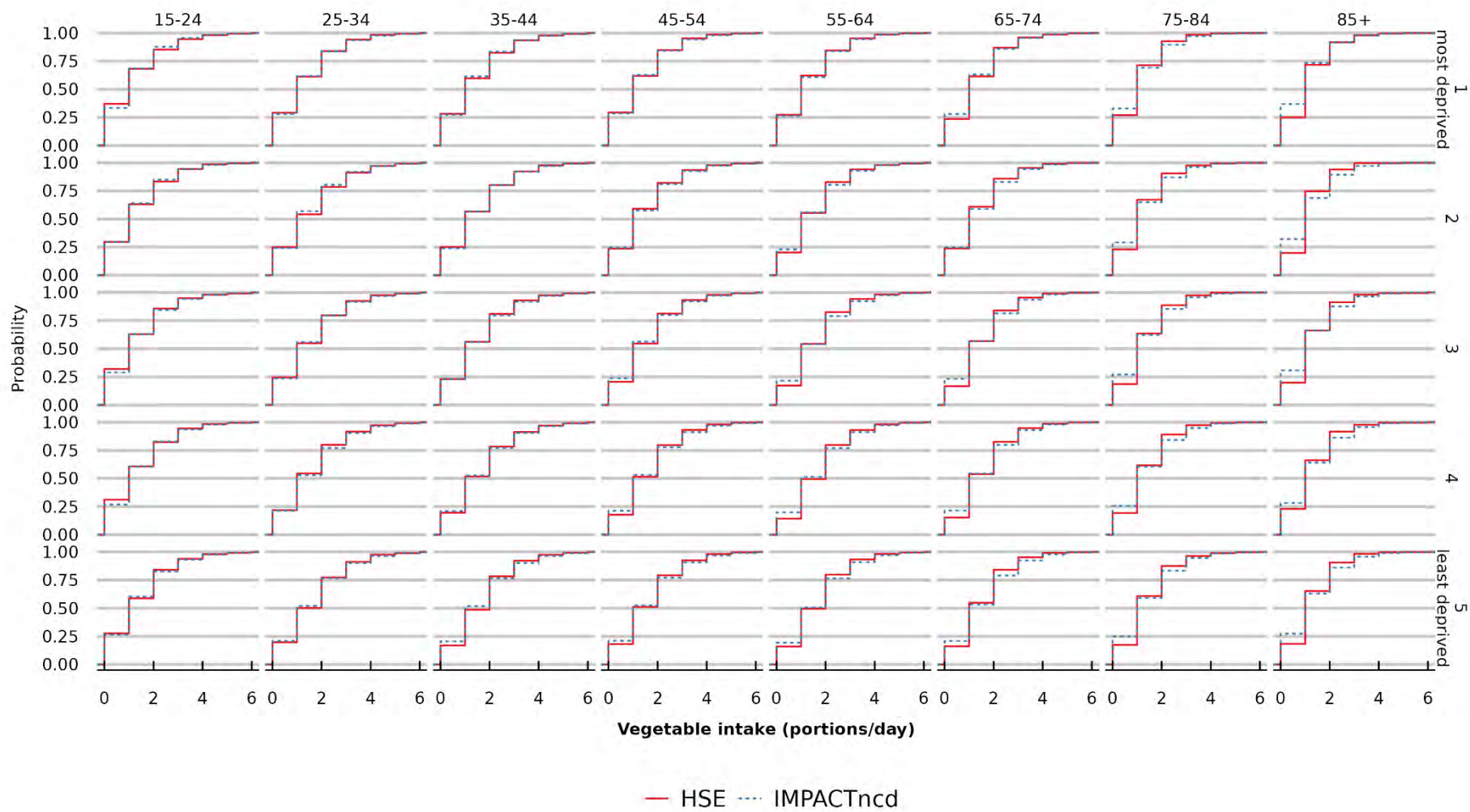


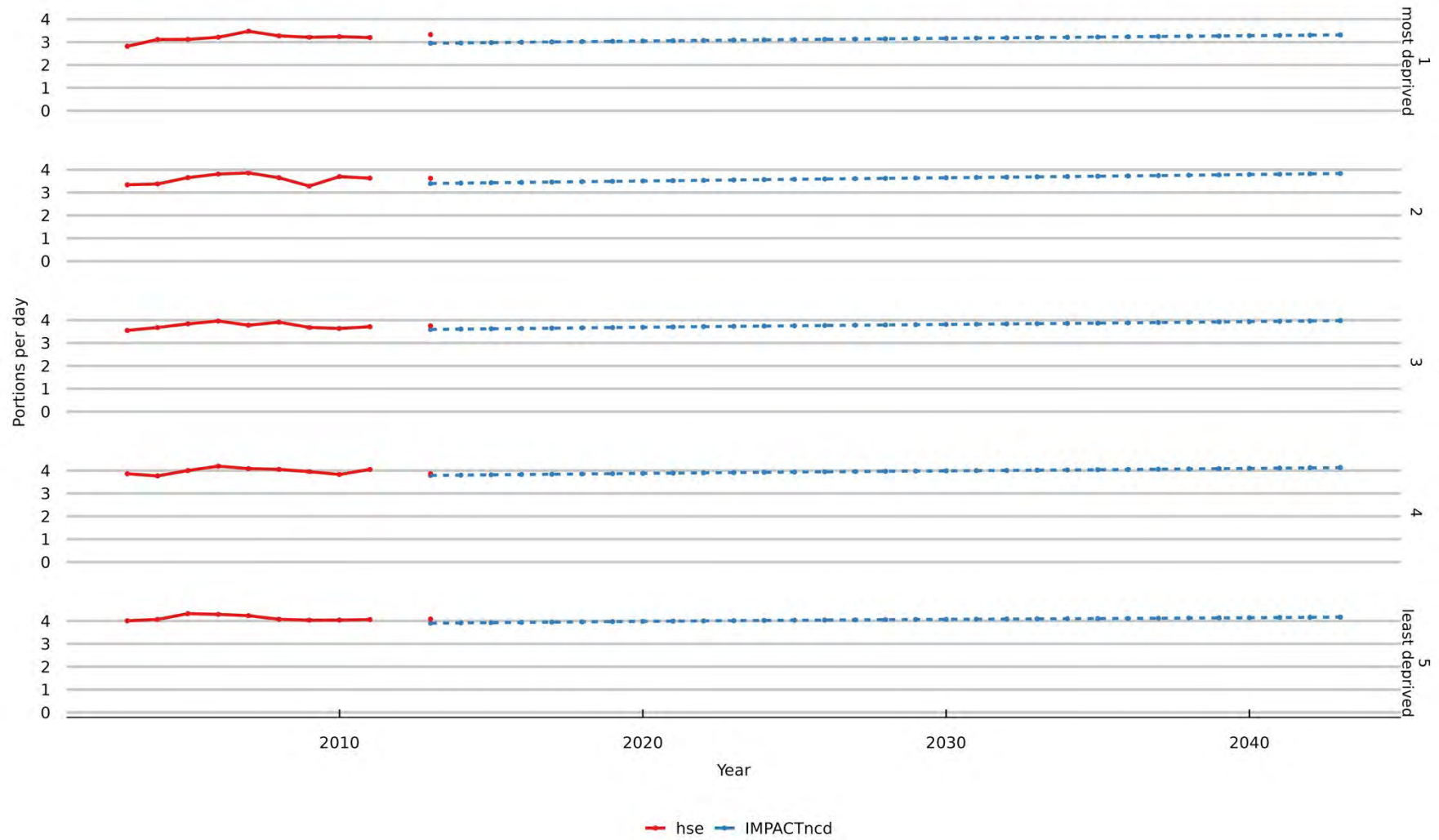


Figure B-19 - Validation: vegetable intake (portions per day) by quintiles of IMD and age



# Fruit and Vegetable intake combined

Figure B-20 - Validation: Fruit and vegetable intake – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)



Statin prescriptions

Figure B-21 - Validation: statins prescriptions by year and age

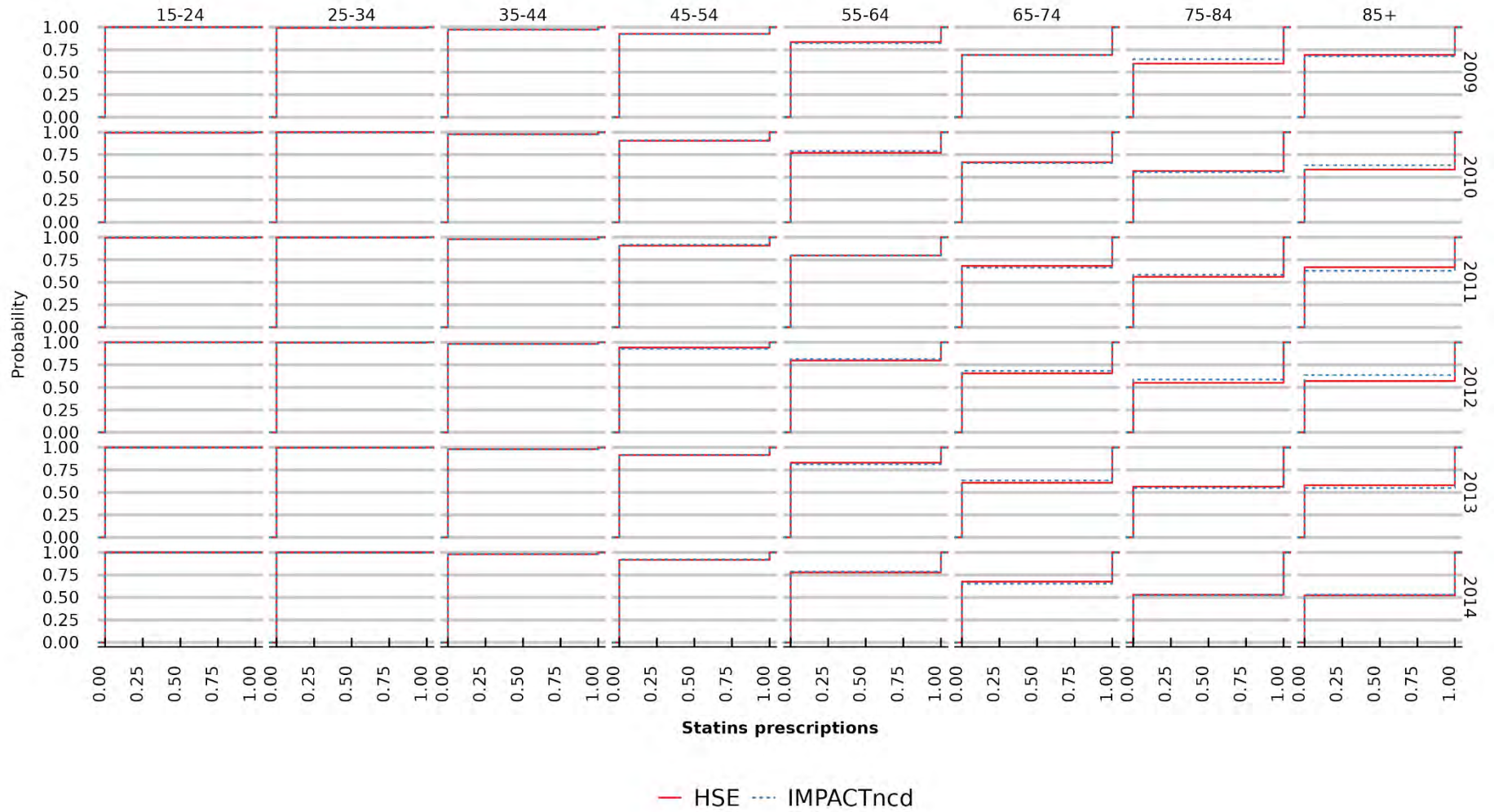
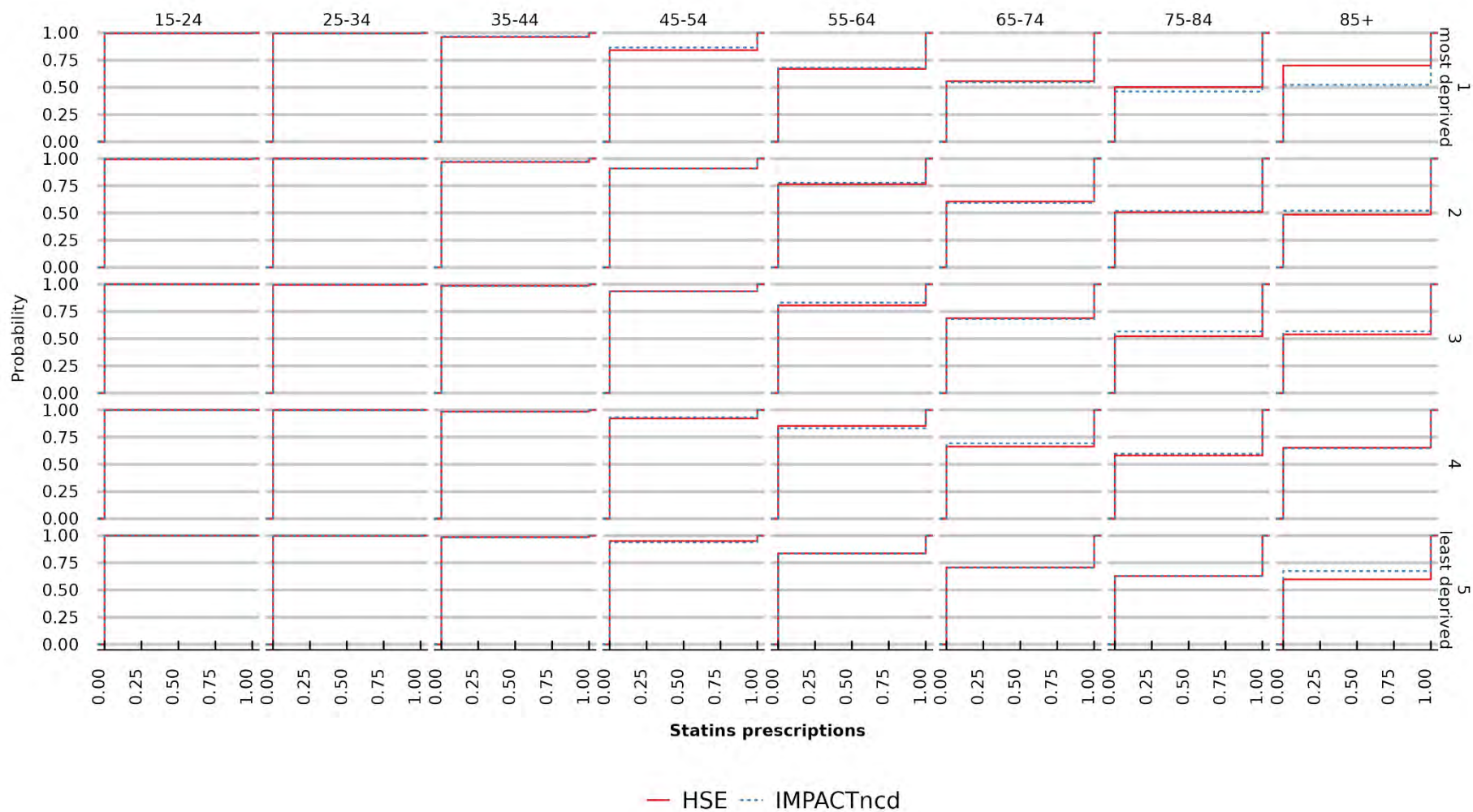


Figure B-22 - Validation: statins prescriptions by quintiles of IMD and age





Number of cigarettes smoked (ex-smokers)

Figure B-23 - Validation: Number of cigarettes smoked by year and age group in ex-smokers

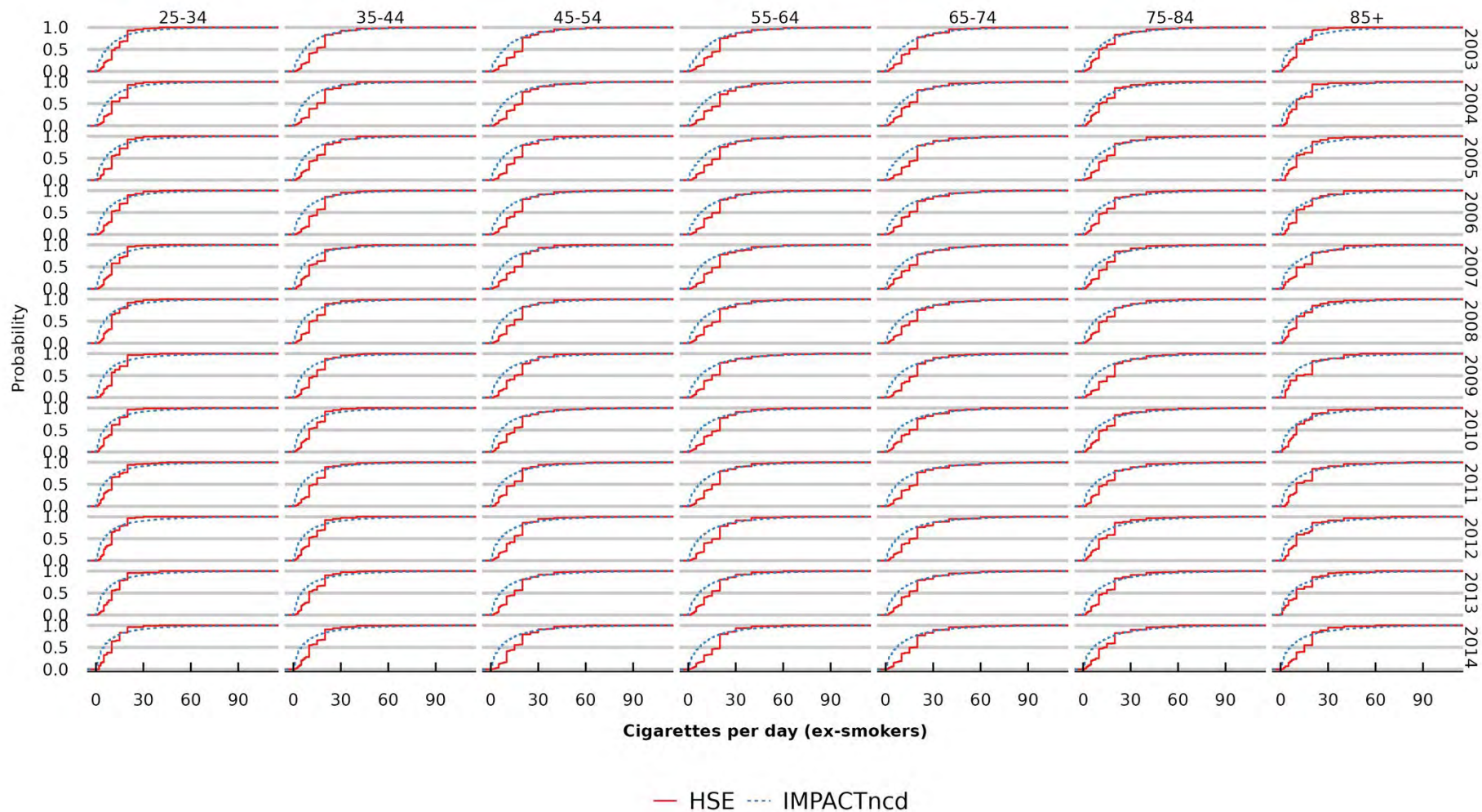
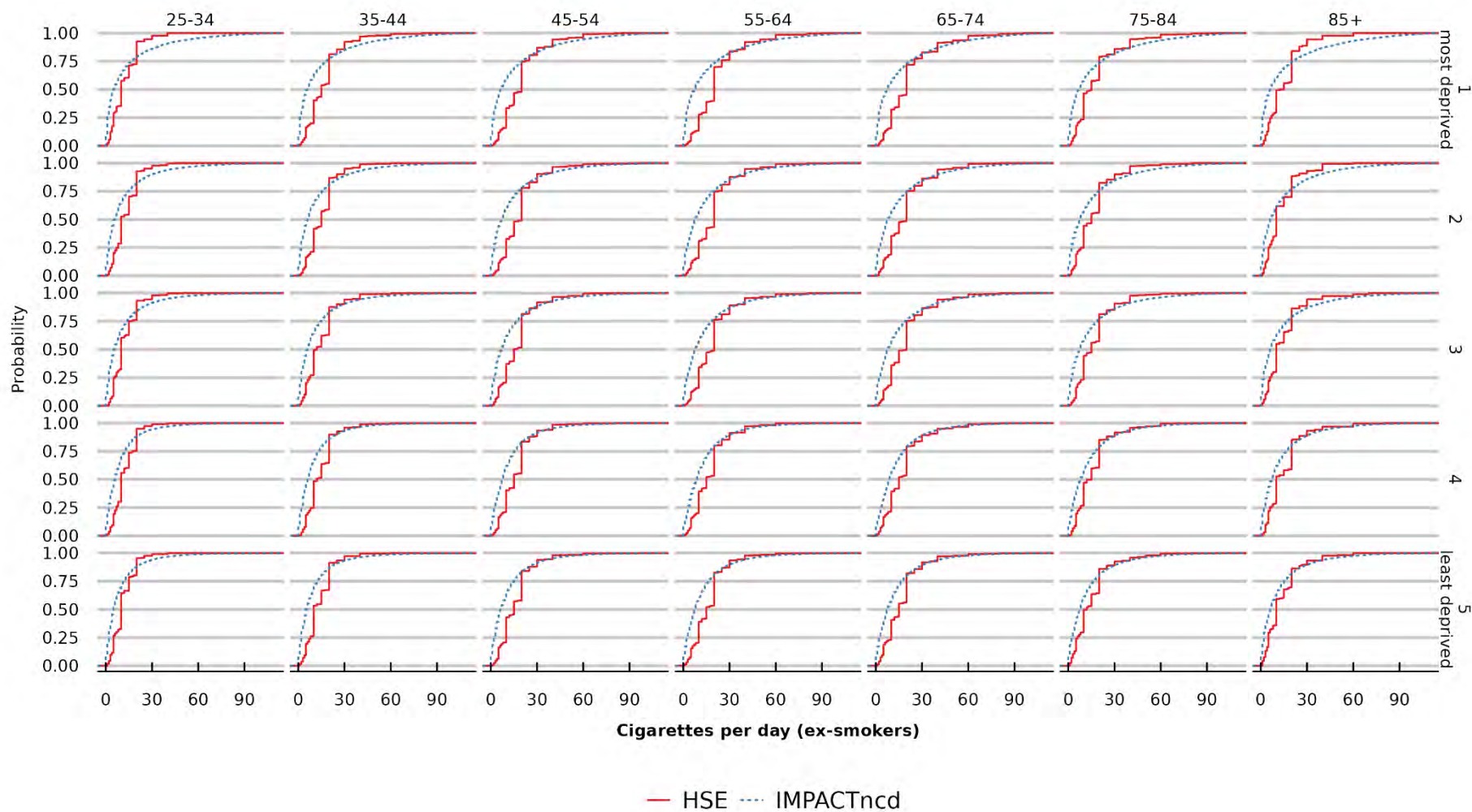




Figure B-24 - Validation: Number of cigarettes smoked by quintiles of IMD and age group in ex-smokers



# Number of cigarettes smoked (current smokers)

Figure B-25 - Validation: Number of cigarettes smoked by year and age group in current smokers

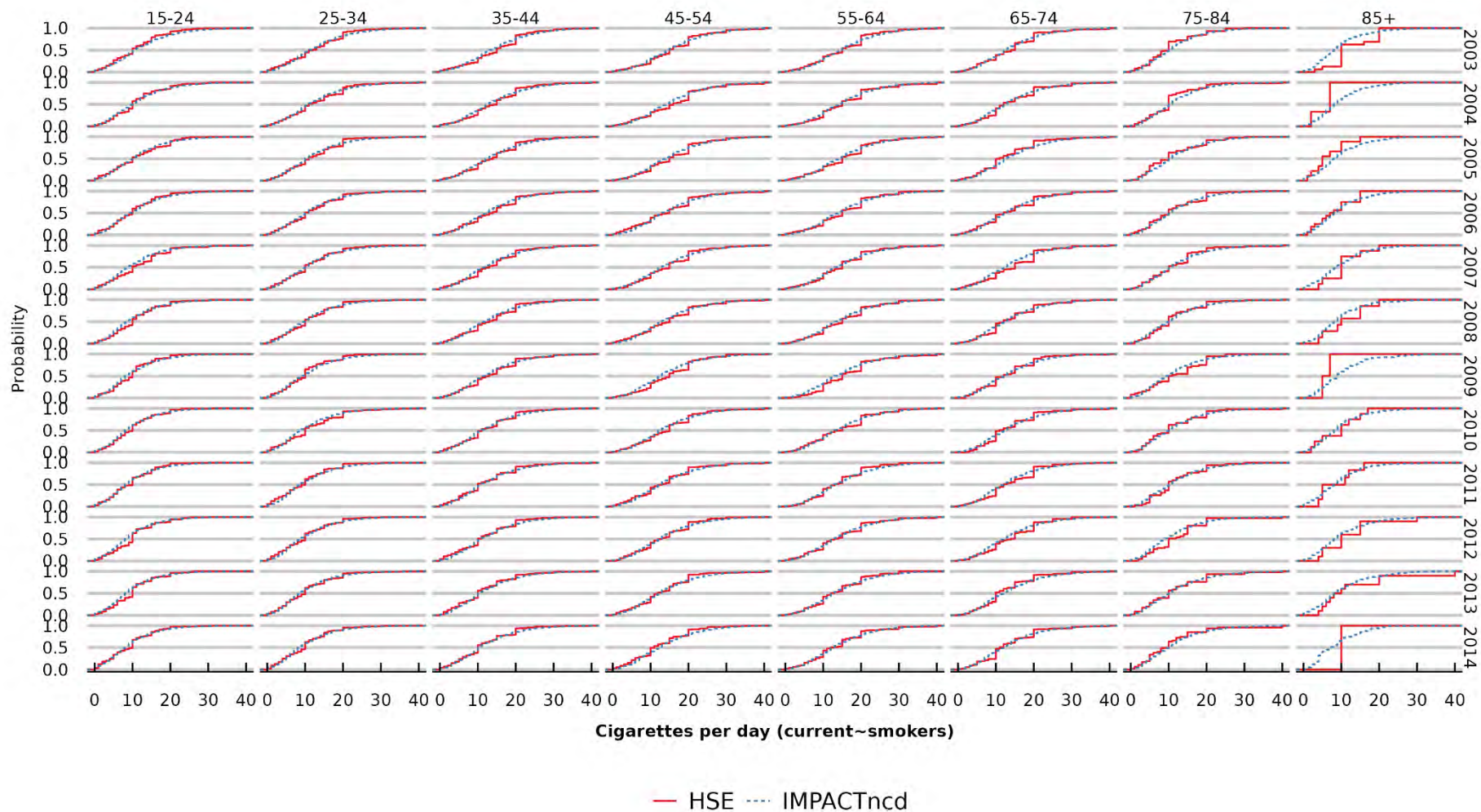
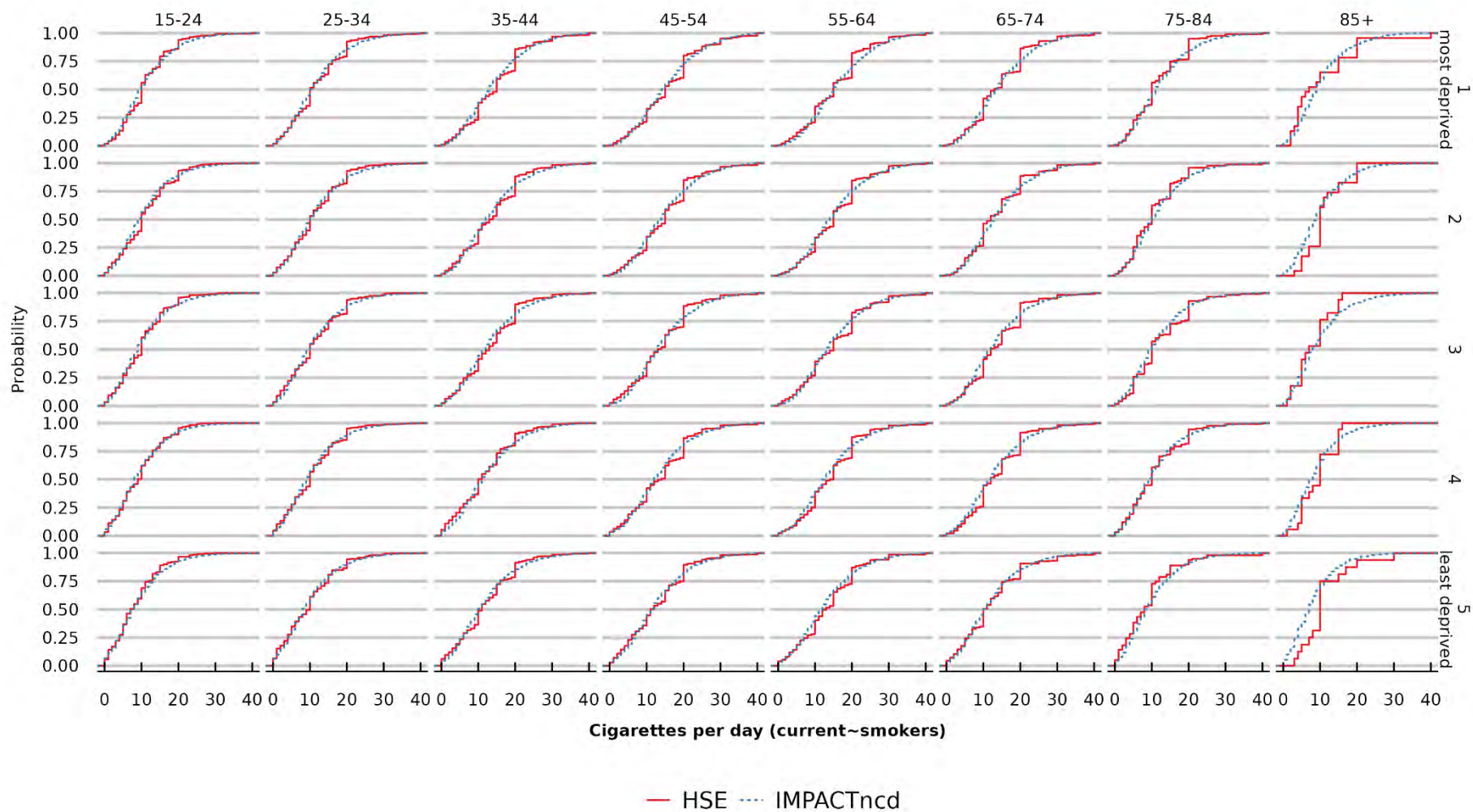


Figure B-26 - Validation: Number of cigarettes smoked by quintiles of IMD and age group in current smokers





# Smoking status

Figure B-27 - Validation: Proportion of active smokers – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

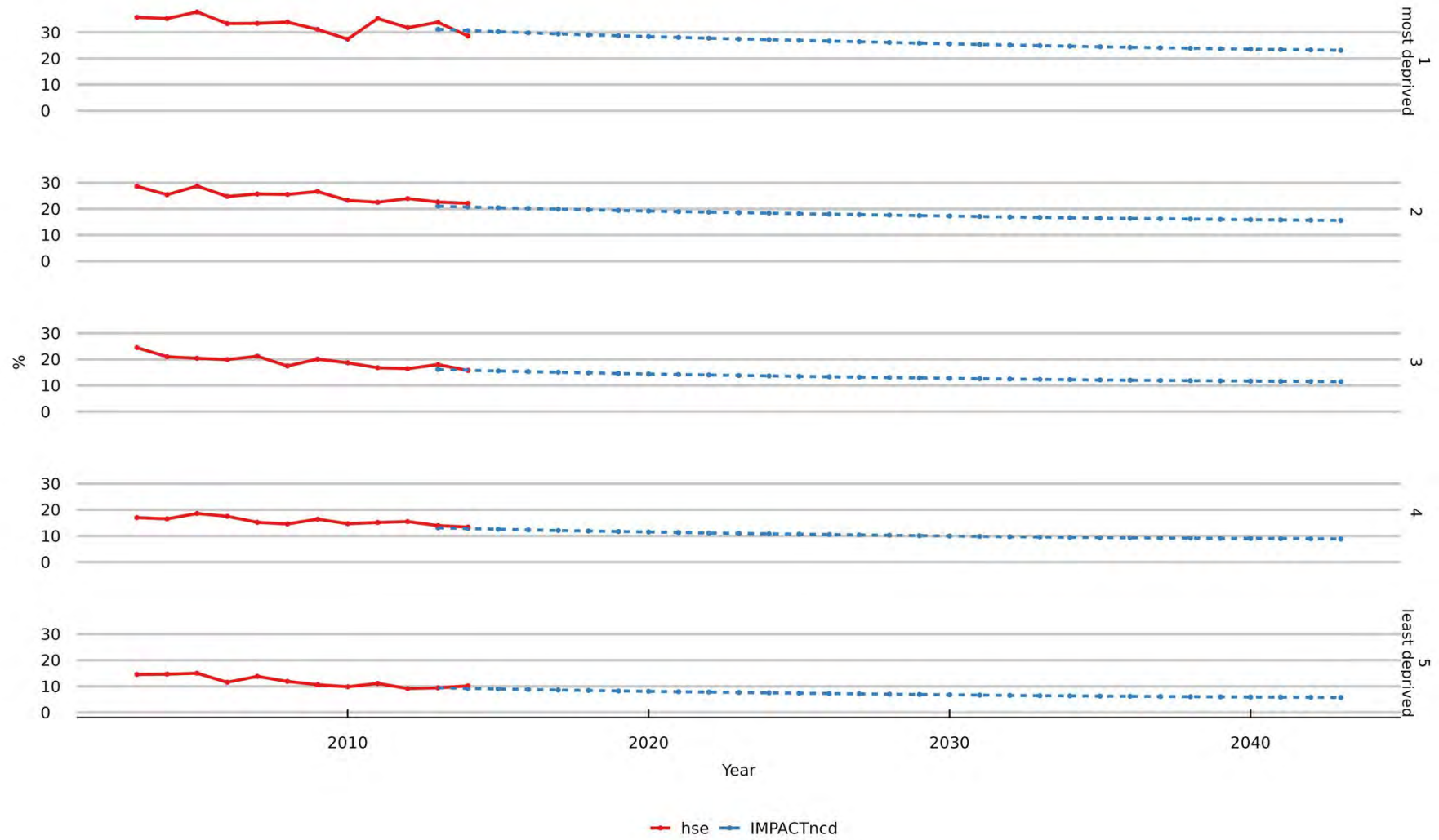


Figure B-28 - Validation: Smoking status by year and age group

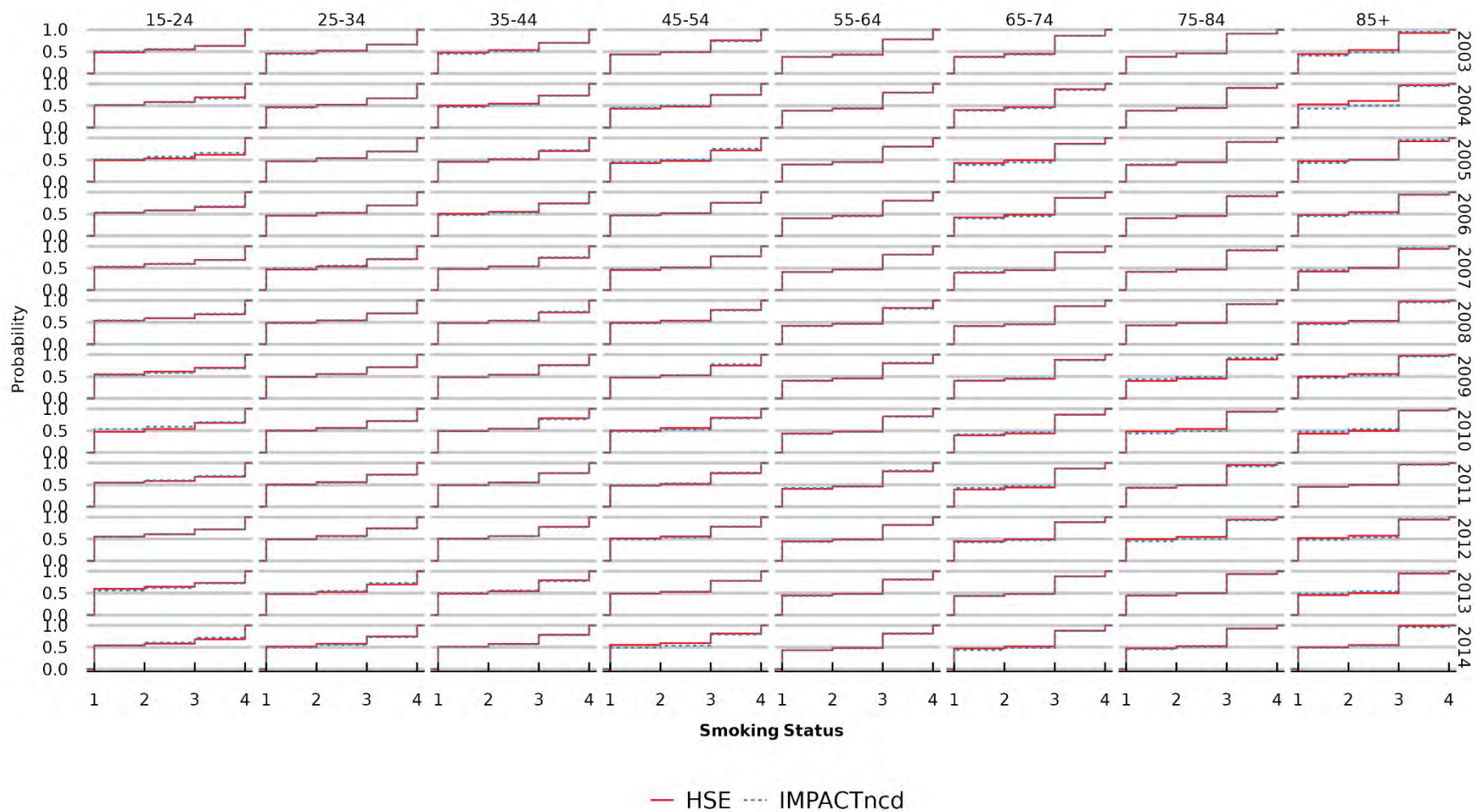
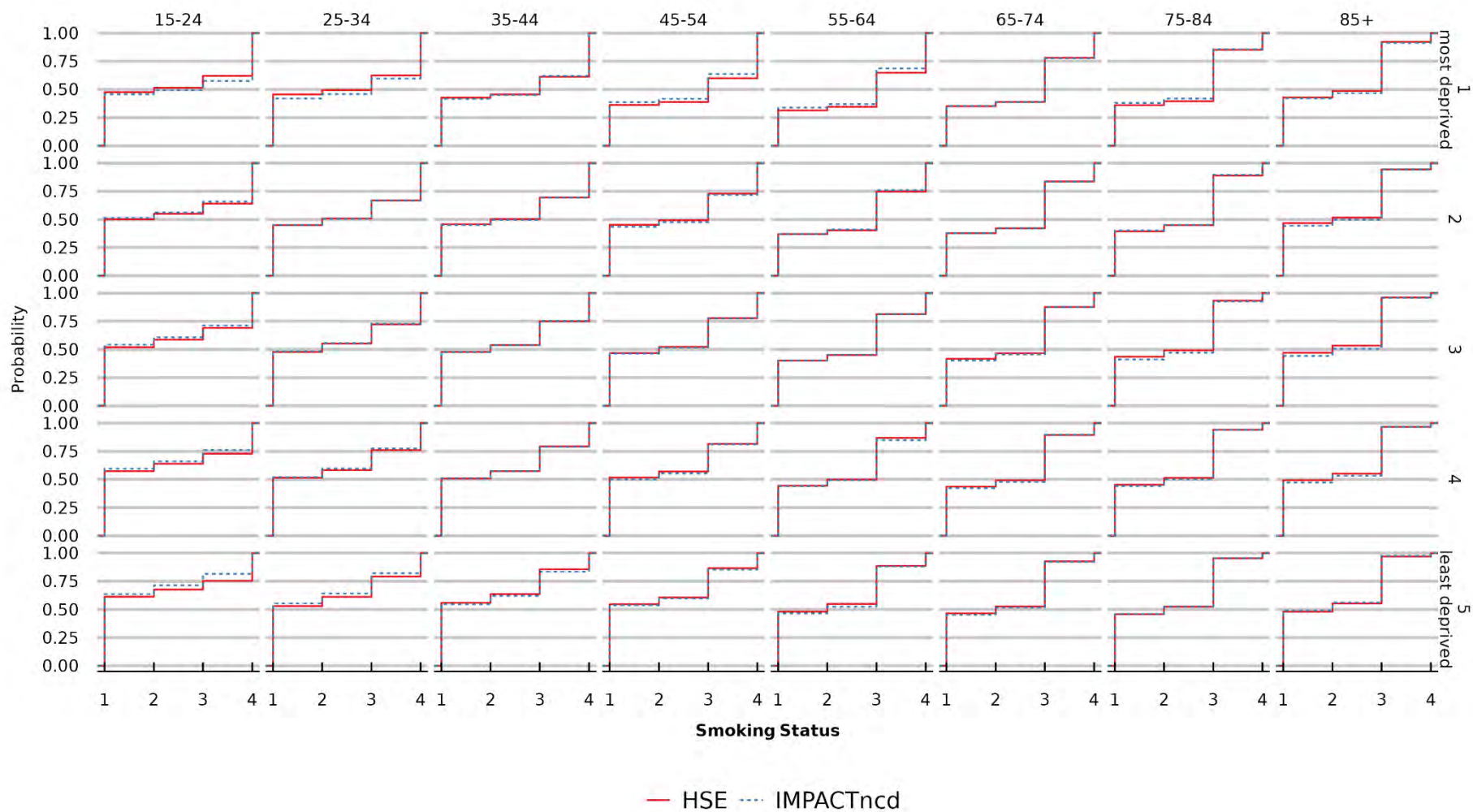


Figure B-29 - Validation: Smoking status by quintiles of IMD and age group





Years of smoking (ex-smokers)

Figure B-30 - Validation: years of smoking (ex-smokers) by year and age

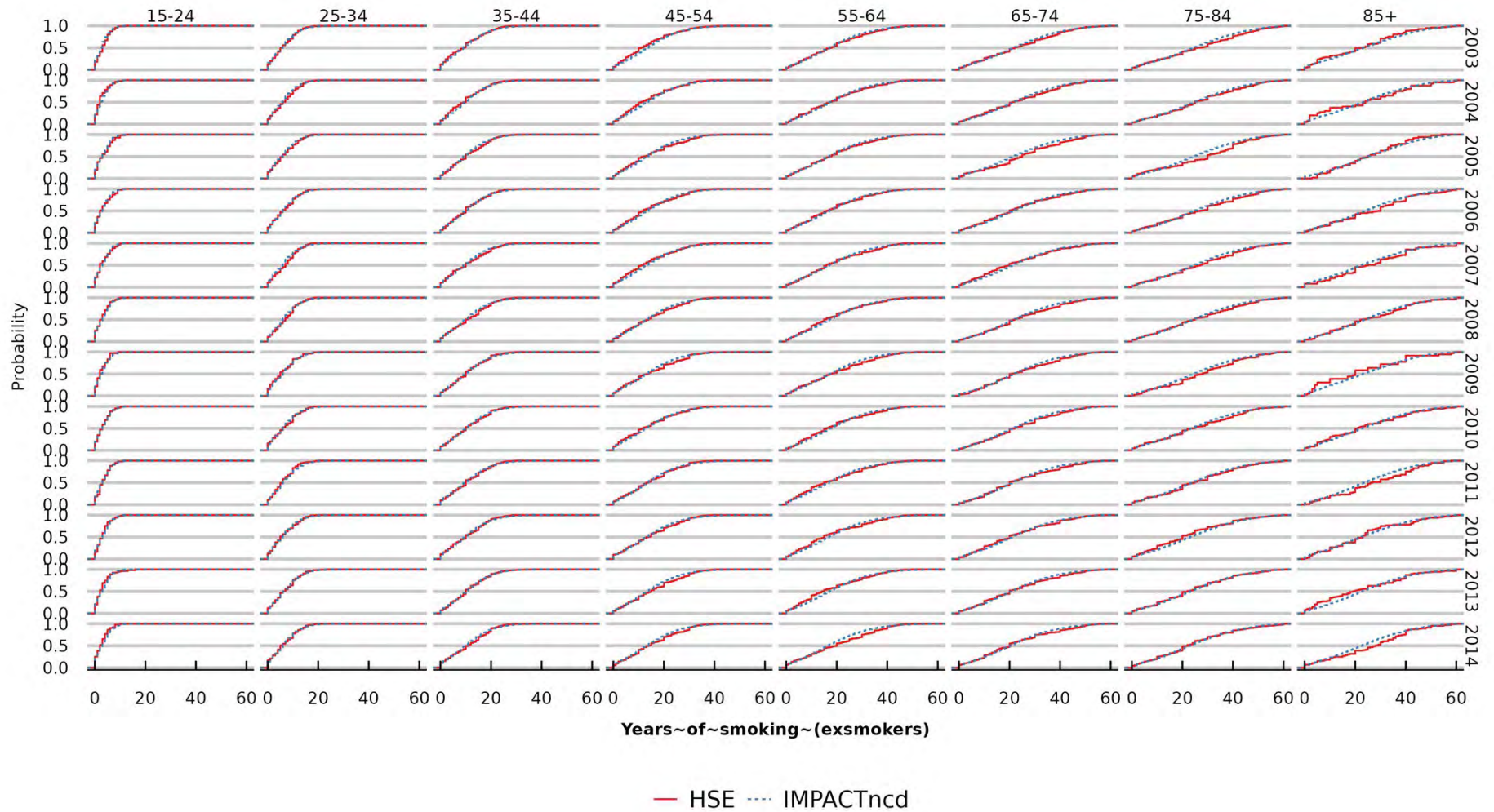
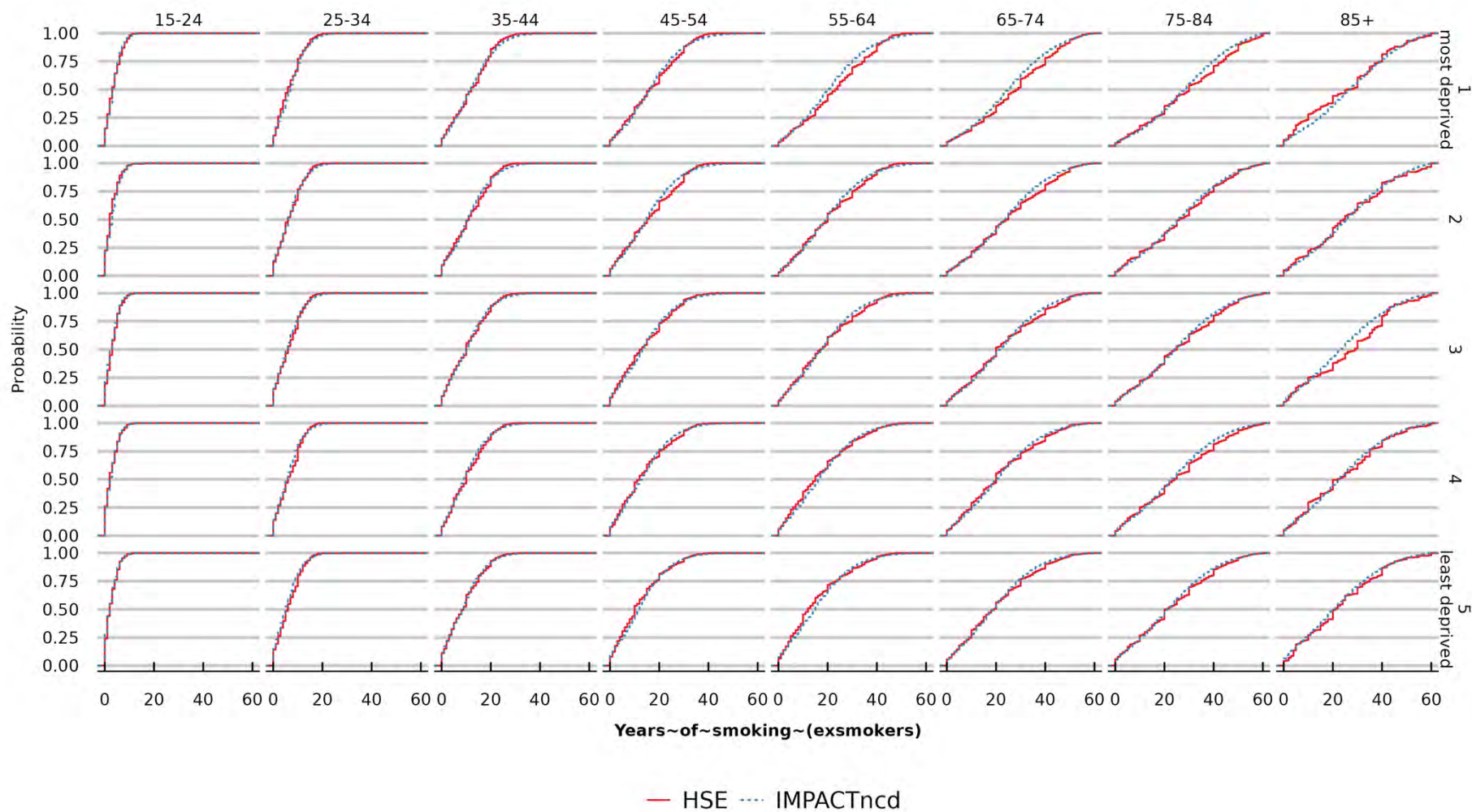


Figure B-31 - Validation: years of smoking (ex-smokers) by quintiles of IMD and age





Years of smoking (current smokers)

Figure B-32 - Validation: years of smoking (current smokers) by year and age

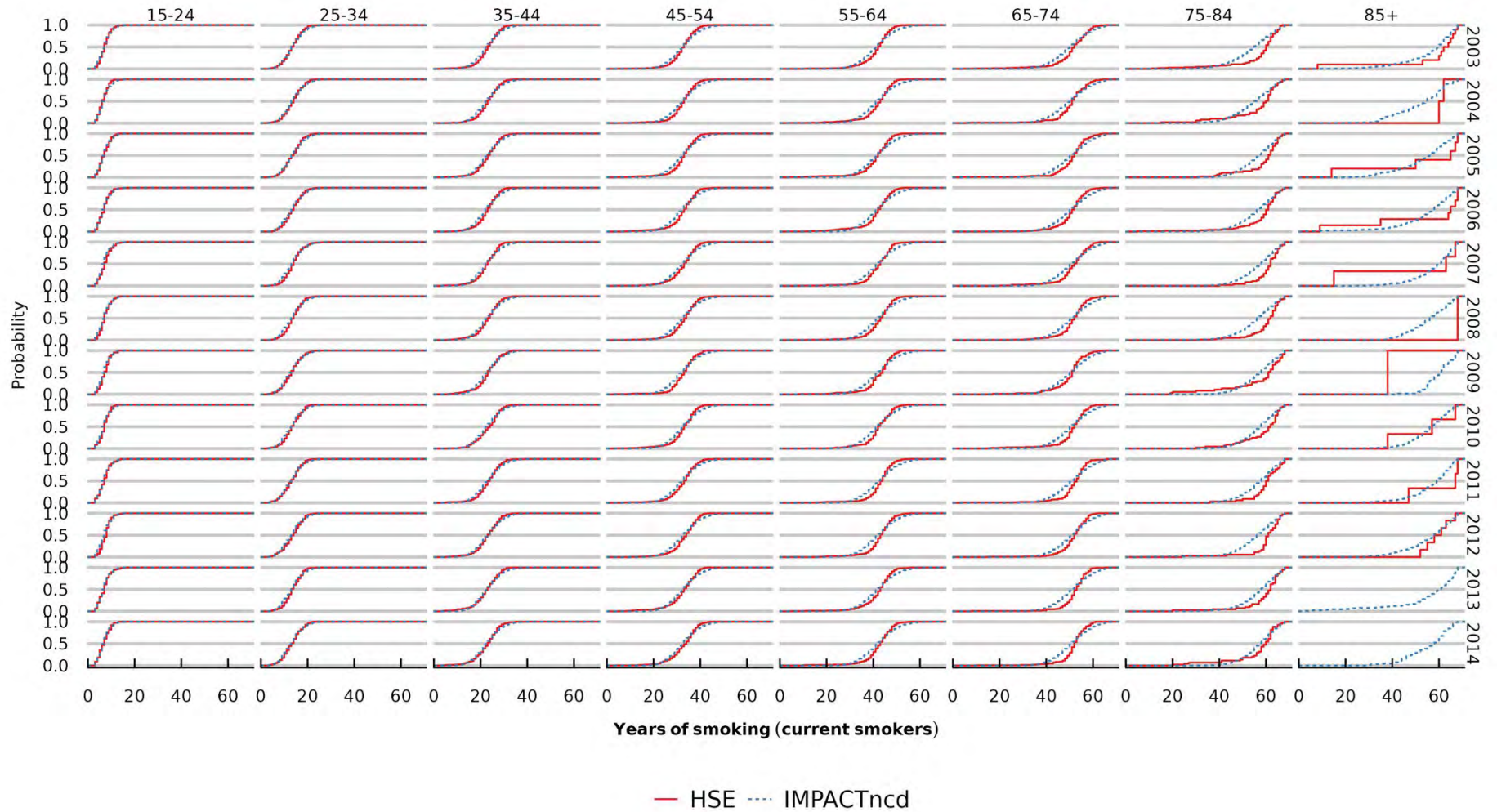
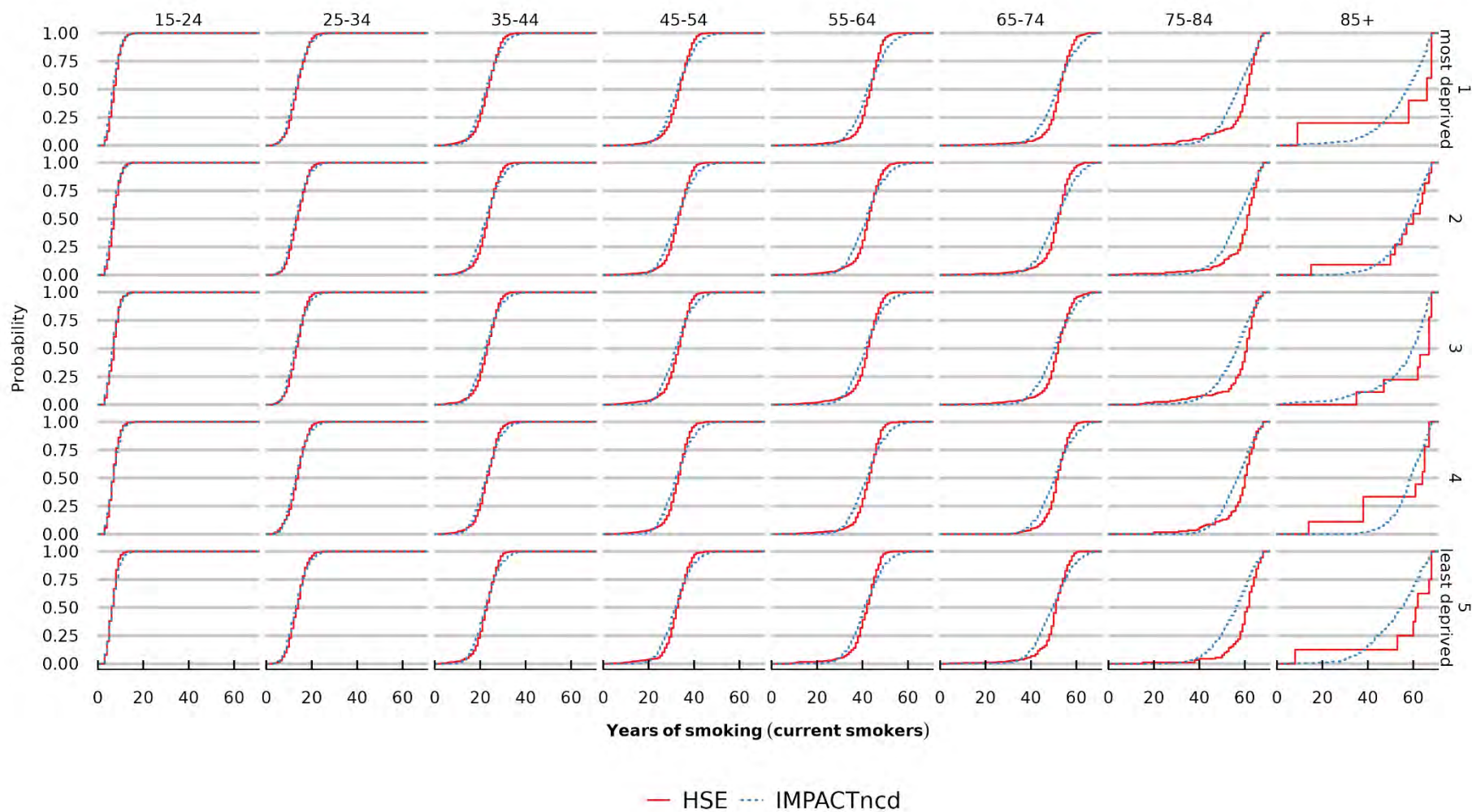


Figure B-33 - Validation: years of smoking (current smokers) by quintiles of IMD and age





Years since smoking cessation

Figure B-34 - Validation: years since smoking cessation by year and age

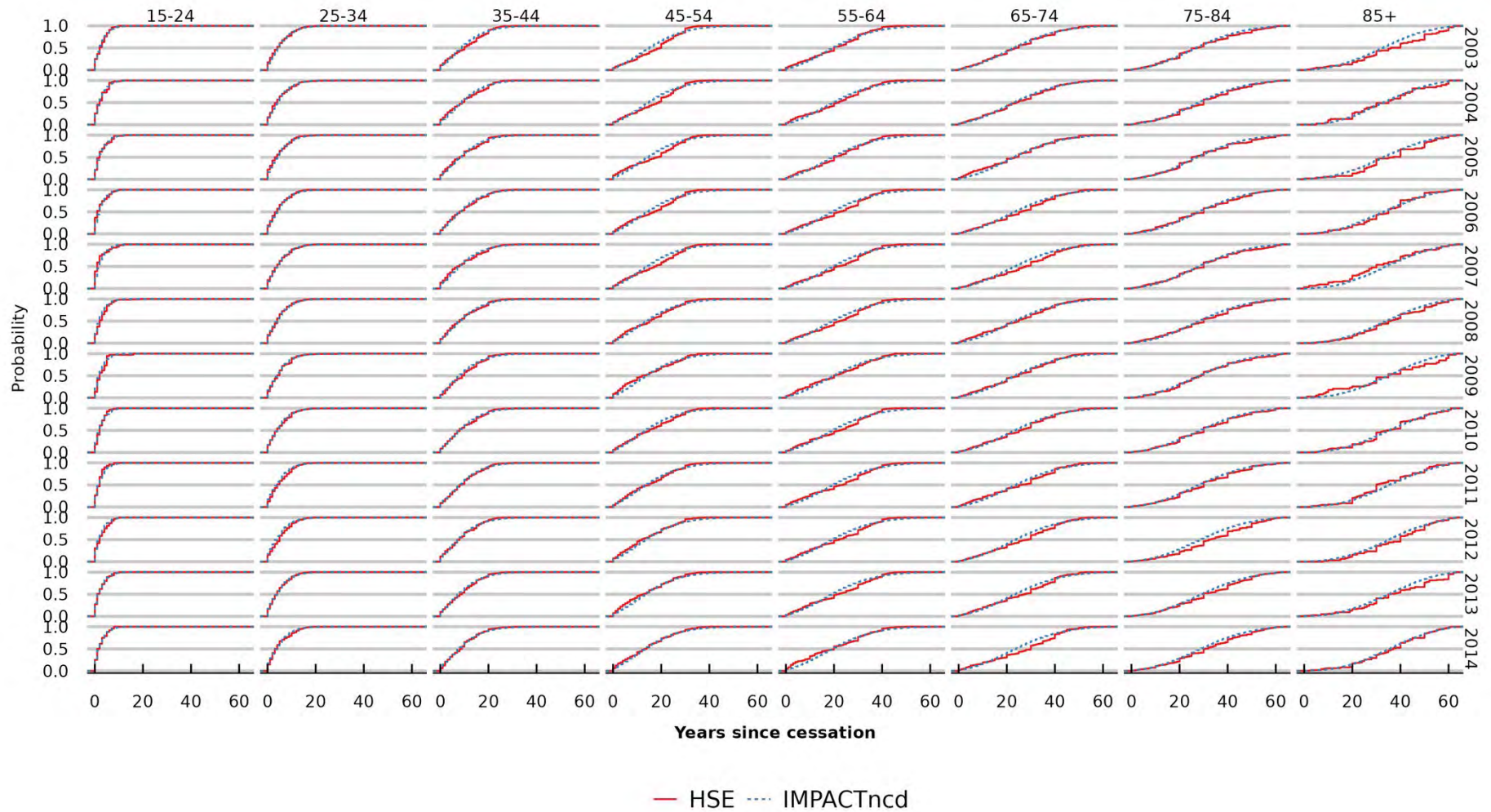
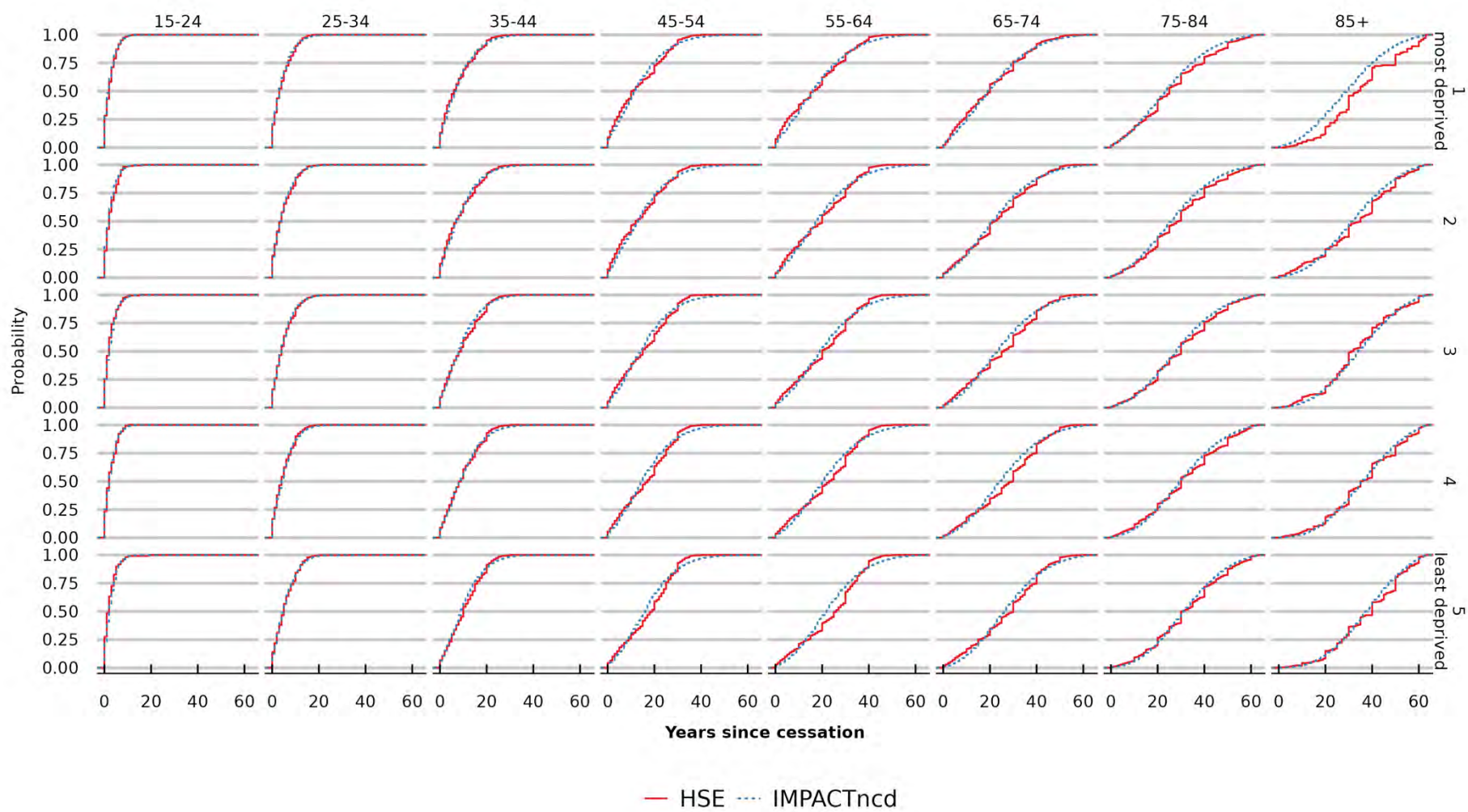


Figure B-35 - Validation: years since smoking cessation by quintiles of IMD and age



Exposure to environmental smoking

Figure B-36 - Validation: Exposure to environmental smoking – HSE and projected IMPACT<sub>NCD</sub> trends by quintile of IMD (unstandardised)

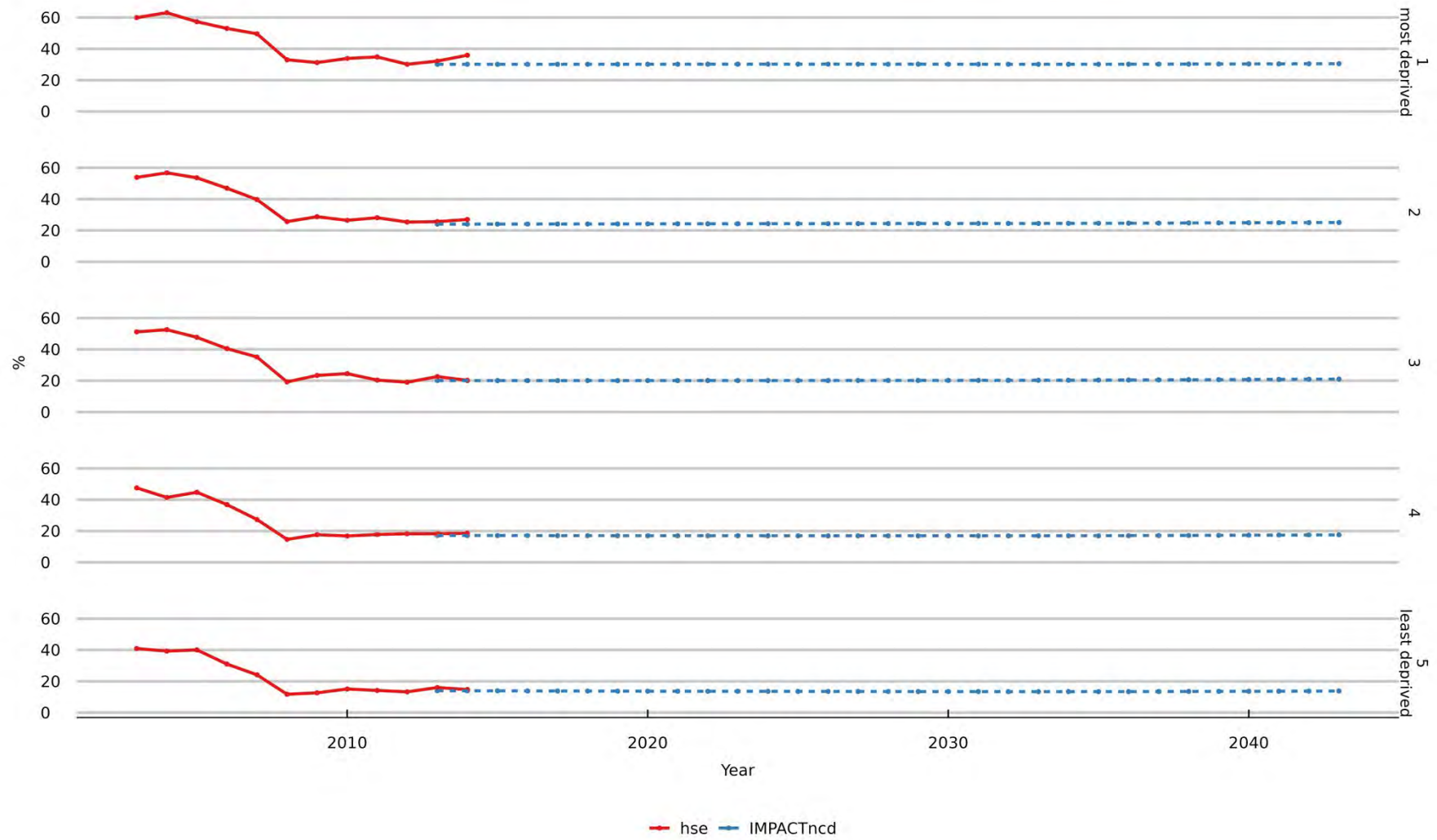




Figure B-37 - Validation: Exposure to environmental smoking by year and age group

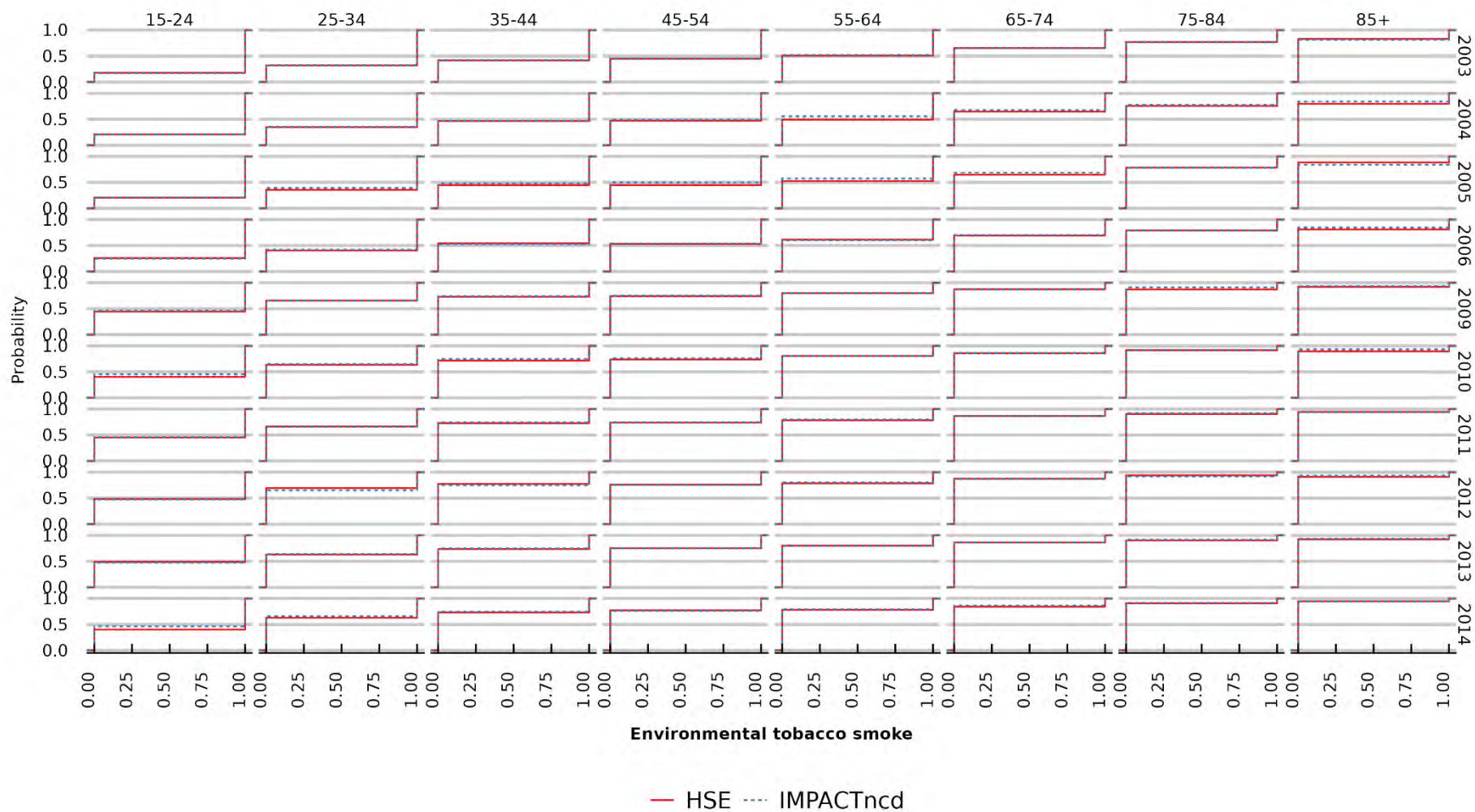


Figure B-38 - Validation: Exposure to environmental smoking by quintiles of IMD and age group

