EConDA
Economics of Chronic Diseases

Work package 7: Model validation

This report arises from the project EConDA which has received funding from the European Union in the framework of the Health Programme. Project number: 2012 12 13

Foreword

This report contains the methods and results of deliverable 07 of the EConDA project: Validation of the model.

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Abbreviations

ARIC - Atherosclerosis and Risk in Communities study

BMI – Body Mass Index

CHD - Coronary Heart Disease

CKD – Chronic Kidney Disease

COPD – Chronic Obstructive Pulmonary Disease

CVD - Cardiovascular Disease

DPP – Diabetes Prevention Programme

DYNAMO-HIA - Dynamic Model for Health Impact Assessment

EConDA - The Economics of Chronic Diseases

FEV1 - Forced Expiratory Volume in one second

GDP - Gross Domestic Product

GP – General Practitioner

HCA – Human Capital Approach

HERG - Health Economics Research Group

ICERs - Incremental Cost Effectiveness Ratios

IFs – International Futures (IFs) modelling system

IGT - Impaired Glucose Tolerance

MI – Myocardial Infarction

NDNS – National Diet and Nutrition Survey

NICE – National Institute for Health and Care Excellence

NPHS - National Population Health Survey

NPV – Net Present Value

NRT - Nicotine replacement therapy

OECD – Organisation for economic Co-operation Development

ONS – Office for National Statistics

OPE – Own Price Elasticity

PE – Price Elasticity

PPP - Purchasing Power Parity

QALYs - Quality Adjusted Life Years

ROI – Return on investment

RR - Relative Risks

SCS – Smoking Cessation Services

SSB – Sugar Sweetened Beverage Tax

T2DM – Type 2 Diabetes

UKHF – UK Health Forum

WHO – World Health Organisation

WP – Work Package

Introduction

The aim of Work Package (WP) 7 is to validate the epidemiological and economic microsimulation model and tool that were developed for the EConDA project in WP5 and 6.

There are five main validation methods (1): face validity, verification, cross validity, external validity and predictive validity. Face validity describes the extent to which the model structure and assumptions have been agreed by experts in the field. Verification checks that the implementation of the assumptions has been carried out correctly. Cross-validation is the comparison of the model outcomes with other published models. External validation compares the model outcomes with the results from a real experiment. Finally, predictive validity involves comparing forecasted outcomes with the actual outcomes several years later.

Face validity and cross-validation have been chosen for this work package. External validation, predictive validity and verification were beyond the scope the project due to the computer power required to calculate these estimates within a microsimulation. For each model or tool comparison, differences in terms of methods, data, intervention and results are discussed at the end of the report.

Face Validity Method: Why microsimulation?

Face validity is a way of validating the modelling methods and assumptions with experts in the field. The EConDA model uses a microsimulation model and the EConDA tool uses a deterministic method applied to a weighted cohort population.

The microsimulation method has been highlighted as the best method for risk factor and chronic disease modelling by the OECD as referenced in their report 'Toward a New Comprehensive International Health and Health Care Policy Decision Support Tool' (2). They state that the 'Foresight Obesity model, developed by the UK National Heart forum[1], is one of the most detailed models available on obesity and related health outcomes and costs'. The EConDA model developed in this project builds on the foresight obesity model (1) described by the OECD.

What is microsimulation?

Microsimulation methods simulate a virtual population. They represent a heterogeneous population by reproducing the characteristics and behaviour of a large sample of individuals from a specific country. The data used in the model will be the most recent and reliable data, which includes population demographics, risk factor status, disease incidence and mortality. The combination of these datasets can be combined and modelled in order to overcome gaps in existing knowledge. Certain characteristics can evolve over the life course of the model, such as the number of new births or changes in exposure to risk factors.

Strengths of microsimulation models

Microsimulation models have a number of strengths over other modelling methodologies. These include:

- enabling the testing of the potential impacts of policies and practices through 'what if scenarios' e.g. what is the expected impact on CVD incidence following the implementation of a tobacco escalator tax

- Time, cost and ethical advantages of using simulation models over experiments, which are not possible with population level policy interventions

- Enabling comparisons of a wide set of interventions to ultimately identify the most promising combinations of prevention (including policy interventions), screening and treatment approaches for different types of patients (as was one of the objectives in the EConDA project [econdaproject.eu])

- Going beyond the follow-up periods of typical clinical trials so that long-term outcomes can be compared and predicted 10, 20, or even 50 years into the future

[1] Note, the UK Health Forum was formally named the National Heart Forum

- Going beyond the typical narrow definitions of study outcomes, and accounting for an array of outcomes relevant to real-world settings where patients are complex and remain at risk of developing a wide range of disease conditions (i.e. accounting for comorbidities)

- Helping to inform and persuade decision makers to make the best, evidence-based choices possible.

Disadvantages of microsimulation models

There are a number of disadvantages associated with microsimulation modelling. These include:

- The intensiveness of the data collection process: data describing the disease, risk factor and population are required at a suitable age and sex stratification.
-The requirement of large computing powers: however, the UKHF model architecture has been developed in a modular manner such that a 'virtual' population of several millions can be run on a desktop computer in a couple of hours.

Disadvantages of existing (non-microsimulation) models

Existing models tend to be either risk factor or disease specific; thus, failing to take account of interactions between these two variables. This can limit the insight into the progression of diseases over the life course, which can be useful for enabling the planning of health policies from prevention, management, treatment and long term care.

Why is microsimulation modelling the right approach for chronic disease modelling?

Microsimulation modelling is the best approach when we consider the following instances:

1. The policy reforms of interest targeted to specific individuals or to different clusters of individuals based on their underlying characteristics.

2. Understanding the granularity of individual's characteristics to estimate the future impact of policy reforms. Microsimulation models enable behaviours and characteristics such as age and BMI to be modelled at the individual level as opposed to an average over a group or population, as seen in many classical models.

3. Understanding the individual's history using a dynamic microsimulation to estimate the future impact of policy reform. For example, an individual's history of risk-taking behaviour, such as smoking and unbalanced nutrition, matters for the development of certain diseases. An individual's history of disease can be used to determine the individual's mortality risk. Microsimulation models are designed with the ability to store an individual's history and use this information when calculating future life events.

Cross-Validation Method

In this section, a number of models and tools will be discussed in terms of their assumptions, methodologies, data and results.

Section 1: BMI and smoking projection validation (module 1)

The EConDA model, developed by the UKHF forecasts risk factor trends into the future using a multivariate non-linear regression model. The EConDA project included body mass index (BMI) and smoking as risk factors and projected these risk factors forward to 2050. We compared these projections against peer-reviewed studies.

Three comparisons were made to investigate the BMI and smoking projections that were carried out for the 8 countries (Bulgaria, Finland, Greece, Lithuania, Netherlands, Poland, Portugal and United Kingdom).

First comparison for BMI projections (3)

Summary

The aim of the study of interest (3) was to estimate the prevalence of obesity and overweight in a range of economies including market economies.

Methods

The projections are based on regional secular trends in the prevalence of overweight or obesity, growth of populations and shifts in demography, all based on logistic regression analyses. Data were mainly extracted from the WHO Infobase (4). These regional projections were summed and used to provide estimates of the global burden and prevalence of overweight and obesity in 2030.

Comparison with results

Since the EConDA countries are all market economies, we used results from market economies as a point of comparison.

Table 1 shows that both models give similar results in terms of the prevalence of obesity and overweight in 2030: 37% (±7%) (EConDA) versus 30% for overweight prevalence and 27% (±10%) (EConDA) versus 22% for obesity prevalence.

Table 1 Comparison of model of interest with EConDA model

Countries	**Bulgaria (EConDA)**	**Greece (EConDA)**	**Finland (EConDA)**	**Lithuania (EConDA)**	**Netherlands (EConDA)**	**Portugal (EConDA)**	**Poland (EConDA)**	**UK (EConDA)**	**Average (EConDA)**	**Established market economies (Kelly et al. 2008)**(3)
Overweight prevalence in 2030	50%	26%	36%	30%	38%	41%	40%	36%	37 ±7%	30%
Obesity prevalence in 2030	16%	47%	22%	26%	15%	31%	23%	37%	27 ±10%	22%

Second comparison for BMI and tobacco projections

The second comparison is based on the International Futures (IFs) modelling system (5).

Summary

For obesity prevalence, IFs uses a driver-based approach, relating adult mean BMI to projections of available calories per capita, the demand for which responds to a function estimated at each cross-section with income. From forecasts of mean BMI, the population percentage of obesity using sex-specific linear equation published by CRA authors is calculated (6).

For smoking use, this approach was not possible because of sparse data. Firstly, a historical series of estimated smoking rates based on the most recent smoking rate data point of each country and the smoking impact forecasts of the Global burden of disease was built. Secondly, cross-sectional relationships that suggest expected rates of smoking (ExpSmoking_Rate) based on gross domestic product (GDP) per capita at power purchasing parity (PPP) was constructed using the following equations (6):

ExpSmoking_RateMales = 0.00224 * GDP – 0.3386 * GDP + 38.3996

ExpSmoking_RateFemales = –0.00573 * GDP + 0.6893 * GDP + 5.6634

Thirdly, the average rates of change in the smoking rate are calculated between 1995 and 2005. These estimates are combined with several assumptions such as the bell shape of smoking with income and rise, in order to estimate the future rates of change in the smoking rate.

Comparison with results

Table 2 to Table 9 show the comparisons of the EConDA obesity and smoking projections with the IFs estimates for the 8 countries of interest. The obesity prevalence results are within confidence intervals for Bulgaria, Finland, Lithuania, Netherlands, Poland and the UK. Smoking prevalence results are within confidence intervals for Bulgaria, Lithuania, Poland and Portugal.

Table 2 Comparison of the EConda model with Pardee estimates for Bulgaria

Bulgaria	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	16% ± 16.7%	28% (30 years and older)
Smoking prevalence in 2030	32% ±- 19%	36%

Table 3 Comparison of EConDA model with Pardee estimates for Greece

Greece	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	47% ±6%	31% (30 years and older)
Smoking prevalence in 2030	33% ±7%	49%

Table 4 Comparison of the EConDA model with the Pardee estimates for Finland

Finland	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	22% ±10%	28% (30 years and older)
Smoking prevalence in 2030	18% ±5%	24%

Table 5 Comparison of the EConDA model with the Pardee estimates for Lithuania

Lithuania	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	26% ±17%	22% (30 years and older)
Smoking prevalence in 2030	28% +±40%	35%

Table 6 Comparison of the EConDA model with the Pardee estimates for the Netherlands

Netherlands	**(EConDA**	**IFs estimates**
Obesity prevalence in 2030	15% ±5%	18% (30 years and older)
Smoking prevalence in 2030	20% ±3%	27%

Table 7 Comparison of the EConDA model with the Pardee estimates for Portugal

Portugal	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	31% ±6%	21% (30 years and older)

Smoking prevalence in 2030	35% ±26%	23%

Table 8 Comparison of the EConDA model with the Pardee estimates for Poland

Poland	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	23% ±6%	23% (30 years and older)
Smoking prevalence in 2030	29% ±17%	31%

Table 9 Comparison of the EConDA model with the Pardee estimates for the UK

UK	**EConDA**	**IFs estimates**
Obesity prevalence in 2030	37% ±7%	33% (30 years and older)
Smoking prevalence in 2030	12% ±2%	22%

Third comparison: DisMod-MR and PyMC versus the EConDA model

The third comparison used the DisMod-MR and PyMC models (7).

Summary

Data from the WHO Comprehensive Information Systems for Tobacco Control were used to i) assess trends from 1990 and 2010 ii) make smoking projections to 2025. Projections made using the DisMod-MR and PyMC models are based on a Bayesian hierarchical meta-regression approach.

Methods

Countries were categorised into 21 regions. The European region was used for comparison here and was composed of the following countries: Andorra, Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Russian Federation, Slovakia, Slovenia, Spain, Sweden, Switzerland, and United Kingdom.

A Bayesian model was used because of paucity of data. It is based on several steps: first, when possible, regional information was used to obtain country level smoking prevalence. Subsequently, a fitting approach was implemented over two periods: 1990-2000 and 2000-2010. Finally, DisMod-MR and PyMC packages were then used to handle non-standard age categories (15 years old or older) and meta-regression analyses and determine projections.

Comparison with results

The comparison between the EConDA model and the DisMod-MR model is presented in Table 10.

There was a significant difference (11%) in the reduction in smoking prevalence by 2025 between results from EConDA (1%) and the DisMod-MR model (12%).

Table 10 Comparison of model of interest with EConDA model

Countries	**Bulgaria (EConDA) 2015-2025**	**Greece (EConDA) 2015-2025**	**Finland (EConDA) 2015-2025**	**Lithuania (EConDA) 2015-2025**	**Netherlands (EConDA) 2015-2025**	**Portugal (EConDA) 2015-2025**	**Poland (EConDA) 2015-2025**	**UK (EConDA) 2015-2025**	**Average (EConDA) 2015-2025**	**EURO (high income countries), 2010-2025**
Smoking prevalence reduction	1%	1%	4%	2%	3%	-6%	-2%	4%	1% ±3%	12 ±4 % (averaged over men and women)

Section 2: Chronic disease model validation (module 2)

This section uses cross-validation to compare the outputs from the chronic disease models found in the literature to the EConDA model (Module 2). Four comparisons were made: DPoRT (8), the model developed by Grover *et al* (9), IDF (10) and the APHO model (11).

Comparison 1: DPoRT: Diabetes Population Risk Tool

Summary

DPoRT is a cohort population tool which can be used to predict the 9-year risk of developing diabetes (8).

Methods

Individuals within the cohort in the start year do not have diabetes and are more than 20 years old. The cohort population was generated by using multilevel cluster sampling from a survey taken from the 1996/1997 National Population Health Survey (NPHS-ON). The probability of an individual having diabetes by a particular follow up point was calculated from a number of variables which include BMI, age and hypertension.

Results for DPoRT model

The results from this tool are referenced from work undertaken by Rosella *et al* (8). Unfortunately, the tool was not accessible due to software requirements. The incidence rates after a 5 and 10 year follow up period as predicted by DPoRT are shown in Table 11. The results show that after 5 years the incidence rate of diabetes within the cohort is predicted to be 4,200 and 3,400 per 100,000 for males and females, respectively.

Table 11 DPoRT 5 and 9 year predictions for the percentage diabetes incidence rates in males and females

	Diabetes incidence rates (per 100,000)		
	Males	**Females**	**Average both sexes**
5-year prediction	4,200	3,400	3,800
9-year prediction	7,000	5,100	6,050

Methods for comparison

The DPoRT tool started with a diabetes-free population. In the EConDA microsimulation model individuals may already have diabetes when the simulation year starts. The EConDA microsimulation model also has a pre-diabetes state which people may enter prior to the diabetes state. The diabetes incidence rates at 5 and 9 years from DPoRT are compared against the total number of incidence cases of diabetes during first 5 and 10 years of the simulation. The microsimulation outputs are generated every 5 years so the 10-year output from the microsimulation was used as an estimate and compared against the 9-year prediction from DPoRT. The cumulative incidence rates at 5 and 10 years as predicted by the EConDA microsimulation model are shown in Table 12. The cumulative incidence rates are shown for

each country which was modelled in EConDA and an average has also been computed. The incidence rates from the EConDA model are for both males and females.

On average the cumulative incidence rate after 5 and 10 years for diabetes as predicted in EConDA is much lower than the 5 and 9 year prediction generated by DPoRT. After 5 years the EConDA model predicted 2,664 cases per 100,000 compared with DPoRT which predicted 3,800 cases per 100,000. The closest comparison between DPoRT and EConDA was observed for Greece and Poland which predicted a 5-year cumulative incidence rate of 3,323 and 3,996 per 100,000, respectively.

Table 12 Cumulative incidence cases for diabetes at 5 and 10 year follow up time points as predicted by the EConDA microsimulation model

	Country								
	Bulgaria	**Finland**	**Greece**	**Lithuania**	**The Netherlands**	**Poland**	**Portugal**	**United Kingdom**	**Average**
Cumulative incidence cases for diabetes after 5 years (per 100,000)	2,021 ± 3	1,086 ± 2	3,323 ±4	1,017 ± 2	5,395 ± 4	3,996 ± 4	2,043 ±3	2,428 ±3	2,664
Cumulative incidence cases for diabetes after 10 years (per 100,000)	3,854 ± 4	2,021 ± 3	6,585 ±5	1,913 ±3	10,073 ±6	7,659 ±5	3,975 ±4	4,552 ±4	5,079

Comparison 2: Years of life lost and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study

Summary

In this study a Markov state-transition model was developed to simulate the annual incidence risk of diabetes and cardiovascular disease among individuals within a synthetic population (9). In this model the synthetic population represents a US population.

Methods

The model simulates changes in an individual's health state throughout their life time. At each year an individual ages and their health state is updated based on a set of transition probabilities. This may result in either: no change to the existing health state or a change to the existing health state in some way: the diagnosis of a new disease, the occurrence of complications from an existing condition; the worsening of an existing complication; or the death from complications related to a disease or other causes. Individuals within the model are assumed to not be able to live beyond 102 years old.

Data from the Atherosclerosis and Risk in Communities study (ARIC) was used to develop the diabetes module. Key predictive risk factors for type 2 diabetes were found using Bayesian information criteria. BMI, waist circumference, fasting glucose and parental history of diabetes were some of the main risk factors identified.

The cardiovascular module considered two types of cardiovascular outcomes. These were: fatal (death from cardiovascular disease such as haemorrhagic stroke) and non-fatal (coronary insufficiency, non-fatal myocardial infarction, a transient ischaemic attack and non-fatal stroke). Individuals could make transitions between different cardiovascular outcome states. The transition probabilities were determined by variables such as age, sex, mean blood pressure and smoking status.

The model produced two main results: the years of life lost (life expectancy) and the healthy life-years lost (years free from diabetes and cardiovascular disease). Both of these outcome measures were used to draw comparisons between different BMI categories (healthy weight, overweight, obese and very obese).

Comparison between the EConDA tool and outputs from the Grover et al model

The EConDA tool (as opposed to the microsimulation model) produced information about the average life expectancy for a particular cohort so these results could be qualitatively compared with that of the Grover *et al* model. The age groups differed between the EConDA tool and the Grover *et al* model. The EConDA tool was able to simulate a cohort of males and females with the following age groups: 18-39, 40-64 and >64 years old. The Grover *et al* model presented results based on the following age groups: 20-39, 40-59 and 60-79 years old. Moreover, the BMI grouping was also different. The EConDA tool grouped all individuals who had a BMI ≥25 kg/m^2 (overweight, obese and very obese) into one 'at risk' group. The Grover *et al* model further stratified the 'at risk' group into overweight (25 to <30 kg/m^2), obese (30 to <35 kg/m^2) and very obese (≥35 kg/m^2).

The numbers of life years lost by BMI group and sex were compared between outputs from the Grover *et al* model and the EConDA tool. Further details are provided in Appendix 1. Figure 1 shows the life years lost for 18-39 year old males and females in the EConDA tool compared with 20-39 year old males and females in the Grover *et al* model.

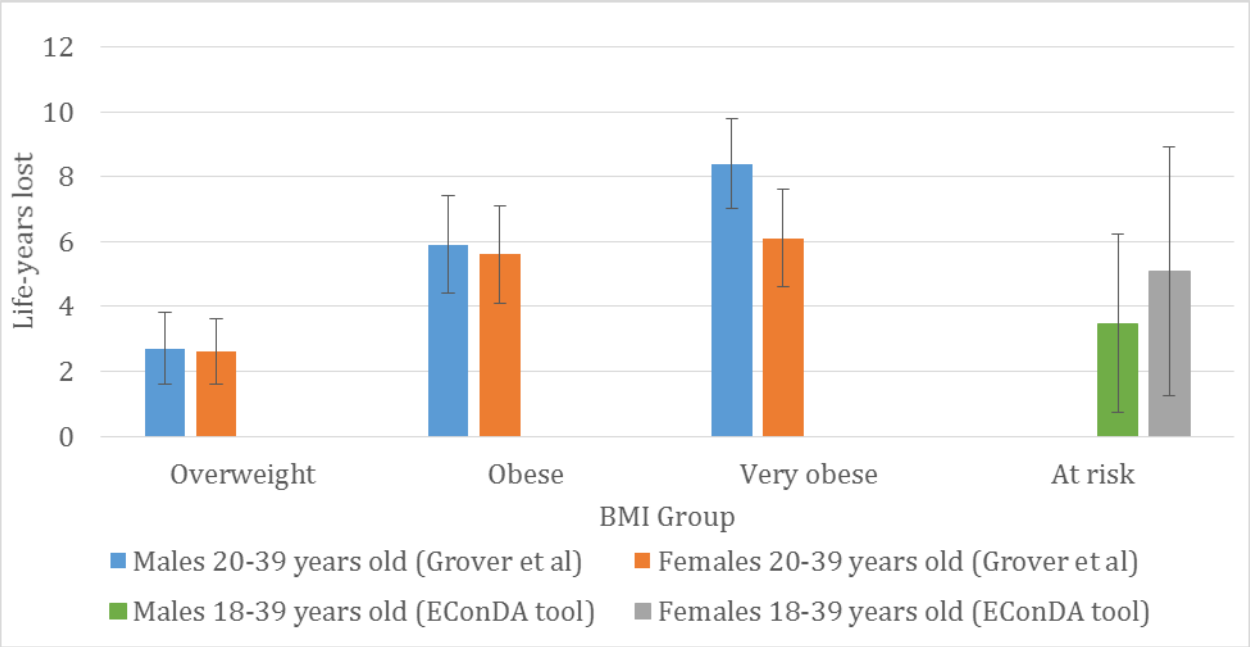

Figure 1 Average life years lost by BMI group relative to a healthy weight group (18.5 to <25 kg/m² Grover et al; 15 to <25 kg/m² EConDA tool) for males and females between 20 and 39 years old (Grover et al) and 18 and 39 years old (EConDA tool). Three BMI group results are shown the Grover et al model: overweight (25 to <30 kg/m²), obese (30 to <35 kg/m²) and very obese (≥35 kg/m²). The EConDA model results are shown for an 'at risk' BMI group (≥25 kg/m²). The error bars represent 95% confidence intervals.

The results show that the Grover *et al* model predicts that the life years lost increases with increasing BMI. The life years lost predicted by the EConDA model for the 'at risk' group was greater than those of the overweight group and less than those of the obese group predicted by the Grover *et al* model.

Figure 2 compares the life years lost for 40 to 64 year olds in the EConDA tool and 40 to 59 year olds in the Grover *et al* model.

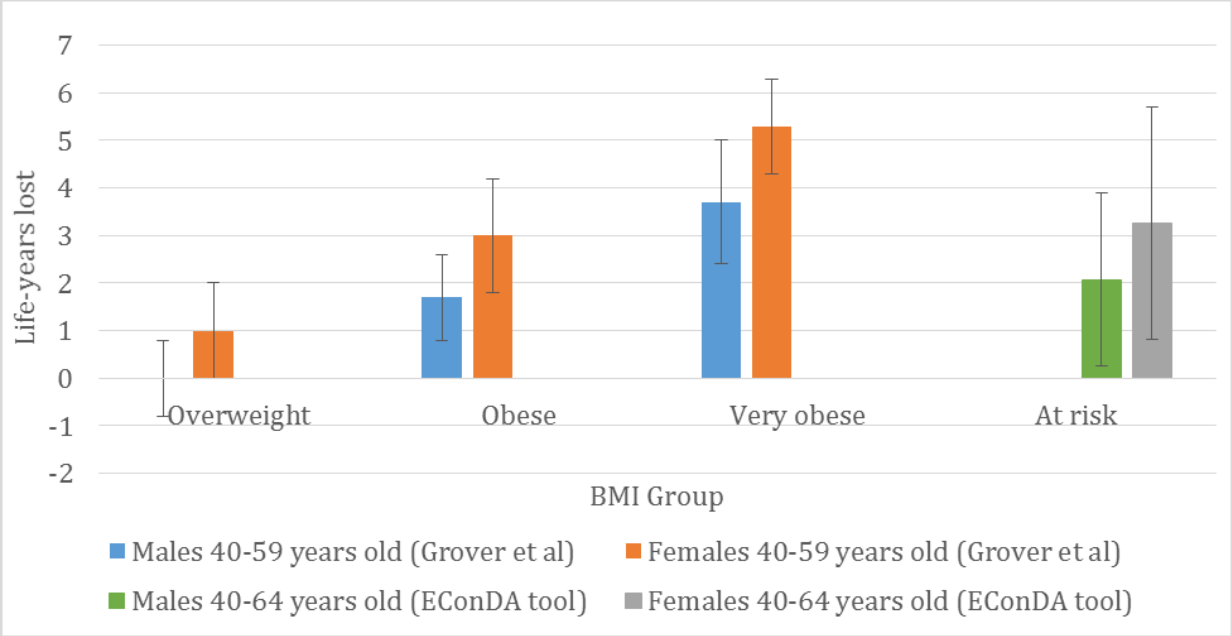

Figure 2 Average life years lost by BMI group relative to a healthy weight group (18.5 to <25 kg/m² Grover et al; 15 to <25 kg/m² EConDA tool) for males and females between 40 and 59 years old (Grover et al) and 40 and 64 years old (EConDA tool). Three BMI group results are shown the Grover et al model: overweight (25 to <30 kg/m²), obese (30 to <35 kg/m²) and very obese (≥35 kg/m²). The EConDA model results are shown for an 'at risk' BMI group (≥25 kg/m²). The error bars represent 95% confidence intervals.

The positive correlation between the life years lost and BMI group reported for the 20-39 year olds age group (Figure 1) remains consistent for this age group (Figure 2). The 'at risk' group results generated by the EConDA tool are slightly greater than the results for the obese group from the Grover *et al* model. However, the error bars are large for both sets of results. The final age group comparison was for 60 to 79 year olds and >64 year olds for the Grover *et al* model and EConDA tool, respectively (Figure 3).

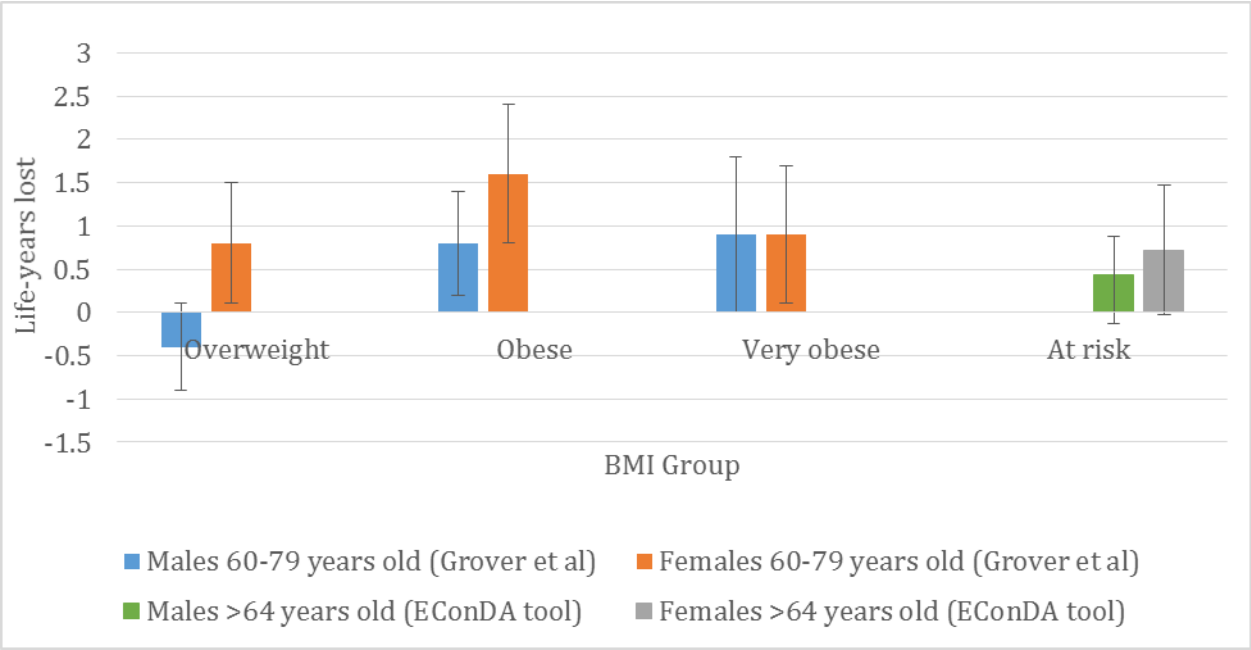

Figure 3 Average life years lost by BMI group relative to a healthy weight group (18.5 to <25 kg/m² Grover et al; 15 to <25 kg/m² EConDA tool) for males and females between 60 and 79 years old (Grover et al) and >64 years old (EConDA

tool). Three BMI group results are shown the Grover et al model: overweight (25 to <30 kg/m²), obese (30 to <35 kg/m²) and very obese (≥35 kg/m²). The EConDA model results are shown for an 'at risk' BMI group (≥25 kg/m²). The error bars represent 95% confidence intervals.

The results for males show that the life years lost of the 'at risk' group falls between the results for the overweight and obese groups (Grover *et al* model), though the error bars for both sets of the results are relatively large.

Overall, the number of life years lost decreases with increasing cohort age. This is a relationship which is observed across both the results from the EConDA tool and results from the Grover *et al* model.

Comparison 3: International Diabetes Federation (IDF)

IDF have predicted that prevalence rates of pre-diabetes (defined by impaired glucose tolerance) to be currently at 318 million (6.7%) and will continue to increase, reaching around 482 million (7.8%) worldwide by 2040 (10). These predictions are generated from the United Nations Population Division by taking into account changes in the distribution of age in the population and urbanisation. These predictions do not consider changes in other risk factors such as BMI.

Baseline model simulations have predicted that the following prevalence of pre-diabetes across the eight countries included in EConDA in 2015 and 2040 (Table 13).

The current prediction for the prevalence of pre-diabetes is on average 6.3% for the eight European countries studied in the EConDA project, compared with 6.7% as reported by IDF. The EConDA model predicted that for 2040 the prevalence would increase to 7.3%, which is similar to the 7.8% figure reported by IDF.

Table 13 Prevalence of pre-diabetes in 2015 and 2040 for eight European countries as predicted by the EConDA microsimulation model.

	Country								
	Bulgaria	**Finland**	**Greece**	**Lithuania**	**The Netherlands**	**Poland**	**Portugal**	**United Kingdom**	**Average**
Prevalence of pre-diabetes (%) in 2015	1.7	5.1	3.5	5.8	8.2	11.8	8.2	6.1	6.3
Prevalence of pre-diabetes (%) in 2040	2.0	5.5	4.8	6.1	9.7	13.2	10.1	7.2	7.3

Comparison 4: Association of Public Health Observatories (APHO) Diabetes Prevalence Model for England

Summary

The model projects diabetes prevalence up to 2030 for England (11).

Method

The variables age, sex, ethnicity, deprivation and obesity trends are used to inform these predictions. The model projects trends for overweight and obesity forward to 2030 using linear extrapolation. The data used to generate the linear extrapolation are from data collected by the Health Survey for England between 2003 and 2008. The projections for the prevalence of diabetes are calculated from these obesity projections which have been adjusted by obesity, deprivation and ethnicity using relative risk data for diabetes. The prevalence estimates for diabetes are adjusted for cases of undiagnosed diabetes using known proportions of the numbers of individuals who are undiagnosed.

Comparison between the Diabetes Prevalence Model in England and the EConDA model in the UK

The prevalence of diabetes from 2015 until 2030 as predicted by the Diabetes Prevalence Model for England is shown in Table 14.

Table 14 Diabetes prevalence as predicted by the diabetes prevalence model in England and the EConDA microsimulation model.

Year	**Prevalence of diabetes in England as predicted by diabetes prevalence model (lower – upper uncertainty limits) (%)**	**Prevalence of diabetes in the UK as predicted by EConDA model (%)**
2015	7.6 (5.3-11.5)	9.6
2020	8.2 (5.7-12.4)	10.0
2025	8.6 (5.9-13.1)	10.5
2030	8.8 (6.1-13.4)	10.9

The prevalence of diabetes in England is predicted to be approximately 7.6% in 2015 and 8.8% in 2030. The EConDA model simulated the UK and predicted the prevalence of diabetes to be 9.6% in 2015 and 10.9% in 2030. The EConDA model has predicted a higher prevalence of diabetes across all of the years when compared to the APHO model. However, the EConDA results are within the limits of uncertainty calculated by the APHO model.

Comparison 5: Chronic Kidney Disease Prevalence model

A chronic Kidney Disease prevalence model has been developed by PHE (Grant Aitken, 2014). The future prevalence of CKD was calculated by applying the estimated CKD prevalence by age groupings (16-34, 35-54, 55-64, 65-74 and 75+) to the 2012 CCG-based subnational population projections (SNPP) produced by the Office for National Statistics (ONS) using multi small area synthetic estimation. The results are shown in Figure 4 and show that, by 2036, the prevalence of CKD stages 3 to 5 among people aged 16 years and over is expected to increase to 4.2 million or 8.3% (Figure 4).

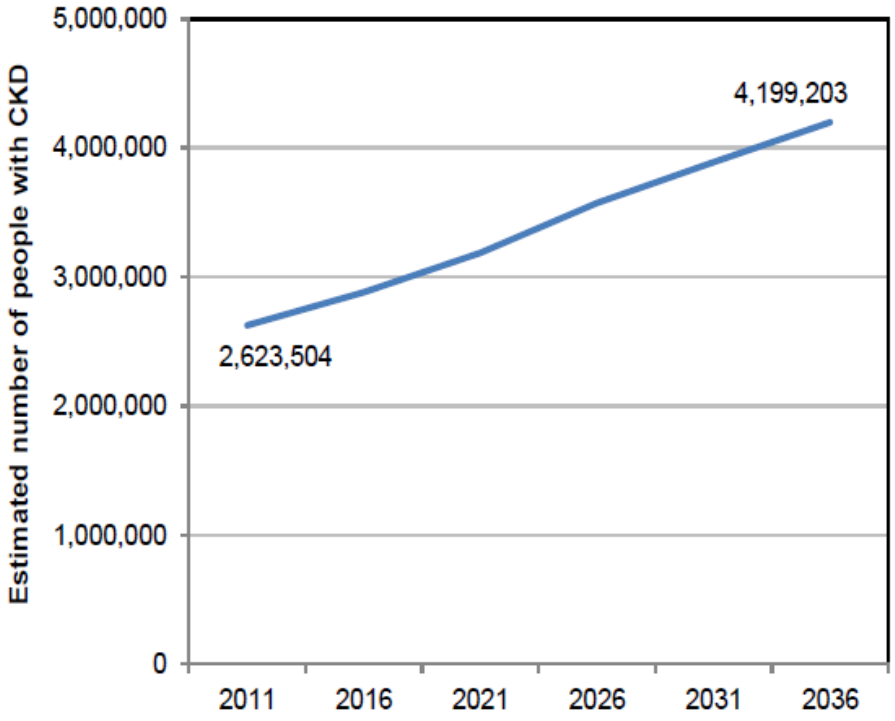

Figure 4 CKD projection using the CKD prevalence model developed by PHE

By 2040, the EconDA model predicts that CKD stages 3a, CKD stage 3b, CKD stage 4 and 5 increase by 25%, 32%, 9%, and -4%, respectively (Table 15). Hence, the average of these stages is 15.5%, which is smaller than the 61% predicted by the CKD prevalence model.

Table 15 Prevalence (per 100,000) for the baseline scenario using the EConDA model

Year	CHD	CKD stage 1	CKD stage	CKD stage 3a	CKD stage 3b	CKD stage 4	CKD stage 5	stroke
2015	1334 [+-3]	2771 [+-5]	3177 [+-5]	4282 [+-6]	1098 [+-3]	115 [+-1]	16 [+-0]	882 [+-3]
2020	1509 [+-3]	2704 [+-4]	3273 [+-5]	4509 [+-6]	1158 [+-3]	115 [+-1]	15 [+-0]	1041 [+-3]
2025	1646 [+-3]	2753 [+-4]	3398 [+-5]	4737 [+-6]	1253 [+-3]	122 [+-1]	14 [+-0]	1142 [+-3]
2030	1757 [+-4]	2791 [+-5]	3503 [+-5]	4932 [+-6]	1317 [+-3]	128 [+-1]	13 [+-0]	1210 [+-3]
2035	1850 [+-4]	2814 [+-5]	3584 [+-5]	5167 [+-6]	1382 [+-3]	128 [+-1]	14 [+-0]	1263 [+-3]
2040	1916 [+-4]	2806 [+-5]	3636 [+-5]	5360 [+-6]	1448 [+-3]	125 [+-1]	14 [+-0]	1314 [+-3]

Section 3: Intervention model validation

Eight models were used to investigate the EConDA results of the following policy interventions: Sugar Sweetened Beverage Tax (SSB) and Smoking Cessation Service (SCS).

Comparison 1: Chronic disease model for simulating multi-stage COPD (developed by RIVM)

The RIVM model is a multi-state model for COPD based on the life table analysis, and is used to project health outcomes of the Dutch population (13,14). A birth cohort is followed through time and updated with a new birth cohort each year. The model simulates the Netherlands and takes into account births, deaths and migration, and these are based on data from Statistics Netherlands. Each year, an individual has a probability of changing smoking state, being diagnosed with COPD (if they don't already have COPD), changing COPD stage (if they already have COPD), and dying. Smoking state transition probabilities vary with age and sex, and are based on the current rates so are constant over time. Individuals greater or equal to 45 years of age have a probability of getting COPD. The progression of COPD is modelled by taking into account the annual decline in forced expiratory volume in one second (FEV1). Individuals are not able to recover from COPD; however, their COPD stage may improve overtime if an individual quits smoking.

The model has been used to simulate the incidence, prevalence and costs by severity stage between 2000 and 2025 and investigates the cost effectiveness of two smoking cessation interventions: the first scenario models the effect of 25% of smoking COPD patients receiving minimal counselling by a general practitioner (H-MIS). The second scenario models the effect of 25% of smoking COPD patients receiving intensive counselling in combination with bupropion (IC + Bupr). Those interventions differ from the EConDA intervention for two reasons. Firstly, there is a difference of 5% in the 'reach of the intervention' (percentage of the population exposed to the intervention) between the two model. For the Netherlands a 'reach' of 20% and 25% is assumed in the EConDA and RIVM model, respectively. Secondly, the EConDA intervention targets the whole smoking population as opposed to RIVM whereby the population sample only contains COPD patients who smoke.

Results and comparison with the EConDA microsimulation model

The severity distribution of COPD incidence in the year 2000 for the Netherlands was analysed and used in the RIVM model. The EConDA model did not simulate the Netherlands for multistage COPD which was due to the model structure and data limitations. EConDA results for the UK and Finland will be used to draw comparisons between the two models. A 'reach' of 30% and 34% were used in Finland and the UK, respectively. The severity distribution of COPD incidence in the start year of the simulation for UK and Finland were compared against the results for the Netherlands (Table 16).

Table 16 Severity distribution of COPD incidence in the Netherlands in 2000 as predicted by RIVM. Severity distribution of COPD incidence in the year 2015 in the UK and Finland as predicted by the EConDA model. The following categories are used mild, moderate, severe and very severe. The EConDA model combines the final two categories.

	COPD stage			
	1	**2**	**3 (Severe)**	**4 (Very**

	(Mild)	(Moderate)		severe)
Netherlands severity distribution of incidence in 2000 (%) in the RIVM model	40	55	4	0.1
Finland severity distribution of incidence in 2015 (%) in the EConDA microsimulation model	69.68	26.45	3.87	
UK severity distribution of incidence in 2015 (%) in the EConDA microsimulation model	64.01	30.29	5.70	

The results show that a higher proportion of COPD patients are predicted to be in the mild stage of COPD in the UK (69.68%) and Finland (64.01%) compared to the Netherlands (40%). However, a higher proportion of COPD patients are predicted to be in the moderate COPD stage in the Netherlands compared to the UK and Finland.

The RIVM COPD model was simulated between 2000 and 2025. The prevalence rates per 1,000 were predicted to 2025 by COPD stage (Table 17). In addition, the EConDA model was simulated from 2015 until 2050. The results from the EConDA model for the UK and Finland in 2025 are shown in Table 17. However, the prevalence rates for COPD in the UK and Finland are different from the Netherlands.

Table 17 Prevalence rates in 2025 per 1,000 by COPD stage (mild, moderate, severe and very severe) for the Netherlands as predicted by the RIVM model and for the UK and Finland as predicted by the EConDA model

	COPD stage			
	1 (Mild)	**2 (Moderate)**	**3 (Severe)**	**4 (Very severe)**
Netherlands prevalence per 1,000 in 2025 (RIVM)	11	14	3.9	1.3
Finland prevalence per 1,000 in 2025 (EConDA)	17.46	5.18	0.6	
UK prevalence per 1,000 in 2025 (EConDA)	67.15	28.38	3.82	

The prevalence of mild stage COPD per 1,000 in the UK is considerably higher than both the Netherlands and Finland. Both Finland and the UK show a similar correlation between the increasing COPD stage and decreasing prevalence. The Netherlands pattern is slightly different as the prevalence is higher for the moderate stage.

Both interventions applied in the RIVM model are shown to cause a decrease in the proportion of individuals in the severe and very severe stages and an increase in the mild and moderate stages of COPD (Table 18). A similar intervention was modelled in the EConDA model. The SCS intervention was targeted at smokers within the model. The proportional change (%) in the number of individuals at each severity stage of COPD between 2015 and 2025 relative to the baseline case is presented in Table 18.

In the RIVM model the intervention results in a reduction in the proportion of COPD patients in the severe and very severe stages (Table 18). Moreover, an increase in the proportion of COPD patients is then observed in the mild and moderate stages. In the EConDA model a reduction in the proportion of the individuals across all COPD stages is observed, except for the moderate COPD stage in the UK where a relatively small increase is observed.

Table 18 Proportional change (%) of the total number of patients in each severity stage between 2000 and 2025 compared to base-case (simulation with no intervention).

		COPD stage			
RIVM scenario	**Sex**	**Mild**	**Moderate**	**Severe**	**Very severe**
25% of the COPD patients gets H-MIS	males	+0.4	+0.1	-0.6	-1.8
	females	+0.4	+0.1	-0.5	-1.8
25% of the COPD patients gets IC+Bupr	males	+1.6	+0.3	-2.2	-6.1
	females	+1.5	+0.5	-2.0	-6.4
EConDA scenario					
Smoking cessation service in the UK	males and females	-0.21299	+0.073584	-0.38241	
Smoking cessation service in Finland	males and females	-0.21526	-0.06978	0	

+ An increase in prevalence

- A decrease in prevalence

Table 19 shows that the smoking cessation interventions in the RIVM model are cost-effective (dominant). H-MIS generates net savings, which indicates that the costs of the H-MIS are offset by the savings in COPD-related healthcare costs (hence H-MIS is deemed to dominate the baseline scenario (i.e. it is cost effective)). Though IC+Bupr is more effective than H-MIS, its savings do not outweigh its intervention costs. Thus, the 'costs per QALY gained' figures for IC+Bupr are positive. To categorically determine whether or not this intervention is cost effective, the figure needs to be compared against a cost effectiveness threshold; however, a threshold was not determined in this project; thus, it remains uncertain whether or not IC+Bupr is cost effective from a payer perspective. This is in line with the EConDA model results.

Table 19 Number of life-years and QALYs gained, total additional intervention costs, total savings and cost-effectiveness: costs per life-year gained and costs per QALY gained for the two scenarios, cumulative for the years 2000-2025 (Euros, year 2000 price level)

Duration of implementation	LYs gained	QALYs gained	Intervention costs (*10^6)	Savings in COPD-related costs (*10^6)	Costs per LY gained	Costs per QALY gained
1 year						
H-MIS	200	400	0.8	2.6	#	#
IC+Bupr	900	1800	13	9.9	2,900	1,500
10 year						
H-MIS	2000	4300	8.4	25	#	#
IC+Bupr	7300	16000	124	93	4,200	2,000
25 year						
H-MIS	2800	7100	24	45	#	#
IC+Bupr	10400	26000	346	160	1,7900	7,200

#H-MIS dominates the base-case, due to net cost savings and higher effects

Comparison 2: DYNAMO-HIA model

Differences in terms of methods

The DYNAMO-HIA is part Markov model and part microsimulation model (to project risk factor behaviour) that uses a deterministic approach (a disease life table). The main methodological difference is that the EConDA model is a full microsimulation i.e. the probability of getting a disease is compared to an application-generated random number to determine whether or not the transition takes place. Table 20 shows the differences in terms of data-input between the two models for the UK.

Table 20 Overview of data sources for disease data used in the example applications for EConDA model and dynamo HIA model

	Incidence		**Prevalence**		**Survival**		**Mortality**	
	EConDA	**Dynamo HIA**	**EConDA**	**Dyna**	**EConDA**	**Dynamo**	**EConDA model**	**Dynamo**

	model		**model**	**mo HIA**	**model**	**HIA**		**HIA**
Diseases								
CHD	BHF 2010	UK GPRD	BHF 2006	UK GPRD	computed from prevalence and mortality	N/A	BHF 2010 (with BMJ correction)	UK GPRD
COPD	N/A	WHO estimates Truelson et al review(2002)	HSE	UK GPRD	Wildman et al. 2009	N/A	ONS 2010	UK GPRD
Diabetes	Personal communication Dr. Craig Currie	IPM based on prevalence & GPRD RR	IDF 2012	UK GPRD	N/A	N/A	N/A	UK GPRD
Hypertension	N/A	N/A	BHF 2012	N/A	N/A	N/A	N/A	N/A
Stroke	BHF 2009	N/A	N/A	IPM based on incidence & GPRD RR	computed from prevalence and mortality	N/A	BHF 2010	UK GPRD
Lung cancer	CRUK 2011	Cancer Incidence in 5 Continents. Vol IX,	N/A	Back calculated using DisMod II	ONS 2011	N/A	CRUK 2012	WHO , mortality database, 100% of population (2000-2002)

First output comparison with Dynamo-HIA: testing the impact of 100% reduction in smoking prevalence using the EConDA microsimulation model and the EConDA tool.

The first comparison investigated the impact of the total elimination of smoking in the UK (15). The EConDA microsimulation was run in order to model the same intervention and the results are shown in Appendix 4. As well as development of the microsimulation model, a downloadable tool was created as part of work package 6. This can be downloaded here: http://www.econdaproject.eu/tools.php.

Table 21 shows the difference in terms of results for both DYNAMO-HIA and EConDA Models. The EConDA microsimulation predicts a decrease in COPD, CHD and stroke prevalence cases by 0.27%, 0.01%, and 0.15%, respectively. The EConDA tool predicts a decrease in COPD, CHD and stroke prevalence cases by 1.5%, 0.1%, and 0.2%, respectively.

Table 21 Results for Dynamo and the EConDA microsimulation (2040) after 25 years of simulations

	Dynamo-HIA	**EConDA Microsimulation**	**EConDA Tool**
Reduction in prevalence for COPD	1.3%	0.27%	1.5%
Reduction in prevalence for CHD	0.9%	0.01%	0.1%
Reduction in prevalence for Stroke	0.4%	0.15%	0.2%
Life Expectancy gain (years)	2.5 years	-	1.5 years

Second output comparison: Intervention: smoking cessation intervention in the Netherlands

The second comparison investigated the impact of a smoking cessation intervention in the Netherlands (16) using both the EConDA microsimulation and the EConDA tool.

Smoking cessation intervention methods

In the EConDA project an intervention 'reach' rate of 20% and an intervention success rate of 17 % was used. In the DYNAMO-HIA model: a reach of 20% and an odds ratio (OR) of 2.0 (reflecting that the ORs quantifying the effects of interventions on cessation rates varied from 1.4 to 2.2 among persons aged 18 years and over) were used.

DYNAMO-HIA predicts (Table 22) a decrease in COPD and CHD prevalence cases by 219/100,000 and 153/100,000 respectively. The EConDA microsimulation (Table 22) predicts a decrease in COPD and CHD prevalence cases by 182/100,000, and 39/100,000 respectively. The EConDA tool predicts a decrease in COPD and MI prevalence cases by 219/100,000 and 137/100,000 respectively. Further results can be found in Appendix 5.

Table 22 Comparison of the EConDA model with the Dynamo-HIA model

Parameters	**Dynamo-HIA**	**EConDA Microsimulation**	**EConDA Tool**
Reduction in prevalence for COPD in 2035	Relative values ~ 219/100,000	Relative values ~ 182/100,000	Relative values ~ 219/100,000
Reduction in prevalence for MI in 2035	Relative values ~ 153/100,000 (IHD)	Relative values ~ 39/100,000 (MI)	Relative values ~ 137/100,000 (MI)

Comparison 3: Sugar Sweetened Beverage Tax Intervention: qualitative and quantitative validation with three models

To assess the SSB interventions, three comparisons have been made: comparison with Children's Food Campaign (17), Briggs (18), and Wang (19).

Differences in results are observed between the Children's Food Campaign with Liverpool University and the EConDA model (17). The reasons for these differences are presented in Table 23.

Table 23 Differences in terms of inputs and outputs between the Food Active model and EConDA model

	Food Active	**EConDA Model**
Method	Microsimulation method for which 10,000 monte carlo trials were run	Microsimulation method for which 100 million monte carlo trials were run
	estimates the impacts of an SSB tax for the England population	estimates the impacts of an SSB tax for the UK population
	scales up the data from a reference (using calories, not BMI)	we have a few stages more (grams to kJ to bmi, etc…); the overall calorie analyses show similar results
	Not an individual based model, not dynamic – i.e. it does not take account of dynamical changes in risk factors over time. Assumes immediate effect.	each individual's BMI drops and not linearly with time (the 1st year is different from the 2nd and 3rd year and is different from the following years based on Kevin Hall's equations (see report methods)
Input data	data from other modelling studies to determine the impact of a 20% SSB tax in England (therefore they model modelled data)	We used raw data
	2008 -2010 years of the NDNS survey were used to determine SSB consumption	data from 2008-2011 years of the NDNS survey to determine baseline SSB consumption
	define SSBs as 'soft drinks, not low calorie'	define SSBs as 'soft drinks, not low calorie', however, we have further stratified our consumption data by various sub-categories as outlined in the project report
	price elasticities from data published by Ng et al, 2012 and used a price elasticity of 0.46	price elasticities by concentrated (0.74) and non-concentrated (0.80) SSBs published by Briggs et al, 2013
	does not take account of substitution effect	based on the assumption by Wang et al, it was assumed that for every 100kJ saved from not consuming SSBs, there would be a 60% net kJ reduction with 40kJ being substituted by other food and beverage intake
	cost references differ	cost references differ

	bowel cancer cost data used in the model for annual cost of cancer	cost data for each cancer was obtained
	4year olds+, manufactured dataset	20year olds+, We did not use a manufactured dataset (just NDNS)
Output data	6.57 kcal/person/day reduction	14.96 kJ/day reduction in total energy intake accounting for substitutions (equivalent to 3.58 kcal/day reduction). Similar findings to Briggs et al, 2012 study (16.7 kJ/person/day; equivalent to 3.99 kcal/person/day)
	BMI not assessed	Mean BMI reduction of 0.05 kg/m2/year. Similar findings to Briggs et al, 2012 study (mean population BMI reduction of 0.07 kg/m2; 95% CI: 0.05-0.09)
	~49,000 fewer cases of diabetes	½ of the Children's food Campaign model results
	33,000 fewer cardio vascular disease and stroke	¼ (only MI and stroke included)
	800,000 QALY gained	1/8 (only 5 diseases included)
	300,000,000 in healthcare costs	1/10 (only 5 diseases included)

Result differences can be seen between the Briggs and Wang article results and the EConDA model (17). Reasons can be seen in Table 24.

Table 24: Differences between the EConDA and the Briggs model

	Briggs	**EConDA Model**
Method	PRIME model, which is a static model assuming that the change in in distribution of BM is a result of the change in mean energy intake (the BMI in the population follows a log-normal distribution)	Monte Carlo, dynamic microsimulation method for which 100 million trials were run
	estimates the impacts on obesity prevalence of an SSB tax for the UK population	estimates the health outcomes impacts of an SSB tax for the UK population
	scales up the data from a reference (using calories, not BMI)	we have a few stages more (grams to kJ to bmi, etc…); the overall calorie analyses show similar results
	Not an individual based model, not dynamic – i.e. it does not take account of dynamical changes in risk factors over time. Assumes immediate effect.	each individual's BMI drops and not linearly with time (the 1st year is different from the 2nd and 3rd year and is different from the following years based on Kevin Hall's equations (see report methods)

Input data		
	2008 -2010 years of the NDNS survey were used to determine SSB consumption	data from 2008-2011 years of the NDNS survey to determine baseline SSB consumption
	soft drinks, concentrated, not low calorie," and "soft drinks, not concentrated, not low calorie,"	define SSBs as 'soft drinks, not low calorie', however, we have further stratified our consumption data by various sub-categories as outlined in the project report
	price elasticities calculated using a Bayesian model to model an almost ideal demand system	price elasticities by concentrated (0.74) and non-concentrated (0.80) SSBs published by Briggs et al, 2013
	not explicitly considered substitution of drinks with food items	based on the assumption by Wang et al, it was assumed that for every 100kJ saved from not consuming SSBs, there would be a 60% net kJ reduction with 40kJ being substituted by other food and beverage intake
	16+ year olds	20year olds+, We did not use a manufactured dataset (just NDNS)
Output data	Similar findings to Briggs et al, 2012 study (16.7 kJ/person/day; equivalent to 3.99 kcal/person/day)	14.96 kJ/day reduction in total energy intake accounting for substitutions (equivalent to 3.58 kcal/day reduction).
	mean population BMI reduction of 0.07 kg/m2; 95% CI: 0.05-0.09	Mean BMI reduction of 0.05 kg/m2/year. Similar findings to Briggs et al, 2012 study

Table 25. Differences between the EConDA and the Wang model

	Wang	**EConDA Model**
Method	Coronary Heart Disease Policy Model, a state-transition computer model that simulates CHD, stroke and diabetes in the US	Monte Carlo, dynamic microsimulation method for which 100 million trials were run in the UK
	estimates the impacts on CHD, stroke, diabetes of an SSB tax for the US population	estimates the health outcomes impacts of an SSB tax for the UK population
	scales up the data from a reference (using calories, not BMI)	we have a few stages more (grams to kJ to bmi, etc…); the overall calorie analyses show similar results
	Not an individual based model, not dynamic – i.e. it does not take account of dynamical changes in risk factors over time. Assumes immediate effect.	each individual's BMI drops and not linearly with time (the 1st year is different from the 2nd and 3rd year and is different from the following years based on Kevin Hall's equations (see report methods)
Input data		

	2003 -2006 years of the National Health and nutrition Examination Survey (US)	data from 2008-2011 years of the NDNS survey to determine baseline SSB consumption
	soft drinks, concentrated, not low calorie," and "soft drinks, not concentrated, not low calorie,"	define SSBs as 'soft drinks, not low calorie', however, we have further stratified our consumption data by various sub-categories as outlined in the project report
	15 % consumption reduction:	price elasticities by concentrated (0.74) and non-concentrated (0.80) SSBs published by Briggs et al, 2013
	25–64 +	20 year olds+
Output data	0.9 pound: 3.150 kcal/day reduction	14.96 kJ/day reduction in total energy intake accounting for substitutions (equivalent to 3.58 kcal/day reduction).
	mean population BMI reduction of 0.9 pound 95% CI: 0.4-1.5	Mean BMI reduction of 0.05 kg/m2/year.
	reduction in diabetes incidence after 10 years: 2.6%	in 2025: 0.016%
	reduction in MI after 10 years: 30,000 (http://www.census.gov/population/projections/data/national/2014/summarytables.html) : 0.01% of the US population	in 2025: 0.005%
	reduction in stroke after 10 years: 8,000: 0.002% of the US population	in 2025: 0.034

Comparison 4: PREVENT Model

Methods

The PREVENT model (20) is a cohort-based model, which relates risk factor change to reductions in incidence, mortality and health service costs of four smoking-related diseases: lung Cancer, COPD, CHD and stroke. The model investigated the effect of three interventions that reduce the smoking prevalence by 3%, 15%, 35%, respectively, for the Netherlands, Austria, France, Germany, Ireland, Poland, Portugal, Romania, Switzerland, and the UK. The present comparison includes the Netherlands, Portugal and the UK.

Comparison with EConDA results

The assumptions included in the smoking cessation service intervention are presented in Appendix C4. The reach of the Smoking Cessation Service intervention in the EConDA model for Netherlands, Portugal and the UK were 20%, 30% and 34% respectively. In addition, there was a success rate for this intervention, which was related to the proportion of people who successfully gave up smoking after completing the intervention. These were 17%, 34% and 34% in the Netherlands, Portugal and UK, respectively. Each year the intervention resulted in approximately 3.4%, 10.2% and 11.6% of smokers giving up in the Netherlands, Portugal and UK, respectively.

Results using EConDA and PREVENT models are shown in Table 26. Projected population totals in 2030 (21) were used to calculate the annual incidence cases avoided from the PREVENT model results (20).

The results for each EConDA country were compared against the PREVENT results with a similar SCS effectiveness rate. The SCS intervention for the Netherlands in the EConDA model was modelled with a 3.4% effectiveness rate which resulted in a 0.02% reduction in the annual incidence in 2030. In the PREVENT model for the Netherlands reductions in the annual incidence were 0.004% and 0.02% for SCS effectiveness rates of 3% and 15%, respectively.

In the UK the EConDA SCS intervention was 11.6% effective which resulted in a reduction of 0.02% in the annual incidence compared with a 0.02% reduction in the PREVENT model (SCS 15% effective). Finally, the EConDA SCS intervention in Portugal was 10.2% effective and resulted in a 0.07% reduction in the annual incidence rate. In the PREVENT model a 15% effective SCS intervention showed a 0.02% reduction in the annual incidence rate in Portugal.

Table 26 Results of SCS interventions for both the EConDA project and PREVENT model

Country	**EConDA annual incidence cases avoided in 2030 with an SCS intervention (%)**	**PREVENT annual incidence cases avoided in 2030 with a 3% reduction in smoking prevalence (%)**	**PREVENT annual incidence cases avoided in 2030 with a 15% reduction in smoking prevalence (%)**	**PREVENT annual incidence cases avoided in 2030 with a 35% reduction in smoking prevalence (%)**
Netherlands	0.02	0.004	0.02	0.05
Portugal	0.07	0.003	0.02	0.04
UK	0.02	0.003	0.02	0.04

ASH reckoner tool

Table 27 shows the differences between the ASH reckoner and the EConDA model.

Table 27 Differences between the ASH reckoner tool and the EConDA model

	ASH reckoner tool (England)	EConDA model (UK)
Aim	Simple tool intended to provide estimates of the cost of smoking at local or regional level	A versatile model – one of its capabilities is that it can provide estimates of the cost of smoking at a local or regional level
Audience	Policy making audience who need to ensure that the overall economic burden of smoking is recognised but do not necessarily need the level of detailed information on specific resource use.	Policy makers, commissioners, health sector professionals including epidemiologists and health economists.
Methodology	No future projections of cost	Future projections of cost
	Cost of illness study (no modelling involved)	Monte Carlo microsimulation, stochastic
	Top-down approach is used to collate costs for input into the tool (multiply total disease cost by the population attributable fraction (PAF)), and a top down approach is used to obtain cost outputs from the tool	Top-down approach is used to collate costs for input into the model (total disease cost divided by the prevalence), but a bottom up approach is used to model progression of disease epidemiology and accretion of costs
	Human capital approach to estimating indirect costs	Human capital approach to estimating indirect costs
Input data	No population data	Population data: population growth projections, fertility rate, all-cause mortality rate
	No disease data	Disease data: incidence, prevalence, mortality, survival, relative risk
	NHS healthcare costs	NHS healthcare costs
	Social care costs	Social care costs
	Indirect societal costs: lost output from early death, absenteeism	Indirect societal costs: lost output from early death, absenteeism
	Environmental costs: smoking related fires, cigarette litter	No environmental cost data
	20+ years old	20+ years old
Output data	Total cost of smoking in the UK	Costs avoided due to an implementation of a smoking cessation service in the UK

ASH reckoner tool: http://ash.org.uk/localtoolkit/docs/Reckoner.xls

It was not possible to make direct comparisons of the outputs between the two models since they modelled different outcomes. The ASH reckoner tool estimates the total cost of smoking, whereas the EConDA model estimates the costs that can be avoided by implementing smoking preventive interventions such as SCS.

This section describes a comparison with the NICE tobacco ROI tool.

NICE Tobacco ROI tool

Another tool of interest is a programme called the Tobacco ROI tool developed by the Health Economics Research Group (HERG) at Brunel University for the National Institute of Clinical Excellence (NICE) in the UK (22).

Summary

The tool investigates the economic returns of a set of tobacco control interventions (pharmacotherapies and support and advice) and compares the outcomes with a "no services" scenario.

Methods

The NICE ROI tool is based on 3 steps:

Step 1: estimates the prevalence of smoker, ex-smoker and non-smoker in the population of interest.

Step 2: using the attributable risk of getting a specific disease (i.e. lung cancer, CHD, COPD, MI and stroke) as a result of being a smoker, the number of cases per year are estimated using the following equation: (22)

$A = (PS \times D1) + (PExS \times D2) + (PNS \times D3)$

Where:

D= prevalence of smoking for each age and gender

PS= prevalence of each co-morbidity for smoker

PExS= prevalence of each co-morbidity for former smokers

PNS= prevalence of each co-morbidity for non-smokers

Step 3: These are then allocated to costs from which the total healthcare cost is calculated. The mortality rates and co-morbidities associated with smoking status are estimated in the same way as those reported in Flack & Trueman, 2007.

Table 28 shows the main differences between the ROI and the EConDA microsimulation.

Table 28 Comparison of the EConDA model with the NICE ROI tool

	NICE-Brunel ROI model (UK)	**EConDA model (UK)**
Aim	Estimate the impact of implementing various kinds of smoking cessation services to reduce costs	A versatile model – one of its capabilities is that it can estimate the impact of implementing smoking cessation services to reduce smoking prevalence and costs
Audience	Health and public sector commissioners who are expected to need not only high-level estimates of the cost of smoking but more granular information on where and when the costs are incurred.	Policy makers, commissioners, health sector professionals including epidemiologists and health economists.

Methodology	Future projections of cost	Future projections of cost
	Markovian, deterministic	Monte Carlo microsimulation, stochastic
	Bottom-up approach is used to collate costs (costs disaggregated by resource consumption level e.g. GP restrictions, hospital bed days)	Top-down approach is used to collate costs (total disease cost divided by the prevalence)
	Diseases modelled: lung cancer, CHD, COPD, MI, stroke	Diseases modelled: lung cancer, CHD, COPD (by stage), stroke, hypertension
	Not an individual based model, not dynamic – i.e. it does not take account of dynamical changes in risk factors over time. Assumes immediate effect.	each individual's risk factor of disease from smoking changes dynamically drops and not linearly with time – mirroring real life
	A baseline scenario and an intervention scenario is modelled	A baseline scenario and an intervention scenario is modelled
Input data	Risk factor data: smoker prevalence (smoker, ex smoker, never smoker; also includes background quit rate)	Risk factor data: smoker prevalence (smoker, ex smoker, never smoker; the dynamic risk factor distribution projection captures background quit rate even though it is not explicitly a form of input data)
	Population data: static population over time	Population data: population growth projections, fertility rate, all-cause mortality rate
	No disease data	Disease data: incidence, prevalence, mortality, survival, relative risk
	Intervention data: success rate, cost per attempt, reach of the intervention	Intervention data: success rate, cost per attempt, reach of the intervention
	NHS healthcare costs	NHS healthcare costs
	Social care costs	Social care costs
	Indirect societal costs: lost output from early death, absenteeism	Indirect societal costs: lost output from early death, absenteeism
	Discounting of health and costs: 3.5%	Discounting of health and costs: 3.5%
	18+ years old	20+ years old
Types of intervention	Smoking Cessation Services described in Appendix C4	2 individual interventions: Local Stop Smoking Service Cessation (LSSS) and Non LSSS Cessation Interventions
Intervention reach	100%	100%
Outputs	No disease incidence/prevalence outputs	Reduction in incidence and prevalence of smoking-related diseases
	Reduction in costs	Reduction in costs
	Health economic outcome measures: DALY, ICER	Health economic outcome measures: QALY, DALY, ICER

NICE-Brunel ROI model: https://www.nice.org.uk/about/what-we-do/into-practice/return-on-investment-tools/tobacco-return-on-investment-tool

Methods for comparison

The ROI was downloaded and run in order to compare with the EConDA microsimulation results that tested the impact of smoking cessation services with those produced from the ROI tool.

A total of 98.8% of UK adult smokers are allocated to individual-level smoking cessation interventions.

A breakdown of the Current Package for your adult population is as follows:
- 49.4% of smokers received Local Stop Smoking Service (LSSS) interventions;
- 49.4% received other, non-LSSS cessation interventions;
- 0.0% receive Nicotine Replacement Therapy to help them cut down;
- 0.0% of pregnant smokers received cessation interventions:
- 0.0% received behavioural support
- 0.0% received incentives
- 0.0% received pharmacotherapies

Comparison with the EConDA results

The parameter that could be compared between the models was the Incremental Cost Effectiveness Ratio (ICER) and the QALY.

Figure 5 shows the ICER results of the UKHF microsimulation model testing the cost-effectiveness of smoking cessation services relative to baseline (no intervention). The negative ICER values, which are comprised of positive 'QALY gained' values in the denominator and negative 'cost avoided' values in the numerator, indicates that the scenario is dominant, which is in line with the results of the ROI tool presented in Figure 6.

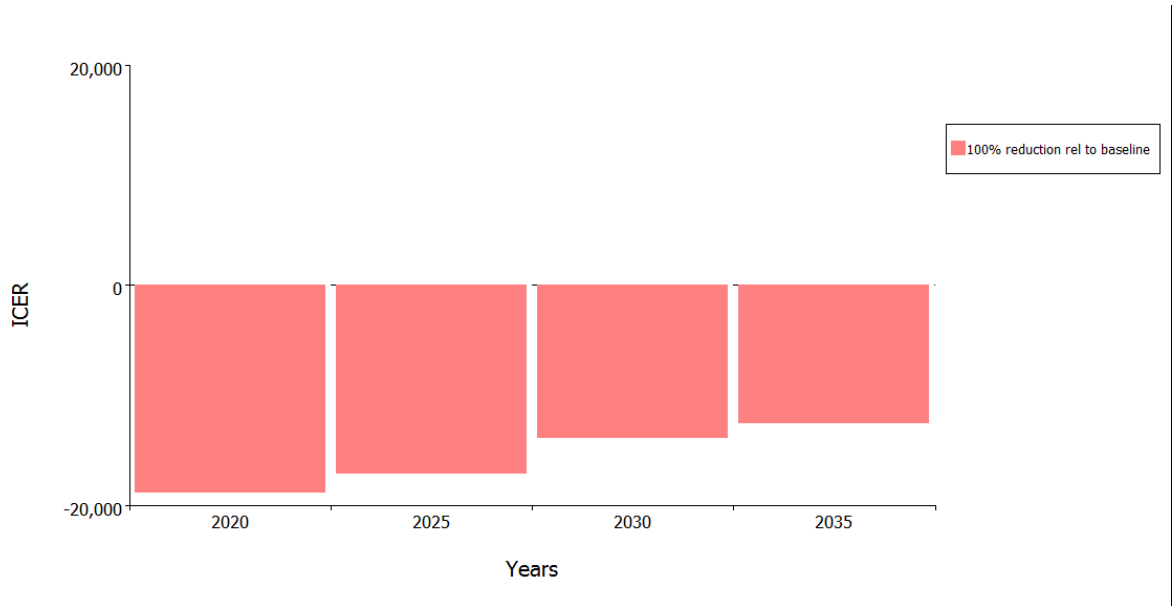

Figure 5. ICER (£ per QALY) over time

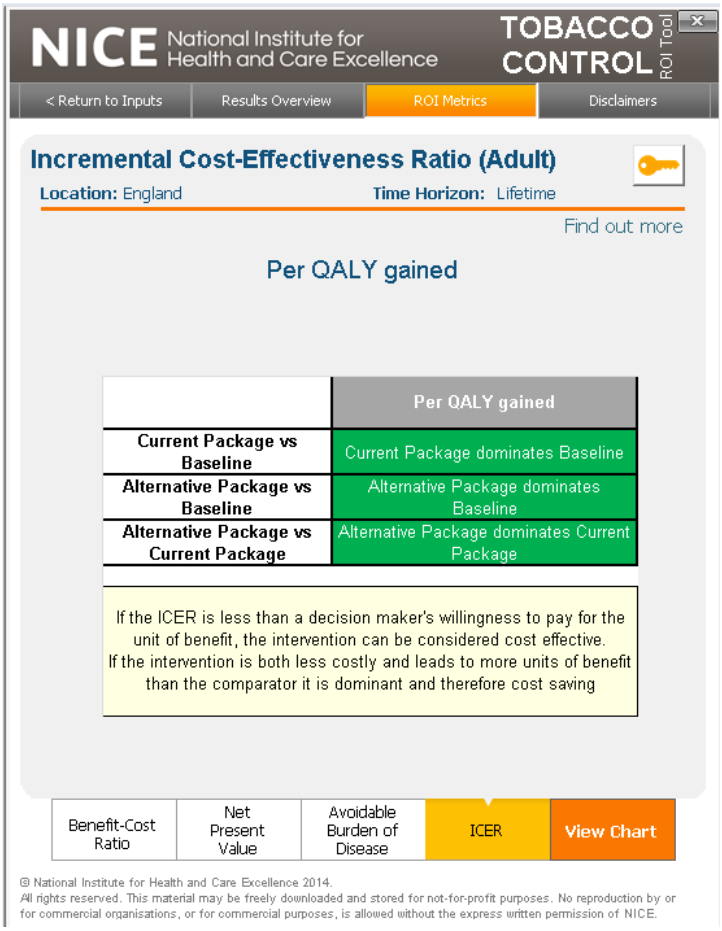

Figure 6: ICER per QALY gained

Section 4: Other chronic disease models

Other models for which no comparison was possible were present in the literature and these are described below.

Impact model

The epidemiological Impact CHD mortality model is a deterministic, cell based model which investigates the impact of CHD treatment uptake and effectiveness, risk factor trends (smoking, cholesterol, blood pressure, obesity, diabetes and physical activity) on patient CHD mortality. It was originally developed for Scotland between 1975 and 1994 (24). It has since then been used for a numerous amount of country (25–27). Comparison was not possible as the EConDA model focused on prevalence, incidence, cumulative incidence, and economic parameters, whereas the Impact model focused on these parameters specifically in the context of CHD treatments and CHD mortality.

POHEM model

The POHEM model is a dynamic Monte Carlo microsimulation model. Like the EConDA model, the POHEM model creates and ages a population (the POHEM model specifically focuses on the Canadian population), one individual at a time. It is based on two modules. The first one is the initialisation. The model can be initialised in two different ways. The first involves the creation of a synthetic population of Canadians

where all the generated individuals are born and then eventually die within the model. The second involves the creation of a real population based on cross-sectional surveys. The second module investigates the dynamic updates and risk transitions. Predictive algorithms and risk transitions models are applied to determine the individuals' disease states, risk factors and health determinants (28,29). No direct comparison was possible.

CORE diabetes model

The CORE diabetes model is a markov model with Monte-Carlo simulations (30). The model simulates either a closed or open cohort. The diabetic cohort can have type 1 or 2 diabetes and this can be defined by the user. The model consists of 4 databases which provide data to inform the model: cohort database, clinical database, treatment database and economic database. For each individual, different risk factors are considered such as age, BMI, gender, systolic blood pressure and glycosylated haemoglobin (HbA_{1c}). The level of risk is defined by a combination of these risk factors. The model focuses on diabetic individuals and their risk of further complication or diseases, relative to the medication they are prescribed and any interventions. The complications of diabetes considered in this model ranges from retinopathy to foot ulcers. Myocardial infarction is one of several diseases considered in the simulation. The length of time the person has lived with diabetes is also considered as a risk factor.

This model is different from the model developed for the EConDA project, as the initial population represents a sample of individuals from the particular country of interest. In the CORE model the entire cohort has diabetes. This has meant that it is not possible to draw any comparisons between the CORE and EConDA model. Also the probability of individuals moving to a state of diabetes is dictated by probabilities based on impaired fasting glucose and impaired glucose tolerance. However, in the CORE model, HbA1c, a different measure of diabetes, has been used.

Discussion

Two validation methods were used in the present report: cross validation and face validity. Cross validation was undertaken using 19 models and was particularly difficult to implement due to differences in methodology, model initialisation, intervention, input data and format of outputs. The first section presents a summary of the results followed by sections which detail the reasons why differences were observed.

Summary of comparisons

In terms of BMI and smoking projections

Similar BMI projections have been observed between the Kelly *et al* model (3) and the module 1 of the EConDA model.

Using the IFs model (5), the obesity prevalence results are within confidence intervals for Bulgaria, Finland, Lithuania, Netherlands, Poland and the UK. Smoking prevalence results are within confidence intervals for Bulgaria, Lithuania, Poland and Portugal.

When comparing the DisMod-MR and PyMC models (7), we found that there was a significant difference in terms of the reduction in smoking prevalence by 2025 between results from the EConDA model (1%) and the DisMod-MR model (12%).

In terms of Chronic Disease models

Compared to the DPoRT model (8), the EConDA model estimates a lower number of cumulative incidence cases of diabetes at both the 5 and 10 year follow ups.

The results from the EConDA tool show that, with increasing age, the difference in life expectancy for different BMI groups decrease. This was comparable to that of the Grover *et al* model (9).

Compared to the IDF projections results of pre-diabetes (7.8%) worldwide in 2040, the EConDA projection result of pre-diabetes rate was lower at 6.3%, averaged over the 8 countries of interest.

In terms of Intervention model

Comparing the results of the SCS intervention between the RIVM model (13) with the EConDA models, revealed significant differences in terms of prevalence of COPD stages between the Netherlands (RIVM model) and Finland (EConDA model) and the UK (EConDA model).

Similar results were observed when modelling a SCS intervention for the Netherlands between Dynamo-HIA and the EConDA tool (15). However, modelling the elimination of smoking within the UK population with the EConDA microsimulation model produced marked differences in results (16).

In terms of SSB interventions, the estimated reduction in energy intake from a 20% excise tax was 14.8kJ/person/day (3.5 calories/person/day). Similarly, Briggs et al (2013) and Collins (17) found reductions in energy intake of 16.7kJ/person/day and 3.3 kcal /person/day, respectively. Wang et al (2012) found a reduction of 9kcal/person/day in the USA. Furthermore, the estimated weight reduction

resulting from a 20% excise tax in this study was 0.05kg/person/year, which is within the confidence interval of the Briggs results. Finally, significant differences in terms of disease prevalence were observed for the SSB tax between the four models compared.

Using the PREVENT model (20), modelling a SCS intervention, similar results in terms of incidence rate were observed for the UK (0.02% in both models). Significant differences were observed in Portugal (0.02% PREVENT model versus 0.07% EConDA model) and the Netherlands (0.004% PREVENT model versus 0.02% EConDA model).

Using the ROI NICE tool (22), modelling a SCS intervention, similar results in terms of health economy analyses (ICER) were observed between this tool and the EConDA model. The SCS intervention was shown to dominate the baseline scenario (no intervention) in both cases.

Comparison was not feasible between the IMPACT (27), POHEM (28) and CORE (30) diabetes models.

The following sections discuss reasons for some of the differences observed between the EConDA models and models from the literature.

Methodology principles

The techniques for acquiring projections of risk factors varied widely between the different models. For example, the IFs model (5) used a driver-based approach for assessing BMI trends, that relate adult mean BMI to projections of available calories per capita. The demand for which responds to a function estimated at each cross-section with income, whereas the EConDA model used cross-sectional BMI data to form population based projections. However, some studies (3) used similar methods to the EConDA methods such as a logistic regression to obtain regional secular trends in prevalence of overweight or obesity, growth in population growth and shifts in demography.

In terms of modelling diseases, the models used to compare our results differ from the EConDA model in a number of different ways: some models were static (fixed in time) such as the PRIME model (18); others were cohort-based models such as the NICE ROI model, and others used a combination of semi-deterministic and semi-stochastic approaches such as that of the DYNAMO-HIA model.

Similarly, there were a number of differences in the approaches taken to modelling chronic diseases such as diabetes, COPD, CKD and CHD. For example, in the case of diabetes, the CORE model researched the impact of treatment and interventions on a diabetic cohort i.e. risk factors for diabetes were not modelled (30). This is in contrast to the EConDA model, which focused on the development of diabetes based on factors such as age, sex and the changing rates of obesity i.e. risk factors for diabetes were modelled. The EConDA model used future trends of BMI levels to influence the risk of a set of diseases in addition to the changes in the population of interest. Some models simulate a dynamic population but do not model how the risk factor BMI changes over time (9). In these models changes observed in the number of cases of a disease may only be related to changes in the population distribution over time.

Initialisation of models

Simulation years

Simulation years for the models compared were not always consistent in terms of the start year, end year and duration. Efforts were made to match these timings but it was not always possible. For instance, in the PREVENT model, the years of interest were between 2010 and 2030 which was different from those used for the EConDA model (2015 to 2050). However, it was possible to generate outputs in 5-year increments from the EConDA model. Therefore, results between the periods of interest (e.g. 2015 to 2030) could be easily accessed and analysed. For DisMod-MR, years of interest were between 2010 and 2025.

Population of interest

The population of interest for the models investigated were generally not entirely comparable for several reasons:

- The countries of interest were different. For example, in Kelly *et al* (3), the market economy estimates were deduced using data from Australia, Belgium, Canada, Denmark, Finland, Germany, Greece, Iceland, Ireland, Japan, New Zealand, Portugal, Spain, Switzerland, United Kingdom and the United States. The inclusion of countries such as New Zealand, US Canada, and Australia may have a significant effect on the estimated prevalence of overweight and obesity. For example, in the NICE ROI tool and the APHO diabetes prevalence model, predictions were generated for England and these have been compared to EConDA results for the UK. In the DisMod-MR model, the European region was composed of Andorra, Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Russian Federation, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom. These were compared to our individual EConDA countries (Bulgaria, Finland, Greece, Lithuania, Netherlands, Portugal, Poland, and UK). For the IDF comparison, EConDA results were compared to results from all around the world.

- There were differences in terms of age categories. For example in the Hughes & Peterson, 2011 paper, the age category of interest was from 30 years old, whereas a threshold of 20 years old has been used for the EConDA projections leading to different obesity and overweight estimates in 2030 (Appendix 3). Another example is the RIVM model for multistage COPD, whereby the prevalence and incidence statistics computed for adults in the model were greater than or equal to 45 years old. For the EConDA model, the population is simulated and the results represent an average over the whole population. For DisMod-MR, 15 years old and older was used. For Briggs *et al* (18), a threshold of 16 years old has been used. Finally, for Wang *et al* (19), a category of 25-64 years old was used.

- There were differences in terms of health of the population of interest. The DPoRT tool assumed an initial zero diabetic population in the start year of the simulation. Additionally, the smoking model developed for the EConDA project did not incorporate diabetes as a smoking related disease (9).

Model stratification

Some models such as the APHO diabetes prevalence model take into account ethnicity, deprivation and undiagnosed individuals, factors that were not included in the EConDA microsimulation results. Projections generated in the EConDA project were stratified by age, sex and education when possible.

Interventions

Comparing the impact of an intervention such as smoking cessation and sugar sweetened beverage tax across the different models was challenging as different assumptions were implemented in each of the models.

For instance, in the ROI NICE tool (22), the smoking cessation interventions were divided into seven different interventions: Local Stop Smoking Service (LSSS), non-LSSS cessation intervention, treatment using nicotine replacement therapy (NRT) to help smokers to cut down, intervention for pregnant smokers, behavioural support, pharmacotherapies and incentives. For the present comparison, around 50% LSSS and around 50% non LSSS were used. In the EConDA model, local and non-local interventions were addressed in the same way.

Another example of difference in terms of smoking cessation intervention assumption is evident in the PREVENT model (20). This model assumes three different effectiveness rates 3%, 15% and 35% which are kept constant and applied to all of the countries in the study. Whereas, the EConDA model assumes different effectiveness rates based on the countries of interest 30% effectiveness, which made a robust comparison difficult.

For SSB tax, an example of a case where the intervention assumption differed is the substitution effect: the EConDA Models and the Wang model (19) includes substitution effects – whereas this was not considered in the Briggs paper (18). Therefore, direct comparison was not possible.

Finally, some differences are seen due to the fact that some SCS intervention targets all of the smoking related diseases and not just COPD patients as observed in the RIVM comparison (13).

Input data

The models outlined in this report were developed in a number of ways. Like the EConDA model, most models used input data from a variety of published sources (30). However, some models used just one dataset to train part of or their entire model. For example, the diabetes model developed by Grover *et al* used data from the Atherosclerosis and Risk in Communities Study (ARIC) (9). Depending on the size of the study cohort, there could be limitations to using just one dataset to determine the risk of individuals. This is especially relevant in the case of some diseases where the prevalence within the population is low.

Format of outputs

In some cases it was difficult to compare outputs from a particular model with the outputs generated by the EConDA model. There were several different reasons:

-Some of the results did not include error bars such as was the case for IFs model (5) and Kelly *et al* (3), which made it difficult to compare the results in a robust manner.

-Some results were not comparable because the risk factor categories and the number of stages for diseases were different. For instance, for the EConDA tool, there were two cohort options: either an 'at risk' group containing individuals who were either overweight, obese or very obese, or an 'all risk' group. Some studies were able to further stratify outputs by the 'at risk' BMI categories such as overweight, obese and very obese (9). Similarly, the COPD model developed with the EConDA project included three stages of COPD whereas, four stages were used in some studies (13,14).

-Finally, some of the EConDA model outputs were omitted such as: 1) mortality, preventing us from comparing results with models such as the IMPACT model; 2) the net present value, preventing us from comparing results with models such as the ROI NICE tool; and 3) the average life years free from a disease, preventing us from comparing some of the data generated in the Grover *et al* model (9).

Limitations

There are many key models in the literature which model similar risk factors and diseases when compared to the EConDA project. The present report provides an overview and examples from the literature, although this is not an exhaustive list. Due to some of the limitations which have been discussed previously it was not possible to compare some models because of the lack of common outputs (31,32).

As mentioned in the introduction, five validation methods exist. External validation, predictive and verification methods were not included here since they were outside of the scope of the project.

Finally, a sensitivity analysis was not included in this project, since the process requires super computers, and thus it was beyond the scope of the project.

Future work and Model improvements

There are a number of improvements which could be made to the current EConDA model based on the methods and assumptions used by other models which have been discussed in this report. The following points could be included in future model developments:

- The use of multiple risk factors. In some of the models multiple risk factors were used in the simulation of disease risk. For example Grover *et al* used both smoking and BMI as risk factors for analysing the risk of diabetes and CHD.

- The inclusion of additional risk factors to more accurately determine the prevalence of diseases. Risk factors such as hypertension (8), waist circumference (9) and cholesterol (total and HDL) (9) could be used to better understand the estimated of the diseases of interest.

- The inclusion of variables related to complications, history and family history are needed to better determine the estimates of interest.

- The inclusion of more health economic related parameters such as ROI or NPV to capture better the economic environment of interventions

-Finally, future work will involve contributing to the implementation of guidelines for modelling since modelling methods need to be fully transparent (33).

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Appendix 1: Using the EConDA tool to calculate life expectancies by EConDA country

Three different age group cohorts were simulated in the tool for both males and females, these were 18-39, 40-64 and >65 year olds. All the cohorts were constructed of individuals who were 'at risk' (≥25 kg/m^2) which included overweight, obese and very obese BMI categories. These cohorts were compared against an equivalent cohort based on age and sex where all the individuals were healthy weight. The average life expectancy was calculated for each cohort. The number of life years lost was calculated by taking the difference between each of these cohorts with the same age and sex. The results for each of the EConDA countries are shown in the tables below for males (Table 29) and females (Table 30).

Table 29 Average life years lost for an 'at risk' BMI group relative to a healthy weight group (15 to <25 kg/m^2) for males and for three different age groups: 18-39, 40-64 and ≥65 years. The results are shown for each EConDA country.

Life years lost	Bulgaria	Finland	Greece	Lithuania	Netherlands	Poland	Portugal	UK
18-39	4.13	6.09	4.05	3.51	1.25	3.75	3.35	1.67
40-64	2.12	3.76	2.64	2.14	0.69	2.35	2.14	0.77
65+	0.38	1.14	0.43	0.47	0.12	0.44	0.38	0.16

Table 30 Average life years lost for an 'at risk' BMI group relative to a healthy weight group (15 to <25 kg/m2) for females and for three different age groups: 18-39, 40-64 and ≥65 years. The results are shown for each EConDA country

Life years lost	Bulgaria	Finland	Greece	Lithuania	Netherlands	Poland	Portugal	UK
18-39	5.11	8.71	4.89	5.58	1.75	5.84	4.99	3.83
40-64	3.11	5.36	3.45	3.59	0.97	3.91	3.2	2.48
65+	0.65	1.55	0.55	0.82	0.2	0.63	0.68	0.67

Appendix 2: ROI NICE data input

Group Code	Description	Age	Current Smoker Male	Former Smoker Male	Current Smoker Female	Former Smoker Female	Source
C00–C14	Lip, Oral Cavity, Pharynx	35 +	10.89	3.4	5.08	2.29	Statistics for Smoking for England 2013: Table B2
C15	Oesophagus	35 +	6.76	4.46	7.75	2.79	Statistics for Smoking for England 2013: Table B2
C16	Stomach	35 +	1.96	1.47	1.36	1.32	Statistics for Smoking for England 2013: Table B2
C25	Pancreas	35 +	2.31	1.15	2.25	1.55	Statistics for Smoking for England 2013: Table B2
C32	Larynx	35 +	14.6	6.34	13.02	5.16	Statistics for Smoking for England 2013: Table B2
C33–C34	Trachea, Lung, Bronchus	35 +	21.3	8.3	12.5	4.8	Thun JAMA 2000 Table 3
C53	Cervix Uteri	35 +			1.59	1.14	Statistics for Smoking for England 2013: Table B2
C64–C65	Kidney and Renal Pelvis	35 +	2.5	1.7	1.4	1.1	Statistics for Smoking for England 2013: Table B2
C67	Urinary Bladder	35 +	3.27	2.09	2.22	1.89	Statistics for Smoking for England 2013: Table B2
C80	Unspecified site	35 +	4.4	2.5	2.2	1.3	Statistics for Smoking for England 2013: Table B2
C92.0	Acute Myeloid Leukemia	35 +	1.8	1.4	1.2	1.3	Statistics for Smoking for England 2013: Table B2
I20–I25	Ischemic Heart Disease	35-64	2.6	1.6	3.2	1.4	Thun JAMA 2000 Table 3
I20–I25	Ischemic Heart Disease	65 +	1.5	1.2	1.7	1.4	Thun JAMA 2000 Table 3
I00–I09, I26–I51	Other Heart Disease	35 +	1.78	1.22	1.49	1.14	Statistics for Smoking for England 2013: Table B2
I60–I69	Cerebrovascular Disease	35-64	2.4	1	3.8	1.5	Thun JAMA 2000 Table 3
I60–I69	Cerebrovascular Disease	65 +	1.5	1	1.6	1.2	Thun JAMA 2000 Table 3
I70	Atherosclerosis	35 +	2.44	1.33	1.83	1	Statistics for Smoking for England 2013: Table B2
I71	Aortic Aneurysm	35 +	6.21	3.07	7.07	2.07	Statistics for Smoking for England 2013: Table B2
I72–I78	Other Arterial Disease	35 +	2.07	1.01	2.17	1.12	Statistics for Smoking for England 2013: Table B2
J10-J18	Pneumonia, Influenza	35 +	2.5	1.4	4.3	1.1	Statistics for Smoking for England 2013: Table B2
J10-J18	Bronchitis,	35	17.1	15.64	12.04	11.77	Statistics for Smoking for

	Emphysema	+					England 2013: Table B2
J40-J44	Chronic Airway Obstruction	35 +	10.8	7.8	12.3	8.9	Thun JAMA 2000 Table 3
K25-K27	Digestive Diseases	35 +	4.5	1.6	6.4	1.4	Callum 2004 (Tobacco in London) Table A1 p. 39
C54	Endometrial cancer*	35 +			0.7	0.7	Callum 2004 (Tobacco in London) Table A1 p. 39
I73.9	Peripheral vascular disease	35 +	16	7	16	7	Callum 2004 (Tobacco in London) Table A2 p. 40
K50	Crohn's disease	35 +	2.1	1	2.1	1	Callum 2004 (Tobacco in London) Table A2 p. 40
K05	Periodontitis	35 +	3.97	1.68	3.97	1.68	Callum 2004 (Tobacco in London) Table A2 p. 40
H25	Age related cataract (45+)	35 +	1.54	1.11	1.54	1.11	Callum 2004 (Tobacco in London) Table A2 p. 40
S72	Hip fracture	55 - 64	1.17	1.02	1.17	1.02	Callum 2004 (Tobacco in London) Table A2 p. 40
S72	Hip fracture	65 - 74	1.41	1.08	1.41	1.08	Callum 2004 (Tobacco in London) Table A2 p. 40
S72	Hip fracture	75 +	1.76	1.14	1.85	1.22	Callum 2004 (Tobacco in London) Table A2 p. 40
K51	Ulcerative colitis*	35 +	0.82	0.82	0.82	0.82	Callum 2004 (Tobacco in London) Table A2 p. 40
D25	Uterine fibroids - women*	35 +			0.7	0.7	Callum 2004 (Tobacco in London) Table A2 p. 40
O03	Spontaneous abortion	35 +			1.28	1	Callum 2004 (Tobacco in London) Table A2 p. 40
G20-G21	Parkinson's disease*	35 +	0.31	0.79	0.2	0.76	Thacker et 2007 (Neurology 68(10) 764-768

*protective effect

Parameter	Source
Prevalence of smokers and former smokers	IHHS (2011) – local area specific data
Population of local area	ONS (2011) – local area specific data
Prevalence of Lung cancer: smokers & former smokers	Copied from Trapero-Bertran et al. (2012)
Prevalence of MI: smokers & former smokers	Copied from Trapero-Bertran et al. (2012)
Prevalence of COPD: smokers & former smokers	Copied from Trapero-Bertran et al. (2012)
Prevalence of CHD: smokers & former smokers	Copied from Trapero-Bertran et al. (2012)
Prevalence of Stroke: smokers & former smokers	Copied from Trapero-Bertran et al. (2012)
Mortality and Life Table	Office for National Statistics
Pregnancy related data	Statistics on Women's Smoking Status at Time of Delivery: England (HSCIC) http://www.hscic.gov.uk/catalogue/PUB11039

Appendix 3: IFs model versus EConDA model

The age category of interest for EConDA is 20 years old and older. For the IFs model, the age category of interest is 30 years old and older. Differences between the EConDA and IFs model are significant for Portugal and Greece. Investigating the EConDA model 20-29 years old projections for these country (Figure 7-Figure 10) explain partly the reasons of the differences: The high obesity prevalence predictions for the 20-29 years males and females in Greece would explain the higher prevalence observed using the EconDA model compared to the IFs estimates.

Figure 7 Projected BMI-group in 20-29 year old males for Portugal

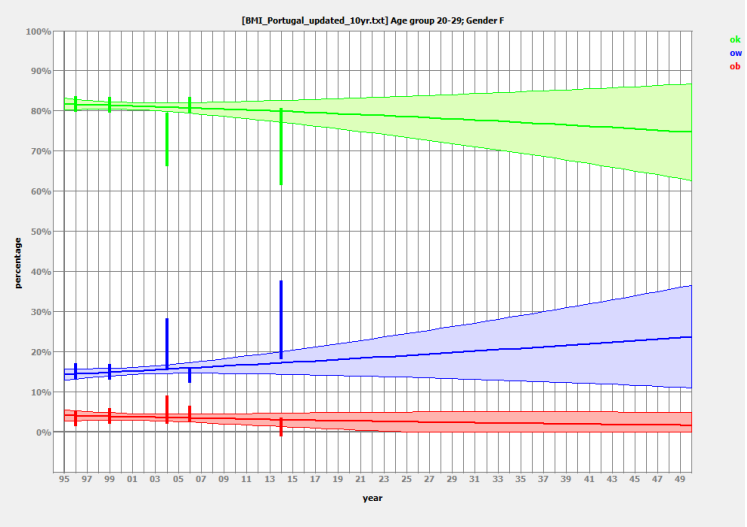

Figure 8 Projected BMI-group in 20-29 year old females for Portugal

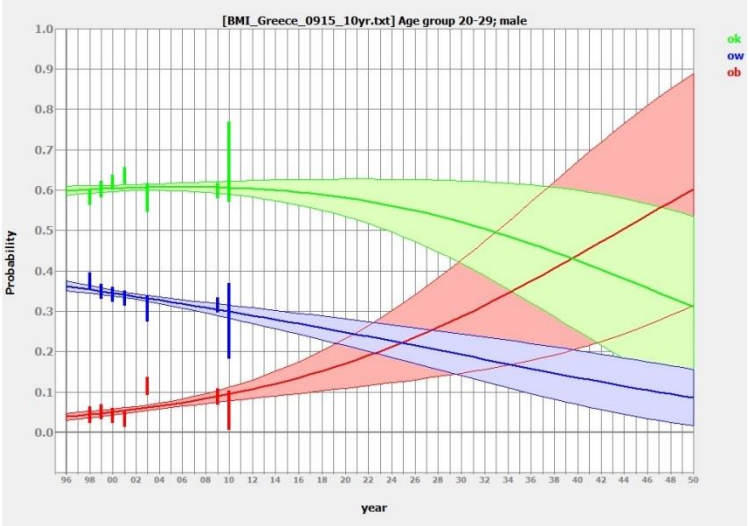

Figure 9 Projected BMI-group in 20-29 year old males for Greece

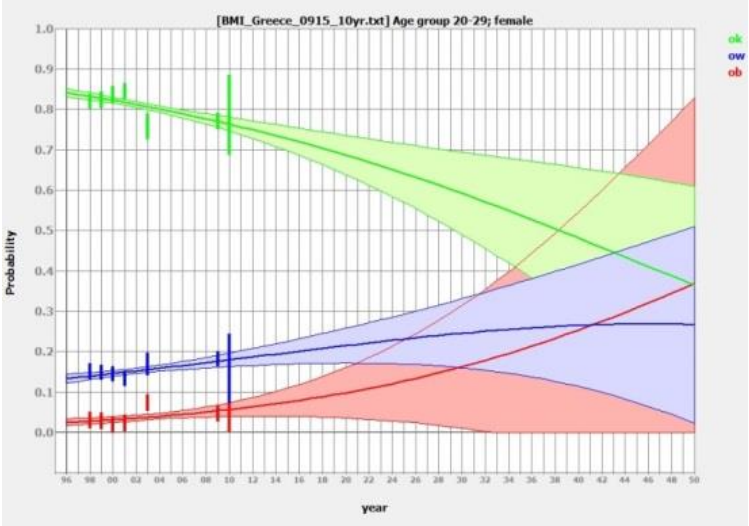

Figure 10 Projected BMI- group in 20-29 year old females for Greece

Appendix 4: UK results

Results from the EConDA model

Impact on disease incidence and prevalence

Figure 11 and Table 31 present the cumulative incidence cases avoided as a result of the intervention compared to baseline. The intervention results in 365, 294, 229 cumulative incidence cases avoided for COPD stage 1, Stroke, and lung cancer respectively.

Figure 12 and Table 32 present the prevalence cases avoided for each intervention relative to baseline, per 100,000. The scenario results in 229, 146 and 36 prevalence cases avoided for COPD stage 1, stroke and lung cancer respectively.

Table 31. Cumulative incidence case avoided (per 100,000)

	Year	CHD	COPD stage 1	COPD stage 2	COPD stage 3	Hypertension	Stroke	Lung Cancer
SCS	2015	0 [+-1]	0 [+-1]	-1 [+-1]	0 [+-0]	1 [+-3]	1 [+-1]	-1 [+-0]
	2020	4 [+-3]	33 [+-4]	-2 [+-3]	4 [+-1]	11 [+-6]	26 [+-3]	11 [+-1]
	2025	7 [+-4]	98 [+-6]	7 [+-4]	10 [+-1]	35 [+-8]	77 [+-3]	43 [+-3]
	2030	15 [+-4]	179 [+-7]	21 [+-4]	20 [+-1]	69 [+-10]	141 [+-4]	92 [+-3]
	2035	25 [+-6]	271 [+-7]	44 [+-6]	34 [+-3]	111 [+-11]	215 [+-4]	154 [+-3]
	2040	31 [+-6]	365 [+-8]	70 [+-6]	52 [+-3]	161 [+-11]	294 [+-6]	229 [+-4]

Table 32. Prevalence case avoided (per 100,000)

	Year	CHD	COPD stage 1	COPD stage 2	COPD stage 3	Hypertension	Stroke	Lung Cancer
SCS	2015	0 [+-3]	0 [+-7]	2 [+-4]	1 [+-1]	10 [+-13]	0 [+-3]	-1 [+-1]
	2020	3 [+-3]	35 [+-7]	-4 [+-4]	4 [+-1]	14 [+-13]	22 [+-3]	8 [+-1]
	2025	5 [+-3]	84 [+-7]	-3 [+-4]	8 [+-1]	27 [+-13]	59 [+-3]	16 [+-1]
	2030	9 [+-4]	137 [+-7]	-4 [+-4]	15 [+-1]	33 [+-13]	97 [+-3]	24 [+-1]
	2035	12 [+-4]	185 [+-7]	3 [+-4]	22 [+-1]	34 [+-13]	126 [+-3]	29 [+-1]
	2040	9 [+-4]	229 [+-7]	7 [+-4]	30 [+-1]	34 [+-13]	146 [+-3]	36 [+-1]

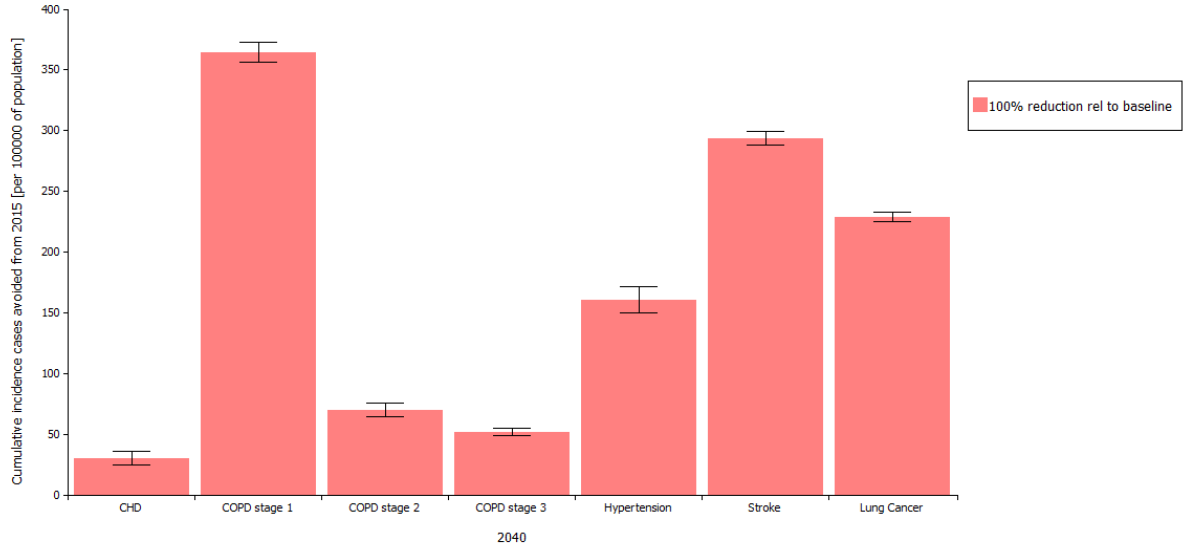

Figure 11. Cumulative Incidence case avoided (per 100,000)

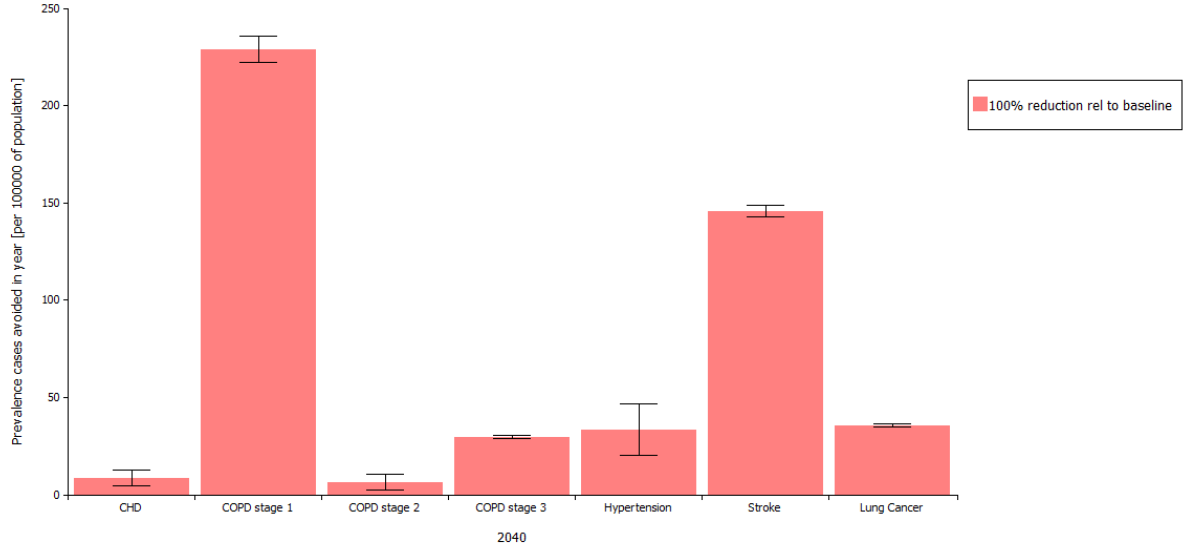

Figure 12. Prevalence case avoided (per 100,000)

Appendix 5: Netherlands results

Results from the EConDA model

The EConDA microsimulation was run in order to model the same intervention and the results are shown below.

Impact on disease incidence and prevalence

Figure 13 and Table 33 presents the cumulative incidence cases avoided by the intervention compared to baseline from 2015 to 2050. The intervention results in 491, 286, 265,143 and 111 cumulative incidence cases avoided for Stroke, COPD, lung cancer, hypertension and CHD respectively.

Table 33. Cumulative cases avoided per 100,000

	Year	CHD	COPD	Hypertension	LungC	Stroke
SCS rel to baseline	2015	0 [+-1]	0 [+-1]	0 [+-3]	1 [+-1]	0 [+-1]
	2020	7 [+-4]	21 [+-3]	14 [+-7]	20 [+-1]	49 [+-3]
	2025	34 [+-6]	76 [+-4]	40 [+-8]	71 [+-3]	160 [+-4]
	2030	67 [+-7]	164 [+-4]	80 [+-10]	153 [+-3]	309 [+-5]
	2035	111 [+-8]	286 [+-5]	143 [+-11]	265 [+-4]	491 [+-6]

Figure 14 and Table 34 present the prevalence cases avoided for each intervention relative to baseline, per 100,000. The scenario results in 297, 182, 61 and 39 prevalence cases avoided for stroke, COPD, lung cancer and CHD respectively.

Table 34: Prevalence cases avoided per 100,000

	Year	CHD	COPD	Hypertension	LungC	Stroke
SCS rel to baseline	2015	7 [+-7]	0 [+-3]	8 [+-13]	0 [+-1]	0 [+-4]
	2020	12 [+-7]	18 [+-4]	18 [+-13]	13 [+-1]	43 [+-4]
	2025	25 [+-7]	58 [+-4]	17 [+-13]	29 [+-1]	126 [+-4]
	2030	32 [+-7]	116 [+-4]	7 [+-13]	47 [+-1]	215 [+-4]
	2035	39 [+-7]	182 [+-4]	-4 [+-13]	61 [+-1]	297 [+-4]

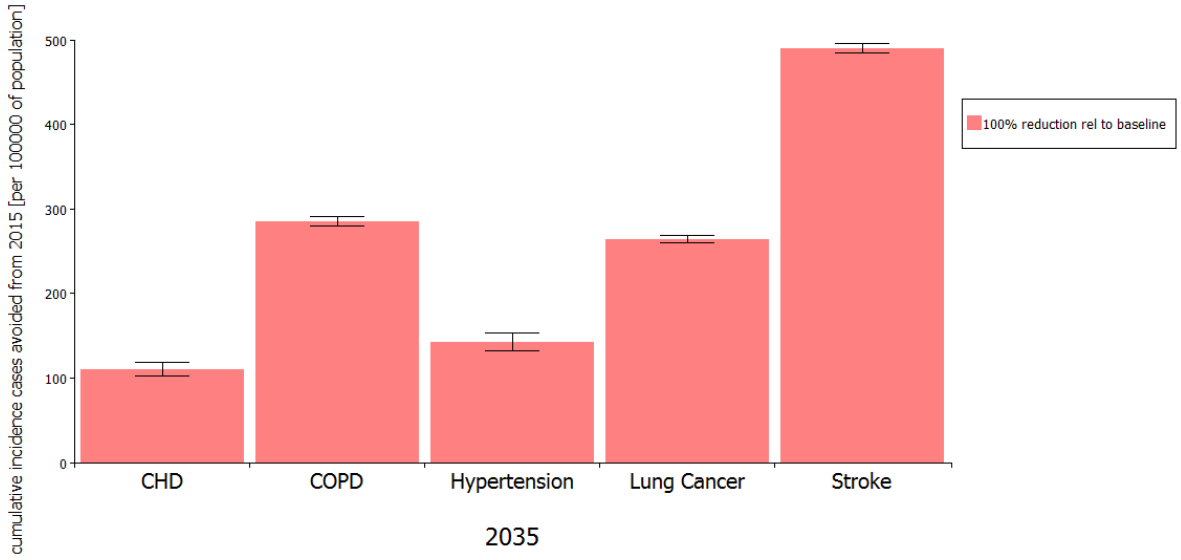

Figure 13. Cumulative incidence avoided from 2015 (per 100,000)

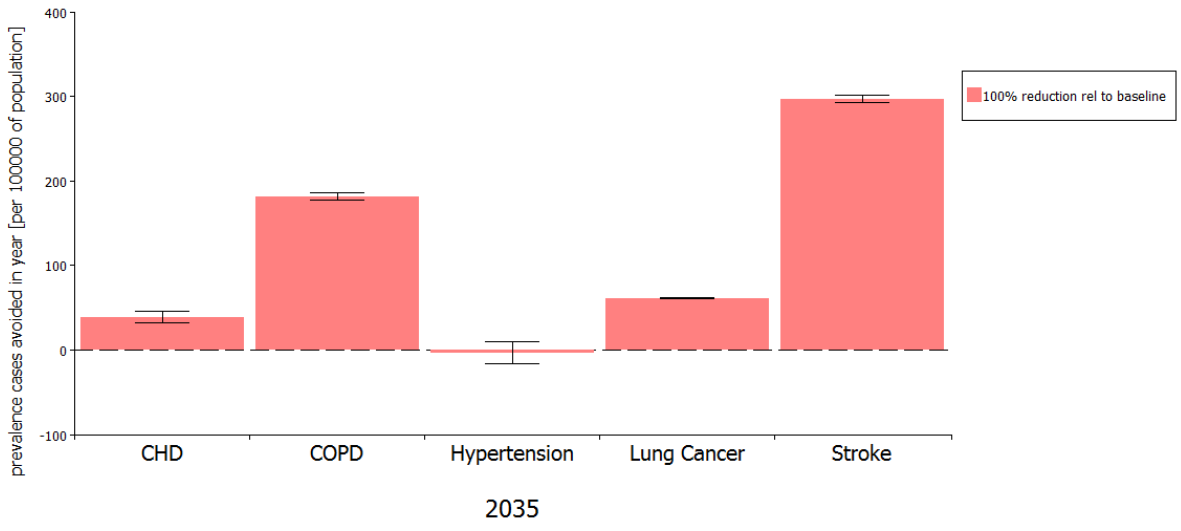

Figure 14. Prevalence case avoided in year 2035 (per 100,000)

Impact on costs, QALYs and ICERs

Figure 15 present the direct health-care costs avoided of each intervention relative to baseline. The graph highlights that the greatest benefit in terms of direct health-care costs avoided is observed for stroke (3.7 million Euro per 100,000) followed by COPD (0.1 million Euro per 100,000), followed by CHD (0.06 million Euro per 100,000).

Figure 16 present the indirect costs avoided of each intervention relative to baseline. Indirect costs avoided compared to baseline were highest for stoke (2.7 million Euro per 100,000) followed by COPD (0.5 million euro per 100,000) and Lung Cancer (0.1 million Euro per 100,000).

Figure 17 and Figure 18 present the QALYs gained (per 100,000) for each intervention relative to baseline for males and females respectively between 2020 and 2050. For males, the scenario of interest results in QALYs gained increasing to 134/100,000 in 2035. For females, QALYs gained (per 100,000) increase to 131 / 100,000 in 2035.

In Figure 19 the negative ICER values, which in this case happens to be comprised of positive 'QALY gained' values in the denominator and negative 'cost avoided' values in the numerator, indicates that the scenario is dominant.

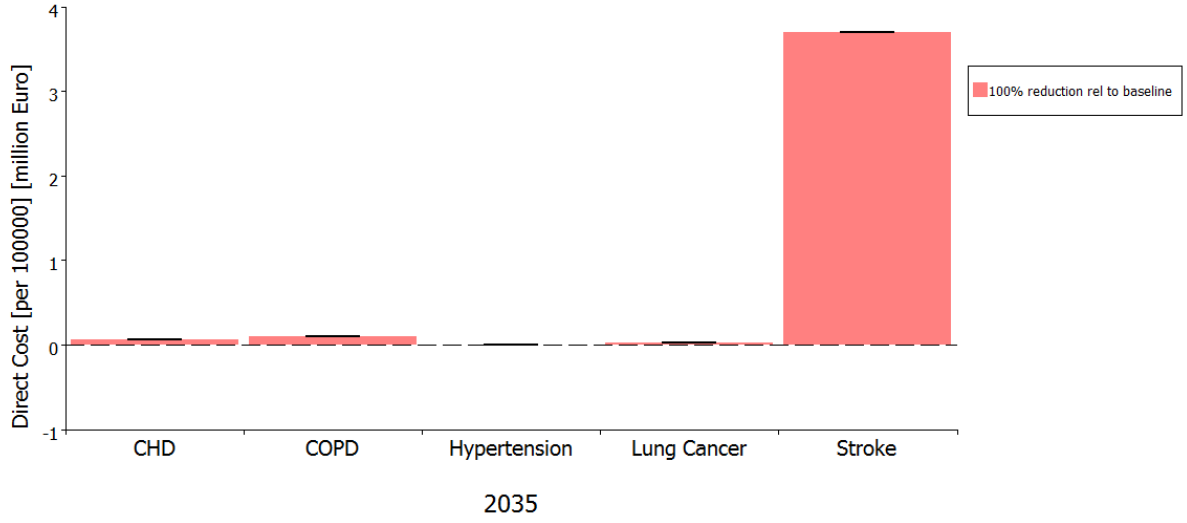

Figure 15. Direct Cost avoided (millions Euros per 100,000)

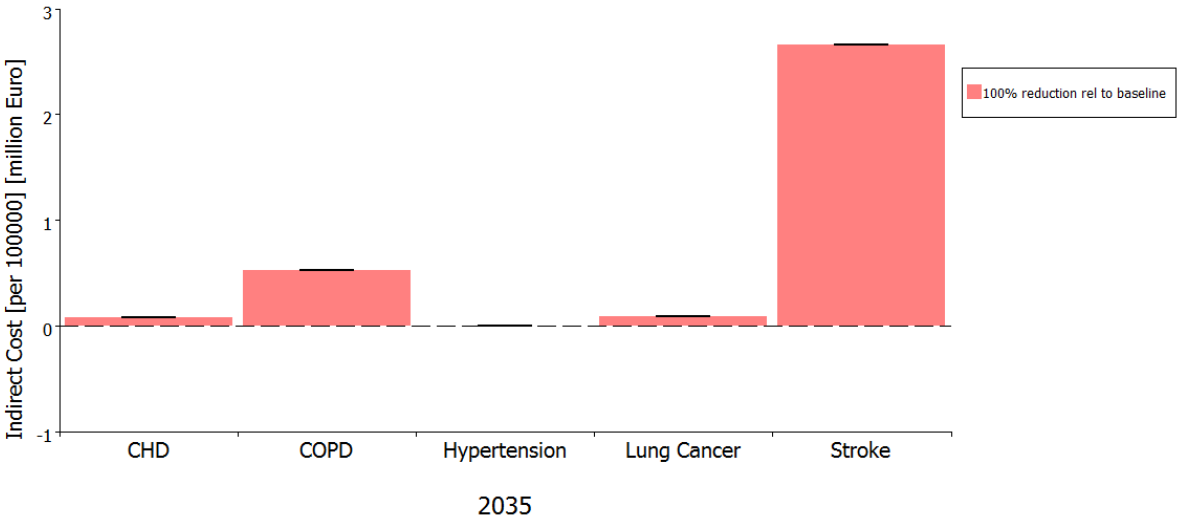

Figure 16. Indirect Cost (millions Euros per 100,000)

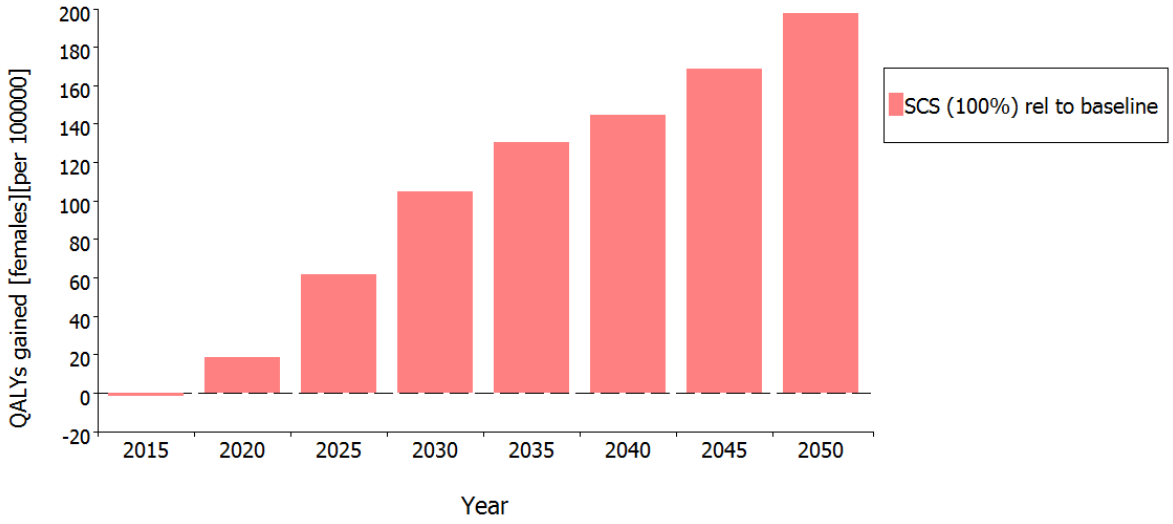

Figure 17. QALY gained for females

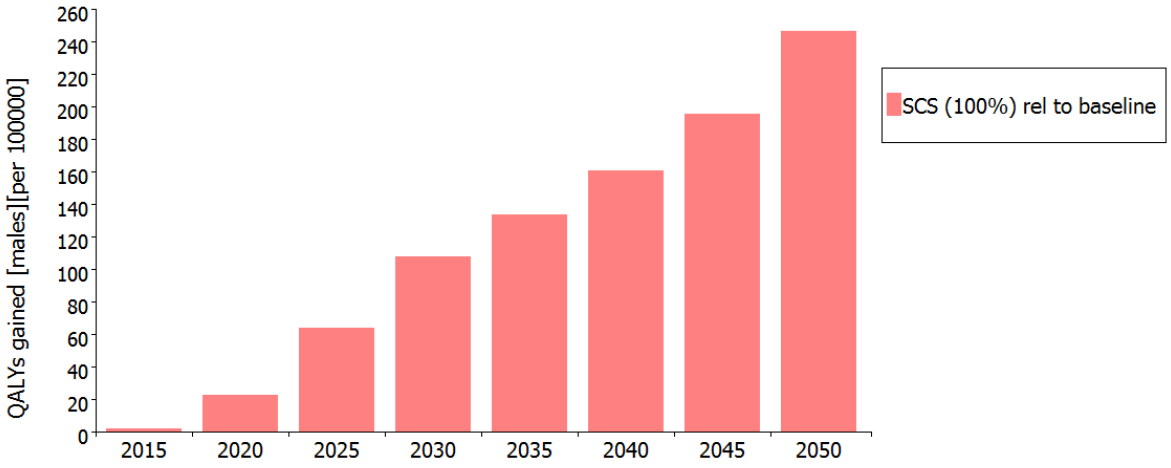

Figure 18. QALY gained for males

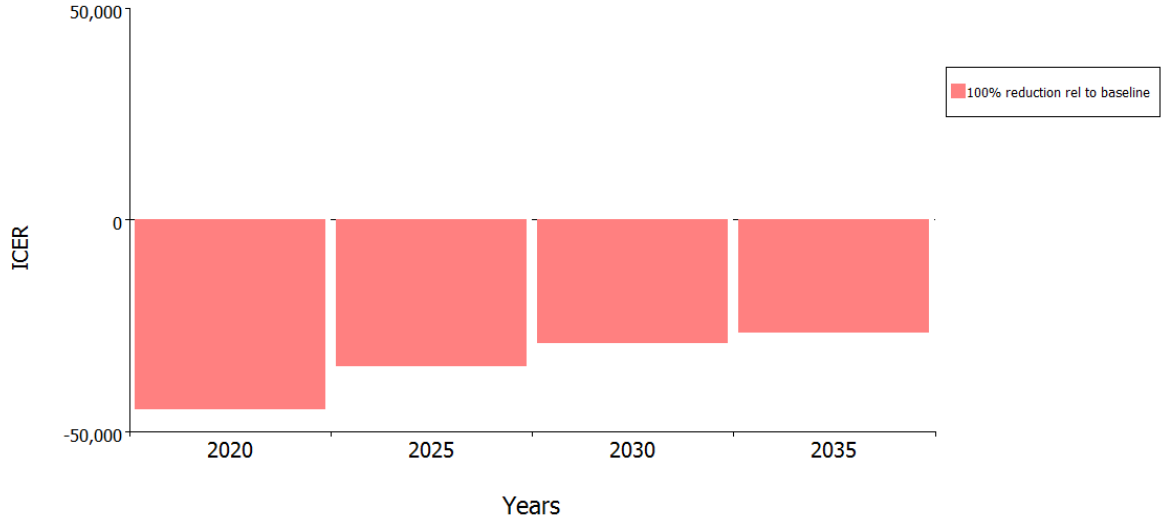

Figure 19. ICER versus time