The smoking epidemic in Europe in the 21st century

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Abstract

Background – Despite smoking being an important public health challenge in Europe, estimates of future smoking-attributable mortality for European countries are rare, and unknown remains how the smoking epidemic will continue in Europe in the 21st century. We shall fill this gap by projecting smoking-attributable mortality in 29 European countries up to 2100 using a novel forecasting approach which takes into account the wave pattern of the smoking epidemic, the importance of the cohort dimension, and likely differences between countries and sexes.

Data and methods – We forecast indirectly estimated smoking-attributable mortality fractions by age (35-84 M; 40-84 F) and sex for 29 European countries from 1950 onwards by means of age-period-cohort modeling with a generalized logit link function. The period parameter is projected by a quadratic curve with correlated errors (women) or by autoregressive extrapolation of the past decline (men). The cohort parameter is projected by autoregressive extrapolation of the recent trend after burning the outer cohorts. We performed 50,000 simulations.

Results – Smoking-attributable mortality among men in the 29 European countries studied will further decline from the 2014 average value of 25% (ranging from 11% in Sweden to 41% in Hungary) to an average value of 11% (range 6.5-11%) in 2040, 7% (5.9-9.4%) in 2065, and 5.9% in 2100. Smoking-attributable mortality among women is expected to reach a peak on average in 2014 (Northern Europe), 2019 (Western Europe), 2028 (Greece, Italy), and 2022 (Central Europe), with maximum levels of smoking-attributable mortality of on average 17% (ranging from 8% in Greece to 28% in Denmark). Smoking-attributable mortality among women is projected to be on average 10% in 2040 (ranging from <5% in Sweden, France, Greece, Slovakia to 20% in Hungary), 5% (3.5-7.6%) in 2065, and 3.5% in 2100. For women, the cohort pattern in the uptake of smoking will result in a shift of the peak of the inverse U-shaped age pattern of SAMF to the right, and crossovers between the age-specific SAMF trends. For men this effect is visible only in the past.

Conclusion – Our novel forecasting method enabled the forecast of age-specific smoking-attributable mortality up to 2100 in line with both the data and the theory. The projected considerable future peak in smoking-attributable mortality among women warrants attention.

Key words: smoking, Europe, future, mortality, smoking epidemic, smoking-attributable mortality

What is already known on the topic

- Past trends in smoking-attributable mortality show a clear (indication of) a wave pattern, which occurred earlier among men than women, and earlier in Northwestern European countries than other European countries
- The few available estimates of future smoking-attributable mortality for European countries for the long-term future are either based on strong assumptions or do not provide age-specific estimates.

What this paper adds

- A new approach to forecast smoking-attributable mortality into the long run, that is data driven, in line with the wave shaped smoking epidemic, and acknowledges the importance of the cohort dimension
- Novel estimates of (age-specific) smoking-attributable mortality up to 2100 in 29 European countries
- Information on the expected timing and level of the maximum mortality impact of smoking for women in Europe

INTRODUCTION

Smoking remains an important public health challenge in Europe. That is, in Europe, tobacco smoking prevalence among adults is still the highest worldwide, and also the share of all-cause mortality due to smoking is – with 16% among adults aged 30 and over - higher in Europe as compared to the global average of 12% (WHO, 2018c). This makes smoking the most important preventable risk factor in Europe (WHO, 2009). For public health policy makers it is highly relevant to know how the smoking epidemic and particularly the mortality impact of smoking, in terms of smoking-attributable mortality, is likely to further develop into the future for Europe as a whole but also for individual European countries.

The smoking epidemic model provides a qualitative expectation / theory on the current and likely future evolvement of smoking-attributable mortality. That is, the smoking-epidemic model, first described by Lopez et al. in 1994, and later expanded by Thun et al. in 2012 to the more recent period and developing countries, describes the general wave pattern of the smoking epidemic and how its timing and strength differs by country and sex. That is, it describes the increase and subsequent decline in smoking prevalence followed about 30 years later by a similar non-linear wave pattern in smoking-attributable mortality. The smoking epidemic started first among men in Anglosaxon countries and Northwestern Europe, followed first by other European countries, then by China, Japan, Southeast Asia, Latin America and North Africa, and finally by sub-saharan Africa. For women, the smoking epidemic started about two decades later than men, and women's smoking prevalence levels remain lower than those observed for men. Europe is currently in the fourth stage of the smoking epidemic model which is characterised by declining smoking prevalence among both men and women, declining smoking-attributable mortality among men, but – in the majority of countries – still increasing smoking-attributable mortality among women. A recent empirical assessment of sex and country differences in the level and timing of the maximum mortality impact of the smoking epidemic from 1950 onwards in Europe, revealed that the timing of the maximum mortality impact differed more between men and women than put forward in the smoking epidemic model, but less between regions. Furthermore, a considerable difference between European countries in the level of the maximum mortality impact among men was revealed (Janssen 2019).

Except for a semiquantitative projection of smoking-attributable mortality, for USA up to 2025, based on current trends in early middle age (Thun et al. 2012), these papers, however, do not provide a formal estimation of smoking-attributable mortality in the future. In fact, studies that estimate future smoking-attributable mortality for Europe and its countries are rare. Projections by WHO as part of the Global Burden of Disease study (Murray & Lopez 1997; Mathers & Loncar 2006; WHO 2013; WHO 2018) provide valuable information on future smoking-attributable mortality in the WHO European region as a whole up to 2030 – and very recently – to 2060, but not for its individual members. Foreman et al. (2018) provide estimates of future smoking prevalence and future smoking impact ratios by country, but not future smoking-attributable mortality. Additional studies with estimates of future smoking-attributable mortality for Europe focused on individual countries that were already quite advanced in the smoking epidemic (Janssen et al. 2013; Stoeldraijer et al. 2015). The more frequent forecasts of lung-cancer mortality – predominantly using age-period-cohort methodology - mostly only deal with the nearby future (Brennan & Bray 2002, Clements et al. 2005, Riebler & Held 2017), and mostly are about non-European countries (Kaneko et al. 2003; Winkler et al. 2015)(see as well Yu et al. 2019). The few available estimates for the long-term future for selected countries are based on strong assumptions – among others on when the peak for women is being reached (Janssen et al. 2013; Stoeldraijer et al. 2015) - and/or important additional information on (future) smoking prevalence (Shibuya et al. 2005).

One important exception is the very recent paper by Li & Raftery (archived) which forecasted smoking-attributable mortality for both sexes for 69 countries up to 2050 (Li & Raftery 2019). They used a four-level Bayesian hierarchical framework to jointly model smoking-attributable mortality for men and women, by means of – among others - a double logistic curve. Their paper and approach are an important contribution to the field. Important to note, however, is that they projected smoking-attributable mortality for all ages combined, thereby not generating age-specific estimates, and ignore the importance of the cohort dimension. Because of differences between birth cohorts in the uptake of smoking and consequently in smoking-attributable mortality levels (Janssen & Kunst 2005; Preston and Wang 2006) previous forecasts included the cohort dimension by means of age-period-cohort modelling (see the previous paragraph).

Our objective is to provide estimates of smoking-attributable mortality, by sex and age, up to 2100 for 29 European countries by means of a new purely data-driven approach which takes into account the wave pattern of the smoking epidemic, the similarities between the countries and the two sexes, and the importance of the cohort dimension.

DATA AND METHODS

Setting

We studied national populations by sex and age for 29 European countries with long-term (lung cancer) mortality data (preferably from 1950 onwards, but at least from 1985 onwards and up to at least 2013). We included those adult ages for which smoking-attributable mortality proves to be most important (35-84 for men; 40-84 for women). Appendix Table 1 provides information on the countries and years included in the analysis.

Main outcome measure

The main outcome measure were age- and sex-specific past and future smoking-attributable mortality fractions: the share of all-cause mortality due to smoking. Although studying and projecting smoking-attributable mortality rates instead of fractions would have been equally feasible, fractions are also used in the smoking epidemic model by Lopez et al. (Lopez et al. 1994) and are easy to interpret.
We estimated age (x)- and sex (s)-specific smoking-attributable mortality fractions ($SAMF_{x,s}$) by country and year by applying a simplified version of the commonly used indirect Peto-Lopez method (Peto et al. 1992; Janssen et al. 2013; Janssen 2019). The method uses lung cancer mortality rates, controlled for lung cancer mortality not due to smoking, as a proxy for past smoking intensities and applies to these intensities the relative risks of dying from smoking (Thun et al. 1997), thereby controlling for the exposure of past smokers to other risk factors. See the supplementary data & methods file for more information on this indirect estimation technique.

Data

To estimate smoking-attributable mortality we used data on lung cancer deaths by country, year, sex and five year age groups (0-4, … , 75-79, 80+) predominantly from the WHO Mortality Database (update 11/04/2018)(WHO 2018). By dividing these numbers with respective exposure data from predominantly the Human Mortality Database (update 29/09/2018)(HMD 2018), we obtained the national lung cancer mortality rates necessary for estimating the smoking-attributable mortality fractions by five year age groups. By means of Loess smoothing we subsequently obtained the smoking-attributable mortality fractions by single year of age.

In addition, we used country, year, sex and age-specific all-cause death numbers from the Human Mortality Database (update March 15, 2019)(HMD 2019) to estimate smoking-attributable mortality across all ages studied (35-84 for men, 40-84 for women) standardized for the population-specific age-distribution of deaths in 2010. This enabled the comparison over time: from the past into the future.

Forecasting approach

Our forecasting approach has three important elements. Firstly, it takes into account the wave pattern of the smoking epidemic. Secondly, it takes into account the important cohort dimension in addition to the age and period dimension of the smoking epidemic. Thirdly, it takes into account expected similarities and differences between countries and the two sexes in the timing and strength of the smoking epidemic.

Forecasting method

More specifically we applied the age-period-cohort model by Cairns et al. 2009 to the fractions using as a link function a generalized logit. The logistic transformation ensures that the projected fractions and their projection intervals (PIs) remain between 0 and 1. The generalized logit function enabled us to even further restrict the projected fractions (and PIs) to more feasible values, by implementing lower and upper bounds.

The model we applied is $logit\left(\frac{SAMF_{x,t}-LB[x]}{UB[x]-LB[x]}\right) = \tilde{\alpha}_x + \tilde{\kappa}_t + \tilde{\gamma}_{t-x}$. ,where $SAMF_{x,t}$ are the smoking-attributable mortality fractions by age (x) and year (t), and LB and UB are the lower and upper bounds, respectively. The age, period and cohort parameters α_x, κ_t, and γ_{t-x} capture the age pattern, the overall time trend, and the cohort patterns, respectively.

Bounds

For women, we ensured that the peak in SAMF would be lower than those for men in the same country, by implementing as upper bounds the maximum observed age-specific SAMF levels among Danish women over the years 1951-2014. Although Danish women experienced exceptionally high smoking prevalences among women (Juel 2000), men in almost all European countries experienced a higher peak in SAMF (Janssen 2019). For men, Danish women, and women in UK, Hungary and Iceland - who experienced at some ages higher SAMF compared to Danish women – we implemented a theoretical upper bound which represents the sex and age-specific SAMF in line with a prevalence of 100%.

As the lower bound we implemented, for both men and women, a future minimum smoking prevalence of 5%. This percentage is based on current fairly equal smoking prevalence levels for men and women in forerunner countries (Eurostat 2019; IHME

2019), a smoking prevalence of already around 8% in Sweden (Eurostat 2019), and the strong emphasis on smoking prevention policies lately (WHO 2013; Department of Health 2017; Dutch Government 2018; Kavanagh & Sheridan 2018; Feliu et al. 2019). This lower bound was implemented by first estimating the associated sex-specific age-standardised SAMF values, by means of the formula to calculate SAMF. Subsequently we applied a linear transformation to the country-specific age pattern of SAMF among men in 2014 so that the resulting sex- and age-specific SAMF values correspond to the sex-specific age-standardized values of 5.9% for men, and 3.5% for women. For Finland and Sweden, we used instead for men the male age pattern in 2011, and for women the female age pattern in 2014.

For women, the implementation of the age-specific lower bounds proved a challenge because their levels were higher than many past observations. To prevent the omission of important observations we based the projection of the period parameter (kt) on the whole time series without the lower bound imposed, and implemented this projection in the model with the lower bound imposed applied to a shorter time series that prevented omissions. Unfortunately, for women in Portugal, Spain, Belarus, Estonia, Latvia, Lithuania, Russia and Ukraine no realistic projections could be obtained.

Projection of the parameters

For women, we projected the period parameter kt deterministically by means of a quadratic curve with correlated errors, because a quadratic curve in the logit of fractions will result in a wave pattern in the normal fractions. The start year of kt that is used for the projections is the first year in which kt increases. For women in the UK, where the quadratic curve is interrupted by a stagnation, we first applied smoothing to the kt.

For men, we extrapolated the linear decline in the period parameter kt after the peak into the future. A linear decline in the logit of fractions will result in a deceleration of the decline in the normal fractions, in line with the wave shape. We projected kt from maximally 10 years after its peak by applying the best fitting ARIMA model (p,d=1,q) with drift, based on minimum AICc, with p and q constrained to maximum 3.

The cohort parameter is extrapolated into the future by extrapolating the decline after the peak of the observed inversed U-shape for women in all countries and for men in the vast majority of countries (N = 15). We applied the same procedure as for the projection of kt among men, to data from 1 to 5 years after the peak. For men in Austria, Netherlands, Denmark, Norway, Switzerland, UK, Sweden, Finland and Luxembourg, for whom the inversed U-shape was followed by a recent increase or a stagnation, we assumed a future stable level, which was implemented by an ARIMA(0,1,0) model with no drift. For men in Czech Republic, Poland, Russia, Ukraine, Belarus and Slovakia, we observed a more fluctuative pattern, which we forecasted by means of the best mean reverting ARIMA (p,0,q) model based on minimum AICc with $p <= 3$ and $q <= 2$. Extrapolation of the cohort parameter was done after excluding outer birth cohorts for which the estimations were not statistically significant (women) or for which the trends were very volatile (men).

Simulations

We forecasted age- and sex-specific smoking-attributable mortality fractions up until 2100, and we estimated 95% projection intervals by performing 50,000 simulations. For the deterministic projection of kt by means of the quadratic curve, we obtained correlated errors and related projection intervals by applying the best mean reverting ARIMA model, thereby omitting the ARIMA(0,0,0) model. Point forecasts and projection intervals for the age-standardised SAMF are obtained by age-standardizing over each sample path separately.

Validation
We validated our projection method by means of backtesting. The backtest for Dutch and Danish men up to 2015, based on data up to 1975 (see supplementary information) revealed that our method can accurately predict the year of the maximum age-standardised SAMF and its level. Moreover, our method can adequately project the observed fractions (1976-2014) at the low and middle ages. At higher ages, however, our projections resulted in lower values than observed from 2000/2005 onwards, which- consequently – also resulted in an underestimation of future age-standardised SAMF. This underestimation could be because the lower bound of 5% smoking prevalence we implemented was too low for that period.

Further information
See the supplementary information for a more detailed technical description of the forecasting methodology and the specifics of the projection of the period and cohort parameter by country and sex.

RESULTS

Past trends in age-standardised smoking-attributable mortality fractions (SAMF35-84 for men, SAMF40-84 for women)(Figure 1) show a clear wave pattern with increases followed by declines among men, whereas among women in most countries SAMF40-84 is still increasing, except for selected Northwestern European / forerunner countries. Among men, SAMF is particularly high and peaked relatively early for the forerunner countries Finland, Luxembourg, NL, UK, Belgium, and is also high – but with a later peak in Eastern European countries. For Iceland, Norway, Sweden and Portugal the levels are considerably lower. For women, SAMF levels are especially high and already peaked in Denmark, Iceland, UK and Ireland, followed by Norway, the Netherlands and Sweden. For women in especially Eastern Europe the levels are still low and only recently increasing (if at all).

Based on these past trends a further decline among men can be expected, whereas for women – in line with the experience in some of the forerunner countries and with the smoking epidemic theory – first a reversal from an increase towards a decline can be expected. That is, indeed, what our projections reveal. See Figure 2 for the sex-specific results by country, Figure 3 for the sex-specific results for the 29 European countries compared, and Table 1 for a summary of these trends by country.

Whereas for men, the peak occurred already in the past, for women in most countries the peak will occur in the future. For women in Northern Europe, the peak was already reached in all countries except Finland. On average, the peak is expected to occur in 2014 (ranging from 2007 in Denmark to 2030 in Finland), with a level of 20% (ranging from 28% in Denmark to 12% in Finland). For women in Western Europe, the peak was only already reached in Ireland and United Kingdom. On average, the peak is expected to occur in 2019 (ranging from 2010 in Ireland to 2032 in Austria), with a level of 17% (ranging from 22% in UK and NL to 10% in France). For women in Greece and Italy, the peak occurs on average in 2028 at 11%. For women in the five included Central

European countries, the peak occurred on average in 2022 (ranging from 2013 in Czech Republic to 2034 in Slovenia) at 16% (ranging from 9% in Slovakia to 26% in Hungary). Across the 21 countries for which reliable projections could be made, the maximum level of smoking-attributable mortality was on average 17%, ranging from 8% in Greece to 28% in Denmark.

For men, the recent decline is extrapolated into the future. In 2040, the SAMF for men is projected to be on average 11%, ranging from 6.5% (Estonia; Sweden) to 15 % (Hungary; Portugal)(see Table 1). This is an important reduction from the 2014 average level and range of SAMF of 25%, ranging from 11% (Sweden) to 41% (Hungary). For women, in 2040 the SAMF is on average 10%, ranging from 20% (Hungary) to slightly under 5% (Sweden, France, Greece, Slovakia). The projected differences between women in the different countries in 2040 are higher compared to men, because some countries (e.g. Slovenia, Italy, Austria, Finland) have then only just experienced the peak, whereas other– especially Northern European - countries have already experienced a decline in SAMF for quite some years. In 2065 the average levels and range have further reduced to 7% (5.9-9.4%) among men, and 5% (3.5-7.6%) among women. In 2100 the projected levels reflect the lower bound we implemented of 5% smoking prevalence, which reflects a SAMF of 5.9% among men, and 3.5% among women.

The projections of age-specific SAMF (Appendix Figure 1) reveal, for men in general, declines for all ages, and a final convergence of age-specific SAMF levels. For women, however, a crossover between the wave-shaped trends for the different age groups can be observed in line with the cohort dimension in the data.
For men we project the same inverse U-shaped age pattern in the future as currently observed, although with lower levels of the age-specific SAMF (Figure 4, Appendix Figure 2). For women, the peak of the age pattern, currently mostly around age 50 to 60, is first shifted to the right, in line with the cohort pattern in the data, and then shifted to the left again in line with the current age pattern among men. The projected shift to the right among women is in line with the shift to the right that is observed in the past among men.

For the full projections by country, including the projection of the period and cohort parameter, please see the two supplementary PDF files.

DISCUSSION

Summary of results

Smoking-attributable mortality among men in the 29 European countries studied will further decline from the 2014 average value of 25% (ranging from 11% in Sweden to 41% in Hungary) to an average value of 11% (range 6.5-11%) in 2040, 7% (5.9-9.4%) in 2065, and 5.9% in 2100. Smoking-attributable mortality among women is expected to reach a peak on average in 2014 (Northern Europe), 2019 (Western Europe), 2028 (Greece, Italy), and 2022 (Central Europe), with maximum levels of smoking-attributable mortality of on average 17% (ranging from 8% in Greece to 28% in Denmark). Smoking-attributable mortality among women is projected to be on average 10% in 2040 (ranging from <5% in Sweden, France, Greece, Slovakia to 20% in Hungary), 5% (3.5-7.6%) in 2065, and 3.5% in 2100. For women, the cohort pattern in the uptake of smoking will result in a shift of the peak of the inverse U-shaped age pattern of SAMF to the right, and crossovers between the age-specific SAMF trends. For men this effect is visible only in the past.

Reflection on the data and methodology

Estimation smoking-attributable mortality

Our projection is based on our indirect estimates of smoking-attributable mortality based on a simplified version of the Peto et al. 1992 method. See Janssen 2019 for a detailed discussion of the estimation technique. The (simplified) indirect Peto-Lopez estimation method is commonly used, also in the previous projections of smoking-attributable mortality (Stoeldraijer et al. 2014; Li & Raftery 2019). That notwithstanding, the resulting levels of smoking-attributable mortality are likely affected to some extent by the estimation method employed. In an earlier evaluation of the effect of different estimation techniques on future smoking-attributable mortality, Stoeldraijer et al. (2014) observed some differences in future levels compared with the use of more recent regression-based indirect estimation techniques (Preston et al. 2010; Rostron 2010), however the year in which the peak year was obtained among women was hardly affected by the estimation technique employed.

Projection smoking-attributable mortality

Our novel method to forecast smoking-attributable mortality has the advantage of coming up with projections into the long-term future thereby taking into account the wave pattern of the smoking epidemic, the important cohort dimension, and expected similarities and differences between countries and the two sexes in the timing and strength of the smoking epidemic. However, the method also relies on some important choices/assumptions, with some drawbacks.

Firstly, we used the logit link function to model smoking-attributable mortality fractions. It should be noted though that the logit assumes a symmetric response to a covariate, and that the outcome probability is not extreme. This could potentially explain the rather fluctuative fit especially at younger ages with very low SAMF. This negative effect of the use of the logit link function, however, is - in our view – largely outweighed by the advantages of its use. That is, the use of the logit link function not only ensured projected values between 0 and 1, but more importantly, a quadratic curve in the logistic transformed values results in a wave pattern in the normal values.

Secondly, we implemented upper and lower bounds, to make sure that the future SAMF and their projection intervals have realistic values in line with the theory and additional insights.

The implementation of the theoretical upper bounds for men did not affect the point estimates. For women, using as the upper bound the max age-specific fractions for Denmark importantly affected the width of the projection intervals, as can, for example, clearly be observed for Slovakia. That is, the uncertainty of the point estimate goes up to the maximum age-specific fractions for Denmark, and can be very wide. However, if we would not have put this upper bound, the uncertainty would have even been larger, leading to – in our view –unrealistic uncertainty intervals.

The implementation of the lower bounds, implies a stronger assumption, with a larger potential effect on our outcomes. We implemented lower bounds in our projection in line with the presumed lower limits and asymmetric wave pattern in the smoking epidemic model (Lopez et al. 1994; Thun et al. 2012). Because the smoking epidemic model does not define the level of these limits, and these have not yet occurred, we had to rely on external information to obtain these lower limits. After careful consideration, we came up with a lower limit that is in line with a prevalence of 5% for both men and women, and an associated age-standardised SAMF of 5.9% for men and 3.5% for women. The implementation of the lower limit and its value does affect the projection outcomes. A sensitivity analysis in which we compared the results with and without the lower limit imposed (see the supplementary results document) revealed – logically – higher future values for men and women when imposing the lower bound – particularly in the long run -, but only minimal differences in the peak year and peak level for women (on average less than a year difference in the peak year, and 0.4 percentage points difference in the peak level), without a uniform direction.

In implementing the lower bounds we furthermore used the current (= 2014) country-specific age pattern for men, both for men and women. This choice was made because important changes over time in the age pattern of SAMF have occurred. That is for men we observed a clear shift in the bell-shaped age pattern to the right up until a couple of years after the peak. After that the peak in the age pattern remained more stable. This observation is in line with the importance of the cohort dimension especially for the uptake of smoking (add sources). Choosing the current age pattern for women (in which in the majority of cases the peak of the smoking epidemic has not yet been reached) was therefore regarded less of an option. It could however be that the current age pattern for men is still different from the future age pattern. To check this we did a sensitivity analysis in which we projected future age-specific values without implementing the lower bound, and compared these to the current projected future age-specific values with the lower bound. See the supplementary results document. For men these two projected age patterns were very similar, except in Ireland, Italy, Norway and particularly Sweden where the peak moved to the left when no lower bound was implemented. In these countries in fact already in 2015 and/or 2016 a different age pattern was observed. For women, when the lower bound is implemented, the peak in the projected age pattern occurs eventually at an earlier age – in line with the peak in the age pattern for men in 2014. This is not yet visible in 2040, when the age patterns are – in general - still rather parallel, with a peak at fairly high ages. It could be argued that this age pattern with a peak at fairly old ages reflects the true future age pattern, but unclear is why we see this shift to the right, as this occurred even after the peak level of SAMF occurred, and is not in line with the pattern for men, and the idea that the uptake of the smoking epidemic is predominantly caused by a cohort pattern, whereas the decline is reflected as a period pattern. Potentially this shift has more to do with non-smoking-related mortality than with smoking-related mortality. In that sense the use of the current age pattern among men for women in the future assumes a similar age pattern of non-smoking-related mortality. It is also important to note that both these age patterns might be different from the actual long-term future age pattern if new policy measures are being taking up differently among different age groups, the largely changing age pattern in recent years among Swedish men could indeed indicate this.

Although the implementation of the lower bound when projecting the logit of the age-specific SAMF by means of a quadratic curve generated a very nice asymetric wave pattern in for example Portugal men, and women in Ireland, Luxembourg, Slovenia, in the majority of countries for women the wave changes rather abrupt from quadratic to level. This most likely results in a underestimation of the projected SAMF levels in the first decades after the peak, which is indeed in line with our validation results. The year

in which the peak is reached and its level, as well as the SAMF values in the long-term future are however most likely not affected.
In interpreting our projection outcomes, it is therefore important to realize that they partly rely on the chosen lower bounds which assume at least a continuation of policy efforts to reduce smoking and its negative health consequences, and that future age patterns reflect the current age patterns observed among men. Without imposing these lower bounds however, our projections would not be in line with the theory, and moreover they would have resulted in very wide projection intervals, as seen in Li & Raftery 2019.

An additional important benefit compared to the Li & Raftery (2019) projection of smoking-attributable mortality is that we were able to obtain future age-specific estimates of smoking-attributable mortality, and that we incorporation the cohort dimension which is necessary to obtain realistic future age patterns. Because the cohort dimension has played an important role in determining smoking-attributable mortality trends, this requires the use of an APC model. (Using an age-period model would result in a similar age pattern as observed now, which – especially for women is not realistic). For this purpose we choose the Cairns et al. APC model, which is based on the commonly used Clayton & Schifflers approach (Clayton & Schifflers 1987a,b) within epidemiology (e.g. Dhillon et al. 2011). The Cairns et al. method uses basically the same function, but involves an additional step to ensure that the drift (=shared linear trend between period and cohort) is completely removed from the cohort dimension and added to the period dimension. Our method could also be applied using other existing APC models (see Yang et al. 2004 for a review), although using models with multiple period or cohort parameters could be daunting and result in less transparent projections.

All in all, we regard our method as a very promising method to forecast age-specific and age-standardised smoking-attributable mortality fractions in the long run, and to determine the year in which SAMF is expected to reach a peak among women and its level. With some minor alterations the method could also be applied to forecast smoking-attributable mortality rates. Moreover, the method could also be utilized to forecast mortality from other factors that evolve as an epidemic (such as obesity-attributable mortality) and in which generational differences play an important role, next to differences over calendar time and age.

Comparison with previous projections of smoking-attributable mortality

Direct comparison of the projected future levels of SAMF with the corresponding levels of two previous projections of smoking-attributable mortality is hampered by the use of different age groups, and different standardisation approaches. Comparing our results with the results for ages 45-80+ by Stoeldraijer et al. 2014 for Denmark, the Netherlands and United Kingdom up until 2050 it can be observed that our projections result in substantially earlier peaks for Denmark and the Netherlands and partly related to this lower projected values in 2050. This is partly due to the exclusion of the ages 85+ in our projections, because for higher ages – in line with the cohort dimension – the peak is reached later compared to younger ages. Most likely, however, the difference foremost stems from our implementation of the quadratic curve, which provides a more data-driven estimation of the peak year and peak level. This conclusion is in line with the observation that our estimate of the peak for the Netherlands is only a few years earlier than the one estimated by Li & Raftery 2019, who employed a data driven approach and included those aged 85 and over (they did not include Denmark in their analysis). Interestingly, Li & Raftery also showcased in their validation for the Netherlands (using data up until 2000 to predict until 2015) a similar underestimation of all-age SAMF compared to us (using data up until 1975 to predict until 2015). This illustrates the difficulty of correctly estimating the decline after reaching the peak, without incorporating additional information, which Stoeldraijer et al. did.

Extension of the smoking epidemic model

Our projections also facilitate the extension of the smoking epidemic model (Lopez et al. 1994; Thun et al. 2012), for Europe (see Figure 5). For men, we can observe the deceleration of the decline from the peak in the mortality impact of the smoking epidemic around 1989 at 35%. For women a clear increase and subsequent decline of age-standardised smoking-attributable mortality shows. According to our projections for the non-Eastern European countries (without Portugal and Spain), the peak in SAMF among women will soon be reached at a level of 17%, and the average SAMF levels of women are projected to stay below the average SAMF levels of men. This, however, is not the case for many individual European countries. For women in Slovenia (2034), Italy (2033), Austria (2032), and Finland (2030) our median projections indicate that it will still take over a decade before the peak in the mortality impact is reached (Table 1). And in 2040 SAMF levels are projected to >=10 % in the majority of countries for both men and women, and even >=15% in Greece (men), Portugal (men), Hungary, Austria (women), and Slovenia (women) (Table 1). For Austria, Belgium, Denmark, Iceland, Ireland, Italy, Norway, Slovenia, Sweden, and United Kingdom we see, for the short term future, substantially higher future SAMF levels among women compared to men (Figure 2).

Overall conclusion

Our novel forecasting method enabled the forecast of smoking-attributable mortality up to 2100 thereby optimally making use of both the data and the theory plus additional insights on the likely progression of the smoking epidemic.
Special attention from health policy makers and society is warranted regarding the projected considerable future peak in smoking-attributable mortality among women in many European countries, and the finding that smoking-attributable mortality among women has already or will soon become higher than smoking-attributable mortality among men.
The current projections of smoking-attributable mortality in Europe require (continued) effective public health action to indeed make sure that the assumed future smoking prevalence of 5% among both men and women is – minimally - reached.

Author contributions: FJ conceived the study. FJ and AB designed the study. AB developed the projection model and performed the initial projections, with input from FJ. SG finalized the projections, with input from AB and SG. All authors interpreted the results. FJ drafted the manuscript. FJ and SG drafted the supplementary data and methods file. AB provided critical comments to both drafts. FJ revised the manuscript. All authors approved the final version of the manuscript.

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Tables and Figures

Table 1 - Current and future (maximum) age-standardised smoking-attributable mortality fractions (M: 35-84; F: 40-84), selected years 2014*-2100, 29 European countries, by country and sex. *Or the latest available year before that for Greece (2013), Russia (2013), Russia (2012)

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Figure 5 - Unweighted average observed and projected age-standardised smoking-attributable mortality fractions (M 35-84; F 40-84) across 20/28 European countries* from 1981 to 2100. *We excluded Slovenia so that we could show the trends from 1981 onwards. Because for women no reliable projections could be generated for Portugal, Spain, and the six Eastern European countries, we also included the trend across these countries for men.

Appendices

Appendix Table 1 - Countries included in the analysis (N=29), data availability and data sources

Appendix Figure 1a - Past and future age-specific smoking-attributable mortality fractions, 1965-2065, 29 European countries, by country, men

Appendix Figure 1b - Past and future age-specific smoking-attributable mortality fractions, 1965-2065, 29 European countries, by country, women

Appendix Figure 2a - Past, current and future age pattern of the smoking-attributable mortality fractions, selected years 1965-2100, 29 European countries, by country, men

Appendix Figure 2b - Past, current and future age pattern of the smoking-attributable mortality fractions, selected years 1965-2100, 29 European countries, by country, women

Table 1 Current and future (maximum) age-standardised smoking-attributable mortality fractions (M: 35-84; F: 40-84), selected years 2014-2100, 29 European countries, by country and sex.

	Men						Women					
Country/Region	2014*	Year max SAMF	Level max SAMF	2040	2065	2100	2014*	Year max SAMF	Level max SAMF	2040	2065	2100
Northern Europe	**0.16**	**1986**	**0.26**	**0.09**	**0.07**	**0.06**	**0.19**	**2014**	**0.20**	**0.07**	**0.04**	**0.04**
Denmark	0.22	1985	0.34	0.10	0.07	0.06	0.27	2007	0.28	0.07	0.04	0.04
Finland	0.16	1974	0.39	0.09	0.07	0.06	0.10	2030	0.12	0.10	0.05	0.04
Iceland	0.15	1997	0.20	0.09	0.07	0.06	0.23	2010	0.26	0.07	0.04	0.04
Norway	0.17	1996	0.22	0.09	0.07	0.06	0.19	2013	0.19	0.06	0.04	0.04
Sweden	0.11	1980	0.17	0.07	0.06	0.06	0.16	2012	0.16	0.05	0.04	0.04
Western Europe	**0.22**	**1982**	**0.35**	**0.11**	**0.08**	**0.07**	**0.16**	**2019**	**0.16**	**0.11**	**0.05**	**0.04**
Austria	0.21	1972	0.33	0.11	0.08	0.07	0.14	2032	0.17	0.16	0.08	0.04
Belgium	0.26	1984	0.41	0.10	0.07	0.06	0.14	2026	0.15	0.13	0.04	0.04
France	0.26	1992	0.31	0.14	0.08	0.07	0.10	2017	0.10	0.05	0.05	0.05
Germany	0.22	1982	0.31	0.11	0.08	0.07	0.13	2021	0.14	0.10	0.05	0.05
Ireland	0.19	1984	0.31	0.09	0.06	0.06	0.22	2010	0.20	0.14	0.06	0.04
Luxembourg	0.24	1983	0.38	0.12	0.08	0.07	0.14	2018	0.12	0.10	0.06	0.04
Netherlands	0.23	1982	0.42	0.13	0.09	0.07	0.22	2017	0.22	0.12	0.04	0.04
Switzerland	0.17	1982	0.30	0.09	0.08	0.07	0.12	2018	0.13	0.06	0.04	0.04
United Kingdom	0.20	1976	0.40	0.10	0.08	0.07	0.22	2011	0.22	0.12	0.04	0.04
Southern Europe	**0.24**	**1998**	**0.28**	**0.12**	**0.08**	**0.07**	**0.06**	**2027**	**0.11**	**0.08**	**0.04**	**0.04**
Greece	0.29	1992	0.30	0.15	0.08	0.07	0.07	2021	0.08	0.04	0.04	0.04
Italy	0.22	1989	0.32	0.08	0.07	0.06	0.09	2033	0.14	0.13	0.04	0.04
Portugal	0.21	2013	0.20	0.15	0.09	0.07	0.03	*NA*	*NA*	*NA*	*NA*	*NA*
Spain	0.24	1996	0.29	0.10	0.07	0.07	0.04	*NA*	*NA*	*NA*	*NA*	*NA*
Central Europe	**0.31**	**1993**	**0.41**	**0.10**	**0.07**	**0.06**	**0.16**	**2022**	**0.16**	**0.10**	**0.05**	**0.04**
Czech Republic	0.26	1987	0.41	0.08	0.06	0.06	0.13	2013	0.13	0.05	0.04	0.04
Hungary	0.41	1996	0.43	0.15	0.07	0.06	0.24	2027	0.26	0.20	0.04	0.04
Poland	0.34	1998	0.42	0.11	0.07	0.06	0.17	2018	0.16	0.08	0.04	0.04
Slovakia	0.29	1993	0.40	0.09	0.07	0.06	0.09	2017	0.09	0.04	0.04	0.04
Slovenia	0.27	1993	0.37	0.08	0.06	0.06	0.15	2034	0.16	0.15	0.07	0.04
Eastern Europe	**0.32**	**1993**	**0.40**	**0.12**	**0.07**	**0.06**	**0.04**	***NA***	***NA***	***NA***	***NA***	***NA***
Belarus	0.31	1996	0.40	0.14	0.09	0.06	0.00	*NA*	*NA*	*NA*	*NA*	*NA*
Estonia	0.31	1994	0.39	0.06	0.06	0.06	0.09	*NA*	*NA*	*NA*	*NA*	*NA*
Latvia	0.32	1992	0.40	0.12	0.06	0.06	0.04	*NA*	*NA*	*NA*	*NA*	*NA*
Lithuania	0.33	1994	0.40	0.11	0.06	0.06	0.04	*NA*	*NA*	*NA*	*NA*	*NA*
Russia	0.34	1991	0.44	0.14	0.08	0.06	0.03	*NA*	*NA*	*NA*	*NA*	*NA*
Ukraine	0.31	1991	0.38	0.13	0.08	0.06	0.02	NA	NA	NA	NA	NA
Europe	**0.25**	**1989**	**0.35**	**0.11**	**0.07**	**0.06**	**0.12**	**2019**	**0.17**	**0.10**	**0.05**	**0.04**

*Or the latest available year before that for Greece (2013), Russia (2013), Russia (2012)

Figure 1 Past trends age-standardised smoking-attributable mortality fractions (M: ages 35 -84; F: ages 40-84), 29 European countries, from 1950 onwards, by sex and region

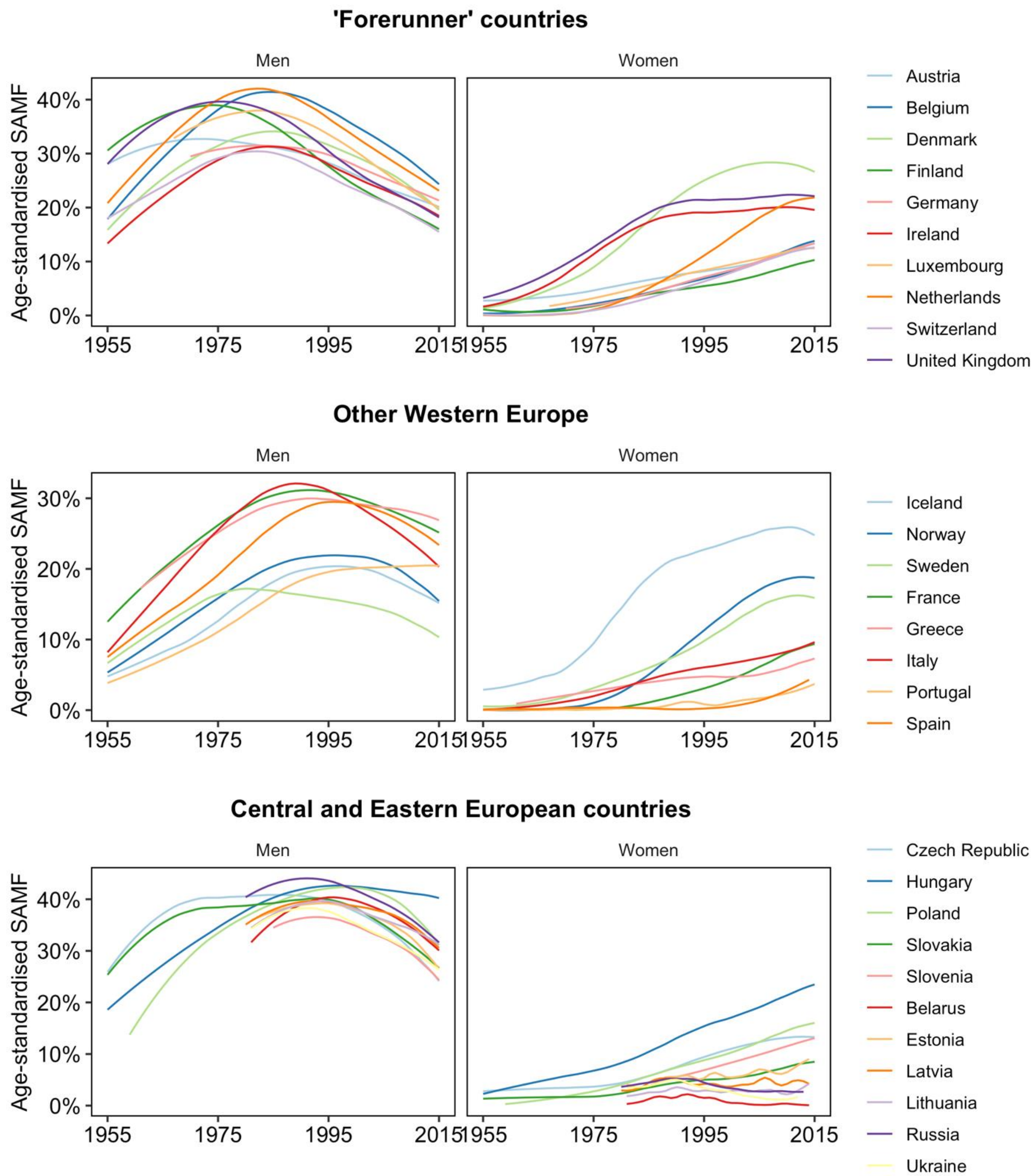


Figure 2 Past and future trends in age-standardised smoking-attributable mortality (M: 35-84; F: 40-84), 1950-2100, 29 European countries, by country and sex

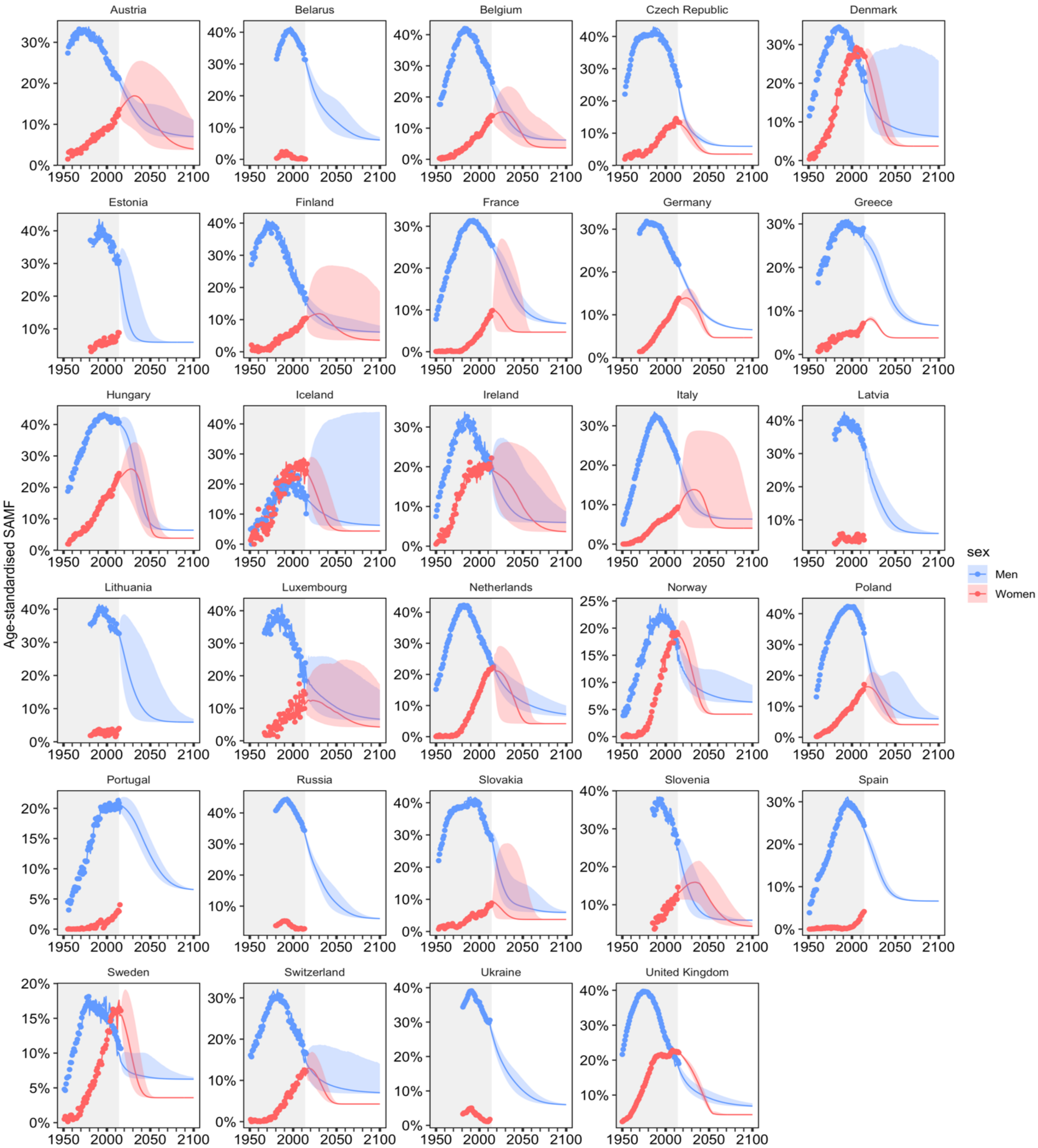
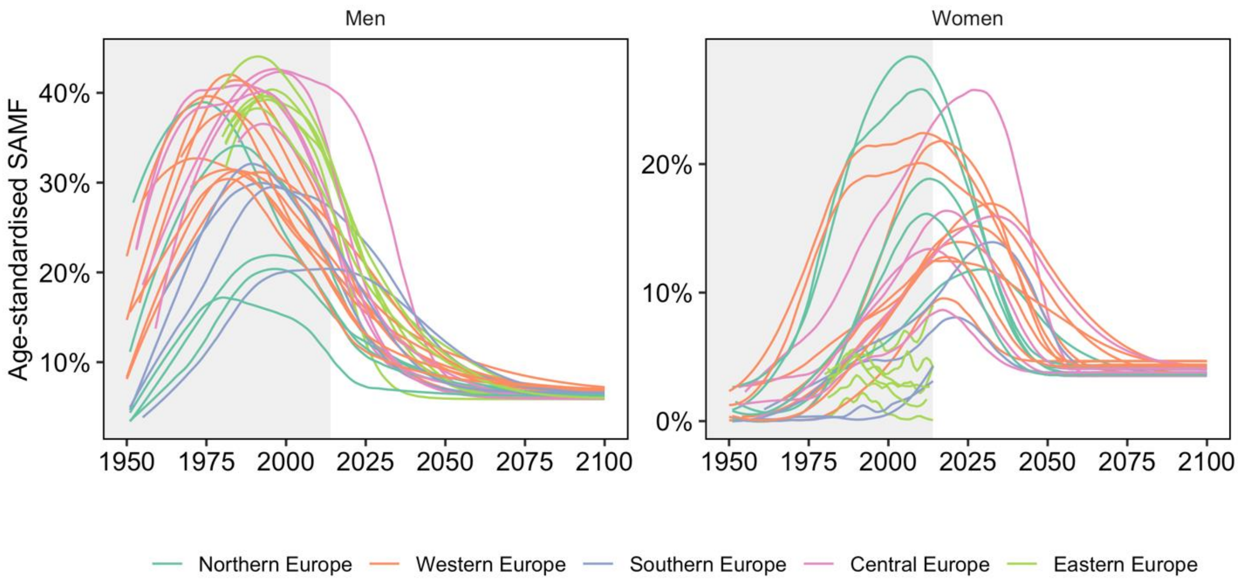
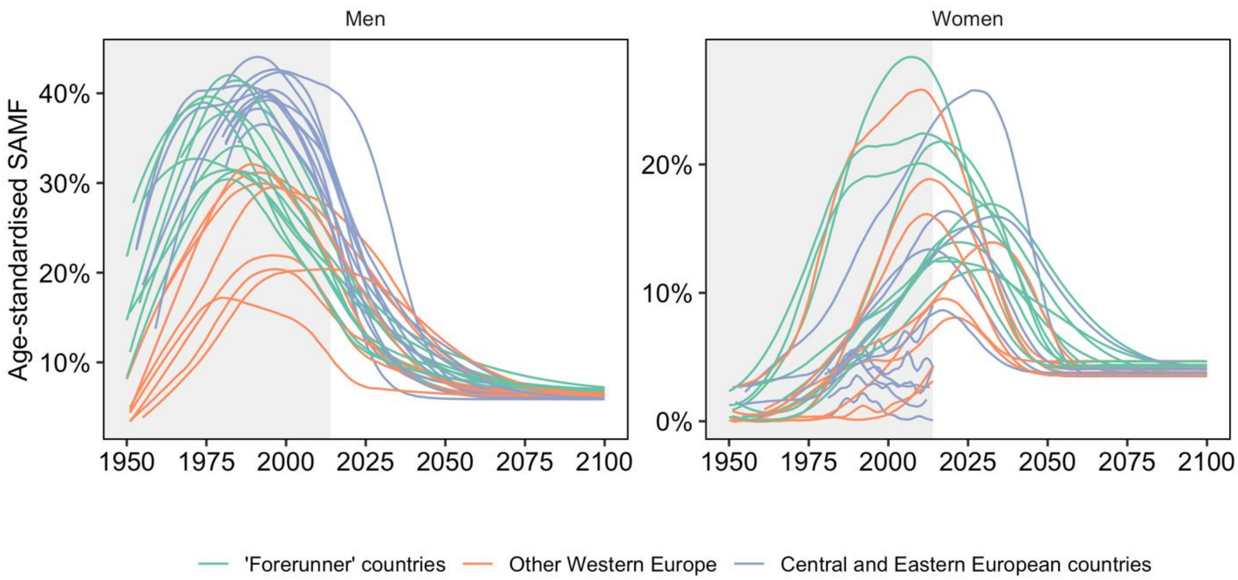


Figure 3 Past and future trends in smoothed age-standardised smoking-attributable mortality fractions (M: 35-84; F: 40-84), 1950-2100, for the different countries compared, by sex



Northern Europe: Denmark, Finland, Iceland, Norway, Sweden
Western Europe: Austria, Belgium, France, Germany, Ireland, Luxembourg, Netherlands, Switzerland, United Kingdom
Southern Europe: Greece, Italy, Portugal, Spain
Central Europe: Czech Republic, Hungary, Poland, Slovakia, Slovenia
Eastern Europe: Belarus, Estonia, Latvia, Lithuania, Russia, Ukraine

Figure 3 alt Past and future trends in smoothed age-standardised smoking-attributable mortality fractions (M: 35-84; F: 40-84), 1950-2100, for the different countries compared, by sex



'Forerunner' countries: Austria, Belgium, Denmark, Finland, Germany, Ireland, Luxembourg, the Netherlands, Switzerland, United Kingdom
Other Western Europe: Iceland, Norway, Sweden, France, Greece, Italy, Portugal, Spain
Central and Eastern European countries: Czech Republic, Hungary, Poland, Slovakia, Slovenia, Belarus, Estonia, Latvia, Lithuania, Russia, Ukraine

Figure 4 Past, current and future age pattern in smoking-attributable mortality fractions, selected years 1965-2100, selected countries, by country and sex

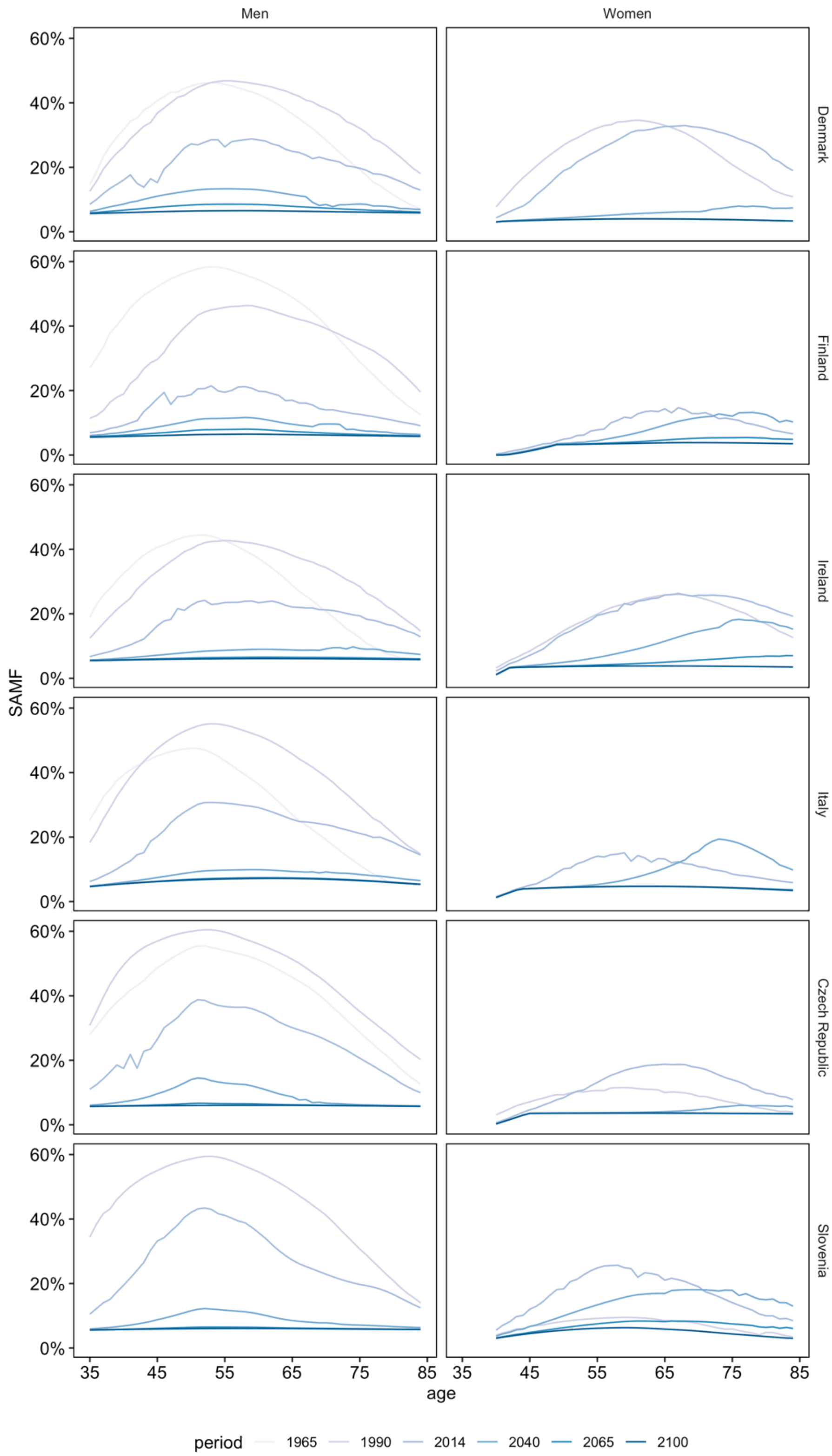
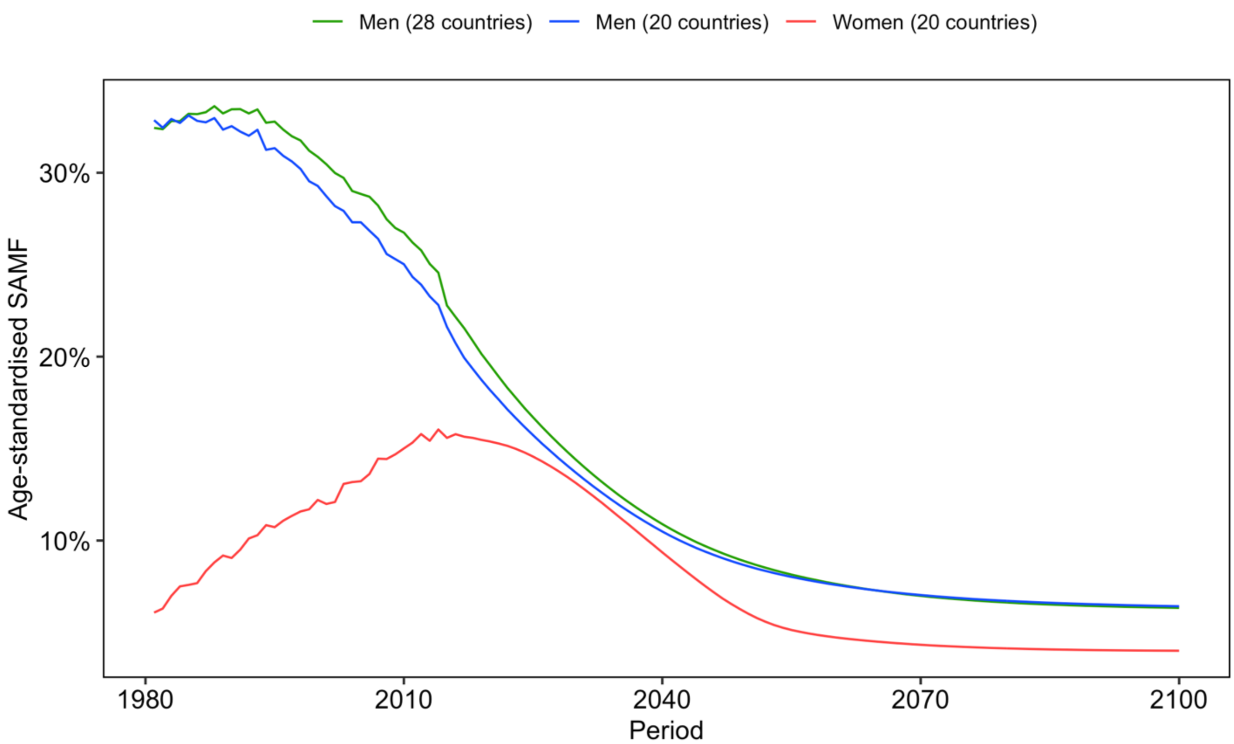


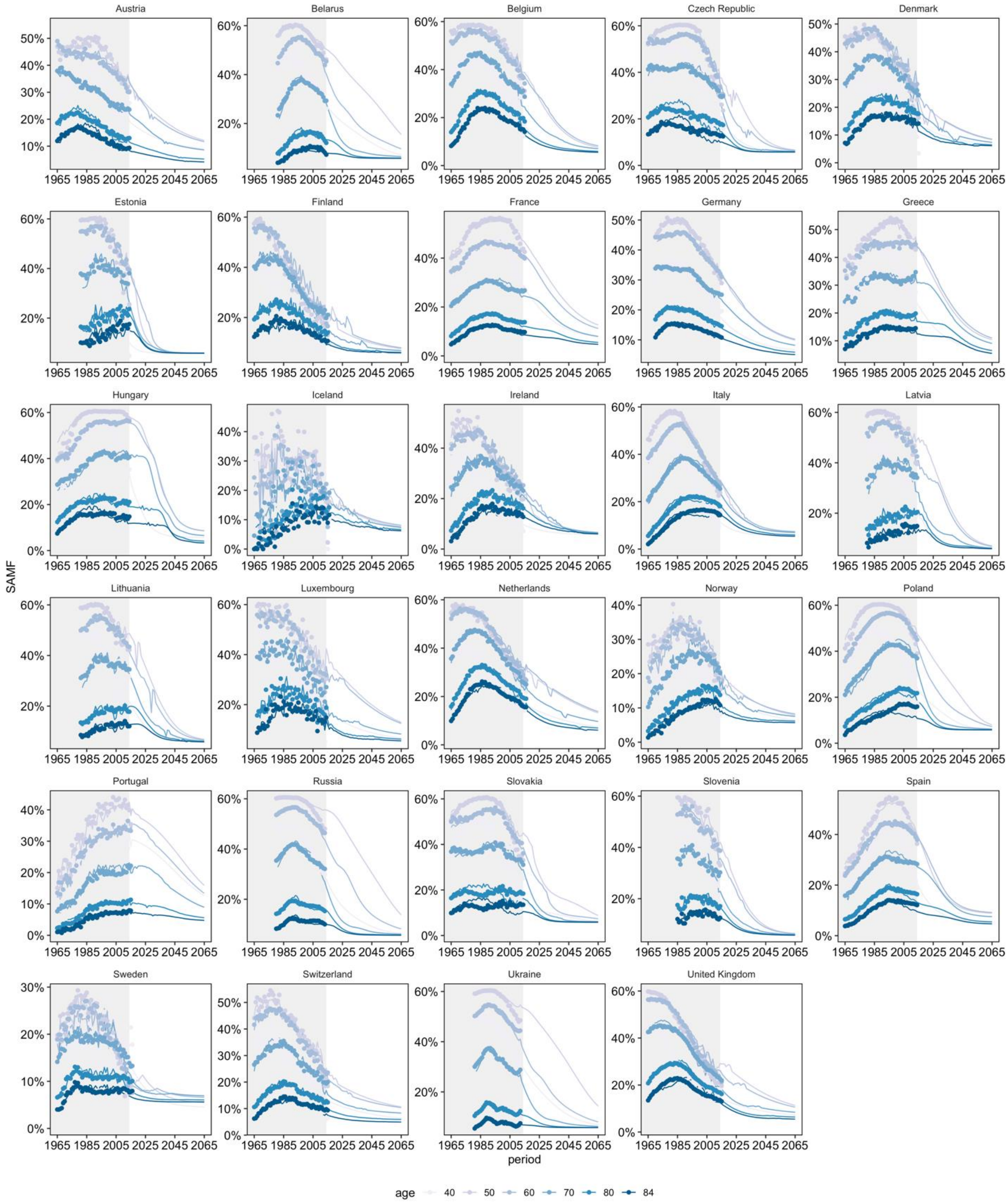
Figure 5 Unweighted average observed and projected age-standardised smoking-attributable mortality fractions (M 35-84; F 40-84) across 20/28 European countries* from 1981 to 2100. *We excluded Slovenia so that we could show the trends from 1981 onwards. Because for women no reliable projections could be generated for Portugal, Spain, and the six Eastern European countries, we also included the trend across these countries for men.



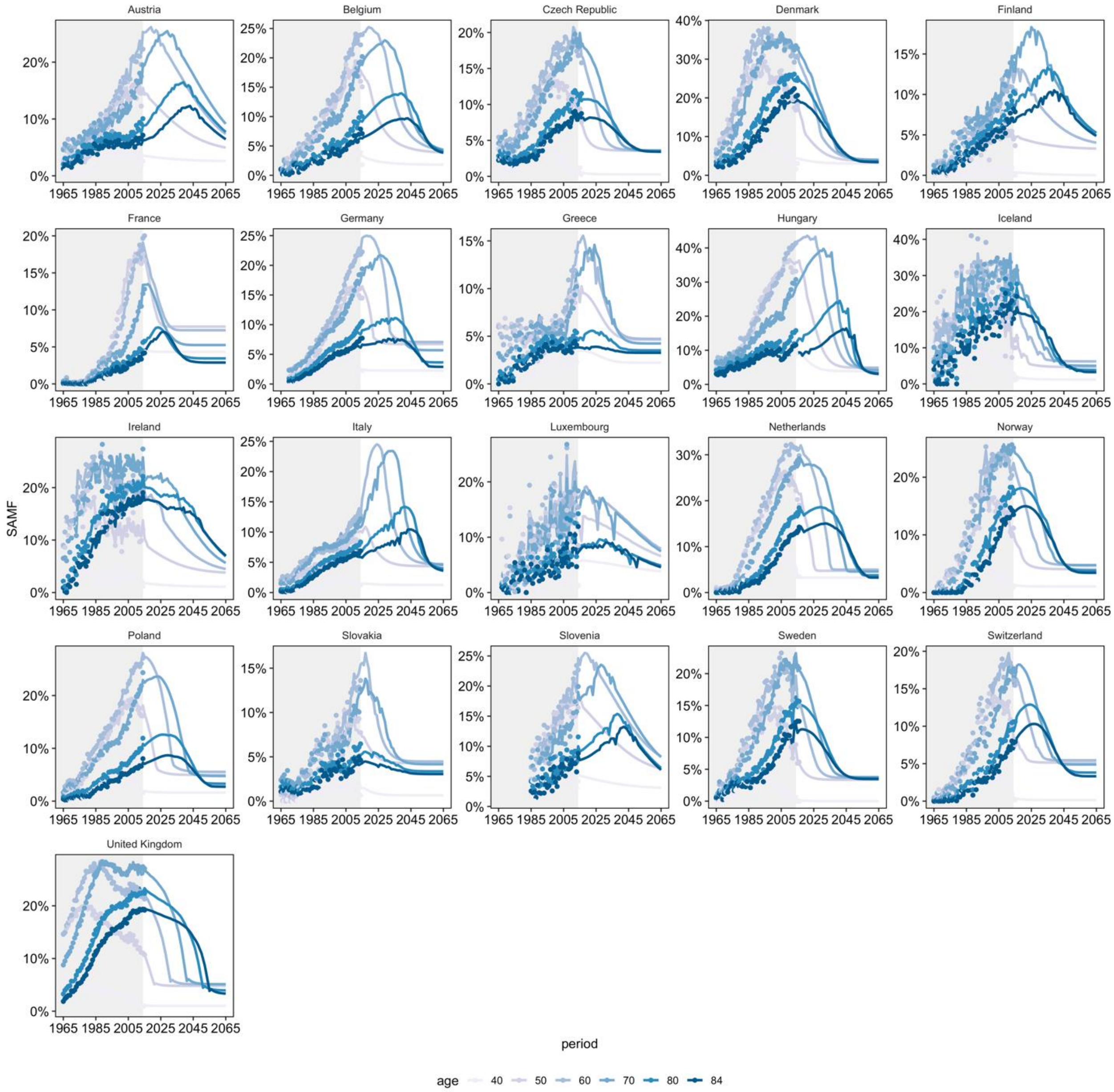
Appendix Table 1 - Countries included in the analysis (N=29), data availability and data sources

Country	Start year	End year	Data sources
Austria	1955	2014	HMD & WHOSIS
Belarus	1981	2014	HMD & WHOSIS
Belgium	1954	2015	HMD & WHOSIS
Czech Republic	1953	2016	HMD & WHOSIS; For 1953-1985, lung cancer mortality data for the Czech Republic were estimated using data from WHOSIS on former Czechoslovakia.
Denmark	1951	2015	HMD & WHOSIS
Estonia	1981	2014	HMD & WHOSIS
Finland	1952	2015	HMD & WHOSIS
France	1950	2014	HMD & WHOSIS
Germany	1970	2015	HMD & WHOSIS
Greece	1981	2013	HMD & WHOSIS
Hungary	1955	2014	HMD & WHOSIS
Iceland	1951	2016	HMD & WHOSIS
Ireland	1950	2014	HMD & WHOSIS
Italy	1951	2014	HMD & WHOSIS
Latvia	1980	2014	HMD & WHOSIS
Lithuania	1981	2014	HMD & WHOSIS
Luxembourg	1967	2014	HMD & WHOSIS
Netherlands	1950	2016	HMD & WHOSIS
Norway	1951	2014	HMD & WHOSIS
Poland	1959	2014	HMD & WHOSIS
Portugal	1955	2014	HMD & WHOSIS; Eurostat data were used to obtain lung cancer deaths for 2004-2006.
Russia	1980	2013	HMD & WHOSIS; WHOSIS exposure data were used instead of HMD exposure data to calculate lung cancer mortality rates.
Slovakia	1953	2014	HMD & WHOSIS; For 1953-1991, data for Slovakia were estimated using data from WHOSIS on former Czechoslovakia.
Slovenia	1985	2014	HMD & WHOSIS
Spain	1951	2014	HMD & WHOSIS
Sweden	1951	2016	HMD & WHOSIS
Switzerland	1951	2015	HMD & WHOSIS
Ukraine	1981	2012	HMD & WHOSIS
United Kingdom	1950	2015	HMD & WHOSIS; Eurostat data were used to obtain estimates of lung cancer deaths for 2004-2006.

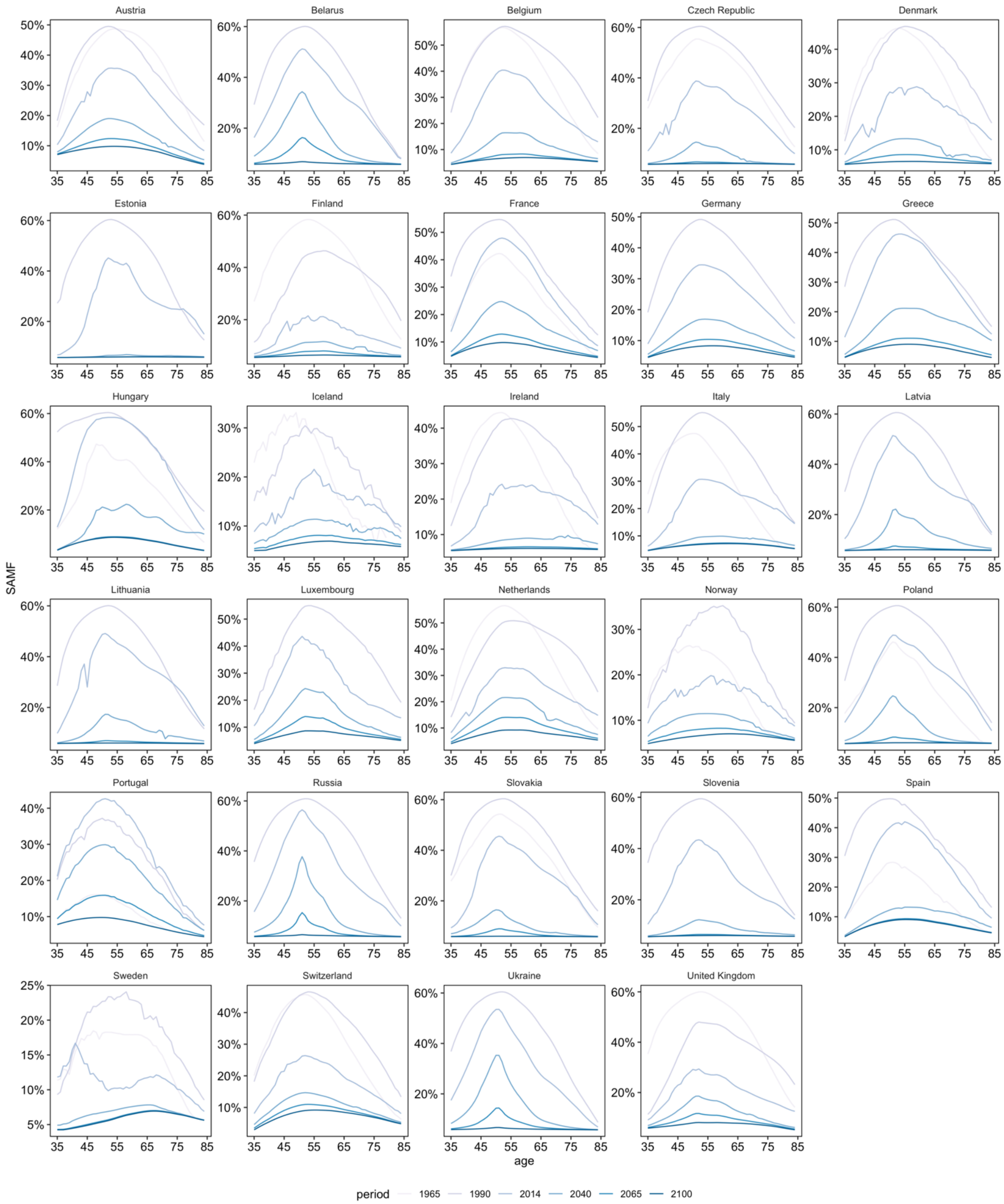
Appendix Figure 1a - Past and future age-specific smoking-attributable mortality fractions, 1965-2065, 29 European countries, by country, men



Appendix Figure 1b - Past and future age-specific smoking-attributable mortality fractions, 1965-2065, 29 European countries, by country, women



Appendix Figure 2a - Past, current and future age pattern of the smoking-attributable mortality fractions, selected years 1965-2100, 29 European countries, by country, men



Appendix Figure 2b - Past, current and future age pattern of the smoking-attributable mortality fractions, selected years 1965-2100, 29 European countries, by country, women