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Impact of a smoking and alcohol intervention program on lung and breast cancer incidence in Denmark: An example of dynamic modeling with Prevent

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ABSTRACT

Purpose: Among the known risk factors, smoking is clearly related to the incidence of lung cancer and alcohol consumption to breast cancer. In this manuscript we modeled the potential benefits of reductions in smoking or alcohol prevalence for the burden of these cancers.

Method: We used Prevent v.3.01 to assess the changes in incidence as a result of risk factor changes. Incidence of lung and breast cancer until 2050 was predicted under two scenarios: ideal (total elimination of smoking and reduction of alcohol intake to maximum 1 units/d for women) and optimistic (decreasing prevalence of risk factors because of a 10% increase in cigarette and alcohol beverage price, repeated every 5 years). Danish data from the household surveys, cancer registration and Eurostat were used.

Results: Up to 49% less new lung cancer cases can be expected in 2050 if smoking were to be completely eliminated. Five-yearly 10% price increases may prevent 521 new lung cancer cases in 2050 (21% less cases). An intervention that immediately reduces population alcohol consumption to the recommended level (below 12 g/d) may lower breast cancer by 7%, preventing 445 out of the 6060 expected new cases in 2050. Five-yearly 10% price increases in alcoholic beverages achieved a reduction of half as expected by the ideal scenario, i.e. 4% (262) preventable cases in 2050.

Conclusions: The future burden of lung and breast cancer could be markedly reduced by intervening in their risk factors. Prevent illustrates the benefit of interventions and may serve as guidance in political decision-making.

1. Introduction

Cancer has become one of the major causes of death in the western world.[1] Behavioral factors are attributable to about 25–50% of all cancer cases.[2,3] Therefore health promotion programs to enhance healthier living have been heavily promoted to reduce the burden of cancer as well as other chronic diseases. However, the effects of such interventions are rarely

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assessed because a long period is needed before changes in prevalence and ultimately in disease occurrence can be discerned in a population. Furthermore, those initiating the intervention may no longer be in office, and the interest in following the effects of a specific intervention may have vanished. Also, overlapping programs further complicate assessment in the efficiency of individual programs. Therefore, a tool that enables simulation of different policy proposals on population health, e.g. cancer, is needed to inform decision-making.[4] Finally, the tool should also be able to project the future prospect of multiple interventions.

In this paper we use Prevent v.3.01 to demonstrate the potential impact of smoking and alcohol intervention programs on future lung and breast cancer incidence in Denmark.[5] These two cancer types were chosen because of their great contribution to cancer deaths (lung cancer)[6] and incidence (breast cancer).[7,8] Logically, smoking was selected as the risk factor to be modeled owing to its strong association with lung cancer: 82% of lung cancer incidence in the Nordic countries was attributable to smoking.[9] As for breast cancer, alcohol consumption is one of the major risk factors that is amenable to intervention, and hence was chosen as the second risk factor to be modeled in our study.[10] Moreover, these two risk factors were frequently observed clustered in a population and have shown strong evidence of success within intervention programs directed at reducing their prevalence.[11,12] The simulation model Prevent estimates the effect of changes in risk factor prevalence on disease occurrence and/or mortality, while accounting for trends and interventions.[13] Prevent is a multi-factorial model that takes into account time dimensions and demographic changes. Good quality, long-term exposure data for smoking and alcohol were available for Denmark through the National Institute of Public Health,[14] as well as good data on cancer incidence from the Danish Cancer Registry.[8]

2. Method

2.1. Data

2.1.1. Risk factor prevalence

2.1.1.1. Smoking. Data were obtained from the Danish National Health Interview Survey in 1987, 1994, 2000 and 2005,[14] since these surveys had details on alcohol that were contrary to the annual survey samples on smoking prevalence, habits and cessation. Table 1 shows smoking prevalence (daily smokers) and five age categories (16–19; 20–24; 25–44; 45–66; 67 + years). Smoking was assumed to be 0 at age below 16. In order to project future smoking prevalence, smoking cessation rates were calculated using the model proposed by Mendez et al.[15] Cessation rates between 1987–1994 and 1995–2005 for three age groups are presented in Table 2. The model used to calculate cessation rates has been fully described elsewhere and is summarized in Appendix 1.[16] To forecast smoking prevalence, 2005 was used as the baseline year and prevalence was simulated until 2050. Future smoking prevalence was estimated by assuming a continuation of cessation rates between 1995 and 2005. Because the proportion of daily smokers only slightly increases or decreases, we assumed that smoking initiation remained stable, as was reported in 2005. We assumed smoking initiation (initiation rates) was completed by age 20. The number of never, current and former smokers for the years 2005–2050 was calculated using the same method and is described in Appendix 1. The proportions were applied to population projection estimates until 2050 retrieved from Eurostat.[17]

Table 1 – Proportion of daily smokers (%) in Denmark according to sex 1987–2005 (14).

	1987	1994	2000	2005
Males				
16–19 years[a]	23	24	31	23
20–24 years	44	34	33	32
25–44 years	48	41	35	32
45–66 years	55	50	40	34
67 + years	40	38	32	29
Females				
16–19 years[a]	34	22	23	20
20–24 years	46	35	29	30
25–44 years	46	43	34	28
45–66 years	47	39	36	32
67 + years	25	27	24	22

[a]Initiation rate is assumed to be completed at age 20.

2.1.1.2. Alcohol consumption. Data were taken from the Danish National Health Interview Survey in 1994, 2000 and 2005 (Table 3).[14] The last reported data were held constant in our modeling exercise. Only female data were used as female breast cancer was the outcome of interest. We retrieved the mean and standard deviation of alcohol intake in g/d for five age categories (16–24; 25–44; 45–66; 67 + years). We also took the mean and standard deviation of alcohol consumption among those who drink alcohol within the safe levels set up by the European Code Against Cancer[18] (for women: 0–7 units/week) to be used as the theoretical minimum exposure (see below). Because alcohol intake was better described by a log-normal distribution, we calculated the parameters μ and σ of the log-normal from the mean (m) and standard deviation (s) using the following formulas.

$$\sigma\sqrt{\ln\left(s^2+\exp(2\ln(m))\right)-2\ln(m)}$$

$$\mu\ln(m)-0.5\sigma^2$$

Table 2 – Cessations rates[a] in Demark according to sex, 1987–2005.

	1987–1994	1995–2005
Males		
20–30 years	0.016	−0.001
31–50 years	0.011	0.012
51 + years	0.017	0.048
Females		
20–30 years	0.027	−0.011
31–50 years	0.013	0.053
51 + years	0.025	0.025

The proportional change can be positive (decline in prevalence) or negative (an increase in prevalence).
[a]Cessation rate: proportional change in smoking prevalence.

Table 3 – Daily average intake of alcohol (g) and standard deviation (sd) among women in Denmark, in 1994–2005 (14).

	Reported intake			Theoretical minimum exposure[a]		
	1994 Mean (sd)	2000 Mean (sd)	2005 Mean (sd)	1994 Mean (sd)	2000 Mean (sd)	2005 Mean (sd)
16–24 years	9.4 (11.9)	10.1 (13.5)	10.1 (14.4)	3.5 (3.7)	3.4 (4.0)	3.1 (4.1)
25–44 years	9.0 (10.9)	8.2 (9.8)	8.6 (16.8)	4.2 (3.9)	3.8 (4.0)	3.3 (3.9)
45–66 years	10.7 (13.3)	10.9 (12.0)	12.9 (18.0)	4.1 (3.9)	4.3 (4.1)	4.4 (4.1)
67 + years	5.8 (9.4)	6.3 (9.7)	9.7 (19.1)	2.4 (3.7)	2.9 (4.0)	3.1 (4.0)

Notes: reported estimates are in normal distribution. In analysis these estimates were transformed to log-normal.
[a]Theoretical minimum exposure is the average intake of alcohol among those who drink alcohol as the international recommendation (0–7 units/week).

2.1.2. *Cancer incidence and its relation to risk factors*

Lung (ICD 10: C33–34) and female breast cancer (C50) incidence rate by sex and 5-year age group in Denmark in 2004 were retrieved from NORDCAN.[8] Lung cancer was related to smoking and breast cancer to alcohol intake. We used a relative risk of 9.9 and 7.6 in getting lung cancer for male and female smokers compared wit non-smokers respectively.[19] As for alcohol intake and breast cancer, a risk function derived from the relative risks as reported by Hamajima et al. was used.[10] By increasing daily alcohol intake to 35–44 g and more than 45 g, the risk of breast cancer was increased by 32% and 46% respectively compared with women who reported drinking no alcohol. We plotted the reported daily alcohol intake in grams on the *x*-axis and the corresponding relative risks on the *y*-axis, and assumed a linear risk function as described by the following formula:

$$R(x) = ax + b,$$

where a was the slope (0.0085) and b was the intercept (0.95). The risk function fitted a linear regression with $R^2 = 0.95$.

2.1.3. *Population data*

From Eurostat we obtained the following data: (1) population size on 1st January 2004 by 1-year age category and sex; (2) forecasted population sizes by 5-year age categories and sex for the years 2005–2050, using the medium national growth estimates; (3) mortality rates for 1987–2005 by 1-year age category and sex; and total births by sex for 1987–2005. The last datasets were needed to estimate smoking cessation rates in that period.

2.2. *Modeling with Prevent*

Prevent was originally developed in 1988 to estimate the health benefits of changes in risk factor prevalence for a population.[13] Prevent is based on the epidemiological effect measure 'potential impact fraction' (PIF), which derives a proportional change in disease risk from a change in risk factor exposure and the relative risk of that risk factor related to the disease(s) under study. Prevent first calculates the autonomous development of a health outcome of interest (here cancer incidence) by applying the trend impact fraction (TIF) on the baseline incidence rates. TIF and PIF are conceptually the same measure where TIF derives from historical changes in risk factor exposure and PIF from change in risk factor exposure due to an intervention. The proportional changes are calculated towards the predetermined theoretical minimum exposure value, the risk factor exposure that would result in the lowest population risk (e.g. in the case of smoking this would equal a smoking prevalence of 0).[20] After the user specifies a change in risk factor prevalence due to an intervention, Prevent calculates the future incidence rates from the current situation using the TIF for the reference scenario and both PIF and TIF for the intervention scenario. The differences between the scenarios are attributed to the intervention, with the output given in terms of rates and number of expected cases in the future (details of the calculations are presented in Appendix 2).

2.2.1. *Model specification*

2.2.1.1. Lag and latency time. The time component is expressed in latency time (LAT) and lag time (LAG). LAT expresses the time until changes in risk factor exposure start being reflected in changes in cancer risk. LAG is the time that is needed for a formerly exposed person to return to the risk of an unexposed person. For smoking and lung cancer we defined the latency time to be 5 years, so changes in smoking will only be reflected in the lung cancer incidence thereafter.[21] For breast cancer and alcohol this was set to be one year.[22] As for the lag time, we set it to be 15 years for smoking and lung cancer[21] and four years for alcohol and breast cancer,[22] declining or increasing in an exponential manner.

2.2.1.2. Theoretical minimum risk exposure. For smoking, the theoretical minimum risk exposure was set to 0 prevalence (all never-smokers).[20] As for alcohol, we calculated and used the average intake (and standard deviation, shown in Table 3) among women who followed the European recommendation of maximum alcohol intake. Such a small amount of alcohol may have still exposed women to a small increased risk of breast cancer, but alcohol abstinence has also been related to an increase of, for example, cardiovascular diseases. Therefore, we chose the above-mentioned value as the counterfactual exposure for alcohol intake.

2.2.1.3. Autonomous disease trend. The autonomous trend is the trend in incidence in the absence of changes in the risk factor under study. For lung cancer, due to its strong relation to smoking, we assumed that incidence of lung cancer to be fully driven by the changes in cigarette smoking. As for breast cancer we assumed the autonomous trends to be equal to the estimated annual percentage change over the past decade.[23]

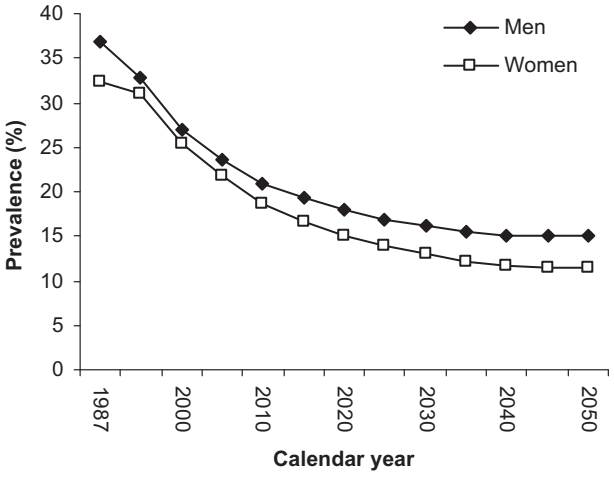

Fig. 1 – Observed (1987, 1994, 2000, and 2005) and predicted proportion of daily smokers in Denmark according to gender.

Because historical cancer incidence trends are not expected to last forever, a five-yearly reduction of 25% was applied.

2.2.1.4. Intervention scenario: ideal and optimistic scenario. In the ideal scenario, we assumed a full elimination of smoking and a reduction in alcohol intake to the level of those who consumed as recommended by the European Code Against Cancer, adopted by the Danish Cancer Society. As for the optimistic scenario we applied a reduction in the prevalence of smokers and alcohol drinkers related to a five-yearly price increase of 10% (assumed that this is always indexed for inflation). The literature review on the price elasticity of cigarettes in adults clustered around –0.40.[24] For young adults price is more elastic and was estimated to range between –0.906 and –1.309.[24] In this paper we chose the more conservative estimate: –0.906. Price elasticity for alcohol has been estimated as –0·48 for beer, –0·75 for wine and –1·31 for spirits.[12] This means that a change in the prices of alcoholic beverages by 10% would be expected to diminish on-premise beer consumption by 4.8%, wine consumption by 7.5% and spirits consumption by 13.1%. Using the reported proportion of alcohol intake by beverage type in Denmark, we weighted these percentages and used it as the average annual decrease in alcohol intake (5.7%) due to a 10% increase in price.[25] For a continuous variable such as alcohol consumption, this means that the mean alcohol intake would shift by 5.7% toward the theoretical minimum risk.

We assumed that the intervention started in 2006 and continued until 2050.

3. Results

Smoking prevalence in Denmark is highest among 45- to 66-year-old men (34–55%) and among 25- to 44-year-old women (28–46%, Table 1). In the latest survey, the proportion of daily smokers among the younger age groups did not change much, causing a slight decrease in the cessation rates (Table 2). Among the oldest males cessation rates increased markedly in the last decade observed (1995–2005: annual cessation rates 4.8%). As for female Danes the large increase in cessation rates was observed among women in the middle age group (5.3%). In the future we projected a continuation of the decrease in the proportion of daily smokers, ending with 15% and 11% of daily smokers in Denmark in 2050, in males and females respectively (Fig. 1). As for alcohol consumption (Table 3, only for female subjects), over the three calendar years a small increasing trend in average alcohol consumption was observed in all age groups except among women aged 25–44 years.

Table 4 shows the decrease in lung and breast cancer cases under the various scenarios by 2050. In the ideal scenario, where smoking is eradicated, the incidence rate of lung cancer was predicted to be 49% and 36% lower, in men and in women, than expected in the base projection. If a five-yearly 10% price increase is enforced, we predicted a decrease in lung cancer of 23% in men and 17% in women. As for breast cancer we estimated 445 (7.3%) and 262 (4.3%) fewer cases when alcohol is reduced to the recommended level and when it is reduced by a five-yearly increase in price of 10%.

Fig. 2 illustrates the impact of the 'ideal' and 'optimistic' scenario on lung and breast cancer incidence. Decreasing cigarette smoking by price increase might reduce lung cancer from 33 to 25 cases per 100,000 person-years in men and from 23 to 19 cases per 100,000 person-years in women. Successfully eliminating smoking might lower lung cancer incidence to only 15 and 14 new cases per 100,000 in men and women in 2050. As for breast cancer, we observed a 7.6% and 4.3% reduction from the expected 157 cases per 100,000 in 2050, if ideal

Table 4 – Number of expected cancer cases according to gender in 2050 with or without interventions to reduce smoking and alcohol intake in Denmark.

Cancer type		Men	Women	Total
Lung cancer	Trend only (no interventions modeled)	1504	1038	2542
	Ideal scenario: Smoking elimination	766	661	1427
	Difference, ideal scenario vs. trend (%)	738 (49)	377 (36)	1115 (44)
	Optimistic scenario: 10% five-yearly price increase	1160	861	2021
	Difference, optimistic scenario vs. trend (%)	344 (23)	177 (17)	521 (21)
Breast cancer	Trend only (no interventions modeled)	–	6060	–
	Ideal scenario: alcohol guideline	–	5615	–
	Difference, ideal scenario vs. trend (%)	–	445 (7.3)	–
	Optimistic scenario: 10% 5 yearly price increase	–	5798	–
	Difference, optimistic scenario vs. trend (%)	–	262 (4.3)	–

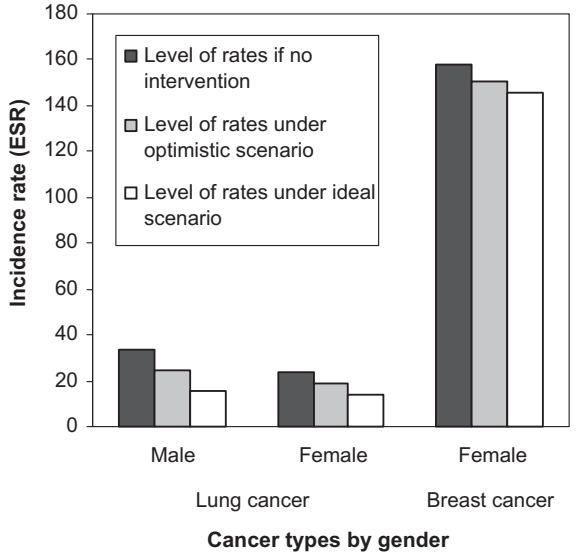

Fig. 2 – Effects of optimistic (total elimination) and realistic (yearly 10% price increase) scenarios to reduce smoking and alcohol consumption on expected cancer incidence rates (European Standardized Rate: ESR) in 2050 by sex. Optimistic scenario: rates if the prevalence of smokers and alcohol drinkers were to decrease because of a 10% five-yearly increase in price. Ideal scenario: rates if smoking is eradicated and alcohol consumption is reduced to that recommended by international guidelines (0–7 units/week).

and optimistic intervention to reduce alcohol consumption is implemented.

4. Discussion

In this modeling exercise, we illustrated the health gain in 2050 of two scenarios on smoking and alcohol consumption. Total smoking eradication may reduce lung cancer incidence up to 49%. A five-yearly 10% price increase (corrected for inflation) could achieve half of the reduction in lung cancer incidence cases compared with the effects predicted by total elimination of smoking. An intervention program to reduce alcohol consumption to the recommended level may reduce the predicted breast cancer rate by up to 7%. If a five-yearly alcohol price increase successfully reduced alcohol consumption as in our assumption, we could expect 4% lower breast cancer incidence in 2050.

The results of our modeling exercises are useful from a policy perspective, as they give an estimate of the potential size of health effects due to interventions that result in certain changes in risk factor prevalence. As only the intervention differs between the models, the estimated projected differences in cancer rates and numbers between the reference and intervention scenarios give a good illustration of the potential for prevention. However, the models are simplification of a very complex reality and are based on many assumptions. Moreover, in the near and more distant future, many expected and unexpected changes may occur in risk factor prevalence and disease occurrence because of factors that are not included in our models. For these reasons, our results should be interpreted as projections that allow intervention effects to be assessed, and should not be interpreted as predictions of future cancer incidence.

We compared the projected lung cancer rate that resulted from Prevent with that of NORDCAN.[8] In our study, Prevent projected lung cancer incidence based on the historical and future projection of smoking prevalence in Denmark, whereas the projection in NORDCAN was computed using an age-period-cohort model based on the past cancer incidence rate.[26] Prevent estimated a lower lung cancer incidence than NORDCAN: in 2020 Prevent estimated a lung cancer incidence rate of 30 per 100,000 for men and 23 for women vs. 40 for men and 33 for women from the projection of NORDCAN. This is probably because of the different projection methods used by the two programs. In the last 5 years (2000–2004), the Danish government has taken several smoking intervention steps. This has resulted in a doubling of the cessation rate compared with those observed in the previous periods. The recent reduction in smoking prevalence will be reflected in the projection of Prevent, but not yet in the lung cancer incidence rate that was used as base for prediction in NORDCAN. If the 'true' future lung cancer rate were higher than the one we projected using Prevent, this implies a larger benefit of intervention, hence more reason to do it.

4.1. *Limitations of Prevent*

Prevent is a state-transition simulation program and assumes homogeneity within age and sex groups. Within such groups the net-health gain on the population level is similar for all members of the population. In our example of smoking, we assumed that intervention would have a similar effect on smoking prevalence for the whole population. This may not entirely be true, because smoking cessation is determined by other factors, e.g. socioeconomic status.[27] Price elasticity is higher for the lower socioeconomic group; hence, it is more influenced by tax/price indexing intervention. If such an analysis for different groups is desired, Prevent needs separate input for all the different classes. On the other hand the population perspective has its own benefits (compared with individual level models), i.e. computation time is shorter and outcomes are not stochastic.

Finally, Prevent makes independence assumptions. Risk factors, incidence rates, and disease-specific causes of death rates (if mortality was studied) are independent. However, alcohol consumption and tobacco smoking are associated risk factors. Although still under debate[10,28,29] smoking may also be related to higher breast cancer risk. Prevent takes the prevalence of each risk factor and relates it to the disease estimates based on the given risk factors-specific relative risk. This may underestimate the incidence of breast cancer as the relative risk of this cancer is higher among those who smoke and drink. Providing separate data on the prevalence of smokers, drinkers and both is one possible solution to circumvent this problem. However, limited data restrict such detailed modeling.

4.2. *Strength of Prevent*

Prevent is a long-standing program that is continuously tested and improved, with reasonable data requirements.

Prevent allows many details in the modeling. First, Prevent allows multiple risk factors and diseases as well as relations between risk factor and disease and vice versa, and leaves it to users to specify the 'causal web'. Risk factors can be in categorical as well as in continuous form. Continuous variables can be specified as normal, log-normal, log-normal with offset or Weibull distributions. For smoking, based on the uptake and cessation rates and excess mortality, users can make projections of future smoking prevalence. Assuming constant prevalence during the simulation period may overestimate the effect of an intervention as smoking uptake at a young age has been decreasing in many European populations, which will continue to reduce future smoking prevalence at older ages. Second, users can opt to let Prevent predict future demographic distributions, or use predicted population projections, e.g. from Eurostat as demographic input. Third, Prevent includes time lags represented by the latency and lag time, allowing delayed changes in disease risk after changes in risk factor exposure. Finally, Prevent can also incorporate autonomous trends in the future prediction of disease risk. Therefore, changes in disease measures with other causes can be incorporated into the model, improving the effect estimate of an intervention.

5. Conclusions

In Denmark, we showed a marked benefit on the burden of lung and breast cancer by price indexing of cigarettes or alcoholic beverages. A program such as Prevent gives insight into the long-term benefits of an intervention to population health and may provide guidance for policy-making in prevention.

Conflict of interest statement

None declared.

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Appendix 1. Calculation of cessation rates

Cessation rates were estimated separately for males and females for three age groups (20–30, 31–50, and 50+) and two time periods (1987–1996 and 1997–2005). They were calculated by selecting a set of cessation values that reproduced as closely as possible the observed past prevalence of smoking using the weighted least-squares method. We used the optimization routine of the generalized reduced gradient algorithm embedded in the 'Solver' add-in function in Excel. The proportion of smokers was determined by the initiation and cessation rates, as well as excess mortality due to smoking. Excess mortality in current and former smokers was determined from population mortality rates, the prevalence of current and former smoking, and relative risk estimates for current and former smokers from the American Cancer Society's Cancer Prevention Study II (CPSII). Smoking initiation was assumed to be completed by age 20. Here we used the prevalence of current smoking in 20- to 24-year-olds. After the age of 20, the number of current smokers was calculated as the number of current smokers in the previous year who survived and did not quit smoking.

1.1. Calculation of probability of dying in never, current and former smokers

The sex-, age- and year-specific mortality rates for never, current and former smokers were then determined by:

$$m_{never_{t,a}} = \frac{m_{total_{t,a}}}{RR_{current_a} \times P_{current_{t,a}} + RR_{former_a} \times P_{former_{t,a}} + 1 - \left(P_{current_{t,a}} + P_{former_{t,a}}\right)}$$

$$m_{current_{t,a}} = RR_{current_a} \times m_{never_{t,a}}$$

$$m_{former_{t,a}} = RR_{former_a} \times m_{never_{t,a}}$$

where:

$m_{total_{t,a}}$ is the mortality rate in the total population aged a at time t

$m_{never_{t,a}}$ is the mortality rate in never smokers at age a, at time t

$m_{current_{t,a}}$ is the mortality rate in current smokers at age a, at time t

$m_{former_{t,a}}$ is the mortality rate in former smokers at age a, at time t

$RR_{current_a}$ is the relative risk of dying in current smokers compared with never smokers from CPSII at age a

$P_{current_{t,a}}$ is the prevalence of current smokers in the population at age a, at time t

RR_{former_a} is the relative risk of dying in former smokers compared with never smokers from CPSII at age a

$P_{current_{t,a}}$ is the prevalence of former smokers in the total population at age a, at time t

The mortality rates were then converted to the probability of dying at age a and time t according to:

$$Q_{t,a} = 1 - e^{(-m_{t,a})}$$

where:

$q_{total_{t,a}}$ is the probability of dying in the total population aged a at time t

1.2. Calculation number of never, current and former smokers at each age

The number of never, current and former smokers at each age and in the years following the baseline year is determined according to:

$$Never_{t,a} = Never_{t-1,a-1} \times \left(1 - q_{never_{t-1,a-1}}\right)$$

$$Current_{t,a} = Current_{t-1,a-1} \times \left(1 - q_{current_{t-1,a-1}}\right) \times (1 - C_{t-1,a-1})$$

$$Former_{t,a} = Former_{t-1,a-1} \times \left(1 - q_{former_{t-1,a-1}}\right) + Current_{t-1,a-1} \times \left(1 - q_{current_{t-1,a-1}}\right) - Current_{t,a}$$

Except for age 20, which was determined according to:

$$Never_{t,20} = Never_{t-1,19} \times \left(1 - q_{never_{t-1,19}}\right) \times \left(1 - P_{current_{t,20}}\right)$$

$$Current_{t,20} = Current_{t-1,19} \times \left(1 - q_{never_{t-1,19}}\right) \times \left(P_{current_{t,20}}\right)$$

where:

$Current_{t,a}$ is the number of current smokers in the population at age a at time t
$Former_{t,a}$ is the number of former smokers in the population at age a at time t
$Never_{t,a}$ is the number of never smokers in the population at age a at time t
$c_{t,a}$ is the proportional change in current smoking prevalence at time t and age a

Appendix 2. Mathematical calculation in Prevent

The calculation in Prevent uses the risk factor prevalence and relative risk to calculate the trend impact fraction (TIF) and potential impact fraction (PIF). The TIF deals with the increased or decreased incident number of cases at a certain time, due to an autonomous change in risk factor prevalence, as a proportion of the incident cases that would have occurred at that time in the absence of the (autonomous) change (or trend). The PIF deals with the incident number of cases prevented at a certain time, by an intervention to reduce risk factor prevalence, as a proportion of the incident cases that would have occurred at that time in the absence of the intervention.

In Prevent, the variables in TIF and PIF are dependent on age, sex, risk factor and disease, and time.

For a categorical risk factor the formula for TIF is as follows:

$$\mathrm{TIF}_t^{r,d,s,a} = \frac{\sum_{c=1}^{n} p_c \mathrm{RR}_{c,0}^{r,j=0,d,s,a} - \sum_{c=1}^{n} p_c^* \mathrm{RR}_{c,t}^{r,j=0,d,s,a}}{\sum_{c=1}^{n} p_c \mathrm{RR}_{c,0}^{r,j=0,d,s,a}}$$

For a categorical risk factor the formula for PIF is as follows:

$$\mathrm{PIF}_t^{r,d,s,a} = \frac{\sum_{c=1}^{n} p_c \mathrm{RR}_{c,t}^{r,j=0,d,s,a} - \sum_{c=1}^{n} p_c^* \mathrm{RR}_{c,t}^{r,j=1,d,s,a}}{\sum_{c=1}^{n} p_c \mathrm{RR}_{t}^{r,j=0,d,s,a}}$$

where pc is the proportion of the risk factor in category c, RR_c is the relative risk for that category, and pc^* is the proportion in category c after the intervention or in the case of TIF pc^* is the proportion in category c after applying an autonomous change in risk factor prevalence. r, d, s, a are indicators for risk factor, disease, sex and age, respectively, whereas j is for reference if 0 and intervention population if 1.

For a continuous risk factor the formulas are as follows:

$$\mathrm{TIF}_t = \frac{\int_l^h \mathrm{RR}(x)P(x)dx_0^{ref} - \int_l^h \mathrm{RR}(x)P^*(x)dx_t^{ref}}{\int_l^n \mathrm{RR}(x)P(x)dx_0^{ref}}$$

$$\mathrm{PIF}_t = \frac{\int_l^h \mathrm{RR}(x)P(x)dx_t^{ref} - \int_l^h \mathrm{RR}(x)P^*(x)dx_t^{int}}{\int_l^n \mathrm{RR}(x)P(x)dx_t^{ref}}$$

where $RR(x)$ is the risk function, $P(x)$ is the original risk factor distribution, $P^*(x)$ the risk factor distribution after the intervention, and l and h are the integration boundaries. In the case of TIF, $P^*(x)$ is the risk factor distribution after an autonomous change in risk factor prevalence.

The TIF is multiplied by the population disease measure (in this paper cancer incidence) to calculate the burden of disease for the reference population. To calculate the incidence of disease among the intervention population both TIF and PIF are applied to the specific disease estimate. The difference between the two populations represents the net effect of an intervention. The model assumes independence between risk factors, using a multiplicative model.

$$I_t^{ref} = I_0\left(1 - \prod_r (1 - TIF_r)\right)$$

$$I_t^{int} I_0\left(1 - \prod_r (1 - TIF_r)(1 - PIF_r)\right)$$

where I_0 is the disease incidence rate in the base year and r is an index for risk factor. I^{ref} is the incidence rate in the reference population and I^{int} is the incidence rate in the intervention population. All measures are age- and sex-specific, and recalculated for each period year based on period-specific risk factor prevalence and constant relative risks or risk functions.

The incidence rates are then applied to the population number (age-, sex-, and period-specific) to calculate the absolute changes in incidence cases due to autonomous trend or intervention.

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