

# Scenarios of future lung cancer incidence by educational level: Modelling study in Denmark.

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## **S**CENARIOS OF FUTURE LUNG CANCER INCIDENCE BY EDUCATIONAL

## LEVEL: MODELLING STUDY IN DENMARK

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## Abstract

Objective: To model future trends in lung cancer incidence in Denmark by education under different scenarios for cigarette smoking.

Methods: Lung cancer incidence until 2050 was modelled using the Prevent software. We estimated lung cancer incidence under a baseline scenario and under four alternative scenarios for smoking reduction: decreasing initiation rates among the young, increasing cessation rates among smokers, a scenario combining both changes, and a levelling-up scenario in which low and mid educated people acquired the smoking prevalence of highly educated. Danish National Health Interview Surveys (1987-2005) and cancer registry data combined with individual education status from Statistics Denmark were used for empirical input.

Results: Under the baseline scenario, lung cancer rates are expected to decrease for most educational groups during the next decades, but educational inequalities will increase further. Under the alternative scenarios, an additional decrease in lung cancer rates will only be observed from 2030 onwards, but only from 2050 onwards under the initiation scenario. The cessation and the combined scenarios show the largest decrease in lung cancer rates for all educational groups. However, in none of these scenarios, the relative differences between educational groups would reduce. A modest decrease in these inequalities will be observed under the levelling-up scenario.

Discussion: Our analyses show that relative inequalities in lung cancer incidence rates will tend to increase. It may be reduced to a small extent if smoking prevalence of low educated people were to converge towards those of high educated people. An important decrease in lung cancer rates will be observed in all educational groups however, especially when focusing both on initiation and cessation strategies.

## **Key-words**

Lung neoplasms; incidence; educational status; socioeconomic factors; smoking; forecasting

## Introduction

Lung cancer is one of the main cancers in developed countries [1, 2]. Between the mid-1990s and early 2000s in Europe, incidence and mortality rates started to decrease in men whereas an increase is still observed among women in most countries [3]. Tobacco is the major risk factor for lung cancer, with a population attributable fraction around 85% [4]. Most European countries have reported higher lung cancer incidence and mortality rates among people with lower socioeconomic position [5-7]. To explain these inequalities, a common hypothesis is that a higher exposure to risk factors explains the higher incidence of lung cancer in low socioeconomic groups. Studies have reported that a substantial part of this inequality could be attributed to differences in smoking prevalence by socioeconomic position [8, 9].

The existence of socioeconomic inequalities in lung cancer incidence and mortality is a major public health concern. Because of the long latency period between exposure to smoking and lung cancer incidence, any public health policy aiming at reducing smoking would only affect lung cancer incidence several years after its implementation. Projections of the incidence of the disease are thus the only mean for public health professionals and policy-makers to decide which one should be implemented [10]. Therefore, it is crucial to develop tools to estimate the timing and the magnitude of the impact of such public health policies. Such projection models will also document short term trends in lung cancer rates that may be expected in view of recent trends in smoking.

The aim of this analysis is to estimate changes in future lung cancer incidence for different educational groups given different types of interventions on smoking, using the software Prevent. In particular, the model will document how long it would take before the changes in educational differences in lung cancer incidence could be expected. The analyses are based

on long-term and good quality Danish data on smoking [11] and cancer incidence [7], both including information about education.

### Methods

We stratified all analyses by sex and education. Education was coded in three categories: less than ten years of education (primary, secondary and grammar school) referred to as low education, 10-12 years of education (vocational education) referred to as middle education, and 13 years of education and more (tertiary education) referred to as high education [7].

Detailed description of the methodology including formulas used in Prevent can be found elsewhere [12]. In our analyses, Prevent estimates the changes in lung cancer incidence in a population due to changes in smoking prevalence. The method is based on the effect measure of "potential impact fraction" (PIF). PIF represents the proportional change in the number of incident cases at a certain time due to changes in risk factor prevalence in the past. The PIF is computed from the proportion of the population exposed to smoking and the relative risk quantifying the association between smoking and lung cancer. We used a relative risk of 9.9 among male smokers compared to never smokers, and a relative risk of 7.6 among female smokers [13]. PIF is specific for each disease-risk factor association (here, lung cancer and smoking), for a specific age, sex and education combination and for a specific point in time.

A time component accounts for the delay between exposure to tobacco and the onset of lung cancer and is represented by latency (LAT) and lag time (LAG). LAT is the time between a change in smoking rate and a change in lung cancer incidence. LAG is the time needed for a formerly exposed (or unexposed) person to return to the risk of an unexposed (or exposed) person, decreasing (or increasing) in an exponential manner. We set LAT at 7 years, and LAG at 25 years. These values are consistent with the available evidence on decrease in lung cancer incidence rates after stopping smoking [14, 15]. As a result, a change in smoking prevalence does not change the PIF for the first 7 years. After that it changes exponentially over the following 25 years until it reflects the full effect of change in smoking prevalence.

Because of the exponential relationship, most of the decrease occurred during the first 10 years of this 25 year decrease.

The PIF associated with a specific point in time is multiplied with the lung cancer incidence rate of the base year to calculate the incidence at that point in time. Baseline incidence by education was obtained from the Danish Cancer Society for the year 2004 [7]. In addition, Prevent also allows an autonomous trend in lung cancer incidence, which is the trend that would be observed in the absence of changes in smoking.

The main results of this paper were based on the assumption that lung cancer trends were fully driven by the changes in smoking. In additional analyses, we assumed an autonomous trend that accounted for past exposure to asbestos, which is the second major risk factor for lung cancer [16]. The excess lung cancer cases due to exposure to asbestos can be estimated from the number of mesothelioma observed, the latter being almost entirely caused by exposure to asbestos [16]. Reviews have estimated the ratio of excess lung cancer cases due to exposure to asbestos relative to mesothelioma cases. We used a ratio of 2 lung cancers for 1 mesothelioma, which is suggested to be conservative in a recent report [17]. Based on this ratio, we derived the autonomous trend for lung cancer incidence from the estimated annual percent change observed in Denmark for male mesothelioma incidence [18]. The trend was assigned to men with low and middle education aged 40 years or older. We did not assign this trend to women and to high educated men as the level of asbestos exposure was very low in these groups.

Demographic data was needed to estimate future lung cancer incidence rates. First, annual all-cause mortality rates for the base year were estimated per education level by taking into account estimates of mortality by education level during the 1990s for a national sample of the Danish population [19]. Further, information on population size projected for the years 2005-2050 is needed to make projections on other outcomes. This information is derived

from the general population and was not available by education level. Therefore, we did not present number of lung cancer cases by education but presented incidence rates only.

Smoking prevalence was estimated as a function of smoking initiation and cessation rates, all estimated per age, sex and educational level. Smoking prevalence was computed cohortwise. We assumed smoking to be 0 below age 20 and smoking initiation to be effectuated and completed at age 20. We then applied age-, sex-, period- and education-specific cessation rates to compute smoking prevalence by age among people over 20.

Historical smoking prevalence data was obtained from the Danish National Health Interview Survey in 1987, 1994, 2000 and 2005 (Table 1) [11]. For the period between 1987 and 2005, cessation rates were computed with the model proposed by Mendez and colleagues [20], taking into account population dynamics (number of people who started smoking, stopped smoking, and died in each age group) and using the historical data on smoking and on population size.

To estimate future cessation rates by age, sex and education, we used unpublished rates available from an Italian study on smoking cessation rates of high and low educated Italian men (Federico et al, 2009) (Table 2). This choice was based on the available evidence but presents limitations that will be discussed later. We computed cessation rates among middle educated people as the average between low and high educated people. The cessation rates were assumed to be similar for men and women. Among low educated people, cessation rates were higher among people aged 50+ years (4.25% smokers successfully quit per year) than among their younger counterparts (2.53% and 2.58% cessation rates for the age group 20-30 and 30-50 respectively). Among high educated people, cessation rates were generally higher and more similar by age group: 4.03% among people aged 20-30, 3.44% among those aged 30-50, and 3.965% among people aged 50+.

We defined a baseline scenario and four smoking reduction scenarios derived from this baseline scenario.

#### Baseline scenario

In this scenario, future smoking cessation and initiation rates remained at the 2005 level. Cessation rates are presented in Table 2 and initiation rates are those observed for the age group 20-24 in 2005 (Table 1).

#### Initiation scenario

This scenario assumed a 50% decrease in initiation rates during the next 15 years, so that initiation rates are halved in 2020 compared to the baseline year (2005). This corresponded to a 4.5% yearly decrease in smoking initiation rates in each educational group.

#### Cessation scenario

This scenario assumed a 50% increase in cessation rates for all age groups during the next 15 years. This corresponds to a 2.9% yearly increase in smoking cessation rates in each educational group.

#### Combined scenario

This scenario combined the two previous scenarios. During the next 15 years, initiation rates were halved and there would be a 50% increase in cessation rates.

#### Levelling-up scenario

We assumed that the cessation rates and the initiation rates of those with lower and mid educational levels converge during the next 15 years towards the levels of the highly educated people as observed at baseline.

#### Measure of socioeconomic inequalities

We computed age-standardised lung cancer incidence rates with the 2005 Danish population as the standard. We computed the rate ratio between low or middle relative to high educated persons as a measure of relative inequalities.

## Results

Smoking prevalence generally decreased between 1987 and 2005 for all education groups among men and women (Table 1). Educational differences were observed in smoking prevalence with higher rates associated with lower education both in men and women. In 2005 smoking prevalence was rather similar for men and women in each educational group. Smoking prevalence decreased at every age for all education groups.

Relative differences in smoking prevalence between the scenarios beg in to change in 2030 (Table 3). The cessation scenario differed the least from the baseline scenario. The lowest smoking prevalence was found with the combined scenario, followed by the initiation scenario. For the levelling-up scenario, smoking prevalence hardly differed between educational groups from 2040 onwards.

Educational inequalities in lung cancer incidence were observed in Denmark in 2004 with higher rates among lower educated persons (Figure 1). Rates for high educated women remained low until age 70. Under the baseline scenario, age-standardised (using 2005 Danish population), lung cancer incidence rates decrease from 140 (per 100,000 person years) in 2004 to 77 in 2050, from 128 to 53 and from 84 to 35 among men with low, middle or high education respectively (Figure 2). The decrease is proportionally smaller for low educated men compared to middle and high educated men. The decrease in lung cancer incidence rates was less pronounced among women. Female lung cancer incidence rates were seen to decrease only after 2020 among low educated women with only slight decreases in incidence rates are expected to decrease from 129 to 90, from 85 to 49 and from 56 to 31 among low, middle and high educated women respectively (Figure 2). In 2004, the gradient was more pronounced among women (ratio IR low/high=2.30) than among men (ratio=1.67). The rate ratios remained stable for middle educated men and

women over the whole period whereas they increased for low educated men and women (Table 4).

Table 4 shows the projected incidence rates and rate ratios under the different scenarios for the years 2020, 2030, 2040 and 2050. The difference in incidence rates between the baseline scenario and the alternative scenarios becomes evident from 2030 onwards. For the initiation scenario, the incidence rates differed from those observed under the baseline scenario in 2050, especially for low educated men and women. The lung cancer rates are substantially lower in the cessation and the combined scenarios for all educational groups. In 2050, the difference in incidence rates between the baseline and the combined scenario was more important for low educated men (20 per 100,000 person years) or women (22 per 100,000) than for the other educational groups.

In terms of rate ratios for educational differences in lung cancer incidence, the most favourable situation will be observed for the levelling-up scenario, where rate ratios will remain stable over the period. Rate ratios were observed to slightly increase for all other scenarios.

## Discussion

We investigated time trends in educational differences in lung cancer incidence under different scenarios aimed at reducing tobacco consumption, either by increasing cessation or lowering levels of initiation. The effect of the alternative scenarios becomes noticeable from 2030 onwards, when compared with the baseline scenario. The largest decrease in lung cancer rates will be observed in the cessation and the combined scenarios. No decrease in relative inequality will be observed over the whole period for all scenarios except the levelling-up scenario.

Strengths and limits of Prevent have been thoroughly discussed elsewhere [12]. Projections is a complex exercise that implies approximations, in which one focuses only on a few variables while ignoring the rest. Because any changes in smoking prevalence will start to have a visible impact on lung cancer incidence about 15 years later, long-term projections are the only way to investigate future impacts of smoking reduction on lung cancer incidence. The drawback is that long-term modelling goes along with more uncertainties in the estimates, stemming from uncertainties in the baseline trends of smoking or in risk factors not included in the model. Results can therefore not be interpreted as exact predictions but will allow us to assess the effect of different smoking reduction scenarios. A difference in estimated lung cancer incidence between two different scenarios will be related to the difference between the two scenarios in terms of smoking prevalence.

As for any modelling exercise, data quality is a major issue as the outcome directly depends on the input data. Lung cancer incidence by educational level was available from a project linking the Danish Cancer Register with education information from Statistics Denmark at the individual level. We had 17 years of historical smoking data from reliable national surveys including information on education with a coding similar to that available for lung cancer data. However, smoking prevalence before age 20 was not available by education in crosssectional surveys as education is not completed for most people. As a result, we had to assume that smoking initiation was completed at age 20 and that nobody smoked before age 20. Consequently, we may have underestimated smoking exposure, and more so among low educated subjects as they take up smoking earlier than their more educated counterparts [21]. Also, we only had information on smoking status, whereas lung cancer risk also is determined by intensity and duration of smoking [16]. However, the amount of cigarettes per smoker does not greatly differ by education level [22].

We assumed no autonomous trend in lung cancer incidence rates. This means that all changes in lung cancer incidence were driven by changes in tobacco consumption. The

literature, however, suggests that smoking does not totally account for socioeconomic inequalities in lung cancer incidence, which partly may be explained by residual confounding from smoking [8, 23] and other risk factors including occupational exposures [24]. We conducted additional analyses with an autonomous trend in lung cancer incidence accounting for past exposure to asbestos among low and middle educated men aged 40+ (results not shown). Expected lung cancer incidence rates including this autonomous trend were slightly higher in these educational groups and socioeconomic inequalities were more pronounced. Our main conclusions however did not change, probably because smoking is responsible for the majority of lung cancer cases.

The education level of the population is increasing over time. In 2005, slightly more than half of the Danish population had tertiary education (53% of men and 58% of women) whereas 34% of men and 22% of women had vocational education. The share of the population with low education was low and is likely to decrease further in future years. The projected incidence rates for the lowest education group would therefore refer to an increasingly smaller group in the future. Despite this, inequalities are likely to be an important problem in future years in Denmark as well, because differences in lung cancer incidence are also observed between the two highest education groups. In addition, studies on time trends in socioeconomic inequality in lung cancer do not report any clear decrease in inequality [25], even when the measure of inequality accounted for changes in the socioeconomic distribution of the population [26-28]. Furthermore, although the mean education level will increase during the next decades, an important degree of educational stratification will remain within the national population.

The parameters of the baseline scenario should be discussed. Little information is available regarding cessation rates by education in Denmark. Estimates that are available are derived from cross-sectional data, which mixes cohort, age and period effects [29]. Danish data on cessation rates therefore could not be directly obtained from this study, and we had to use

the estimates that were available from an Italian study. We selected male cessation rates as smoking histories strongly differ between Italian and Danish women, but much less so for men. The Italian data indicate higher smoking cessation rates among higher educated people as consistently suggested by indirect estimates for Denmark [30] and elsewhere [29, 31-33]. The education-specific cessation rates used were in line with those observed for Spain [31], Italy [34] or the US [33].

Tobacco price increase, bans on smoking advertising, smoking bans at school and antismoking education have all been found to affect smoking initiation rates in the population [35]. The most effective policies for smoking cessation were taxation policies and smoking bans: cessation rates were increased by 3-5% with a 10% increase in price and by 12-38% with comprehensive clean indoor laws [36]. Moreover, little is known on the differential effect of these policies by socioeconomic status (SES), although it has been suggested that bans on TV advertising or anti-smoking education may be more effective in reducing initiation rates among young people from low SES groups [35, 37, 38]. Although recent evidence suggested that high and low educated smokers benefit equally from the nationwide tobacco control policies [39], specific policies may have differential effect by SES on smoking cessation. There is no evidence regarding a differential effect of smoking bans in public places and in the work place [35, 38]. Media campaigns are generally shown to have a larger effect on high SES smokers or no differential effect by SES. They may nevertheless be most effective among low SES smokers when implemented within a part of more comprehensive tobacco control policies [37, 38, 40]. Bans on TV advertising may be more successful among low SES smokers [37]. Support for smoking cessation via telephone help lines has been shown to be effective among low SES smokers, especially with a follow-up from the counsellors, whereas the price of nicotine replacement therapy may be a barrier for low SES smokers if not offered freely [37]. Conflicting findings have been reported regarding the effect of price increase by SES, with some observing greater effect among high SES smokers [41] or among low SES smokers [35]. In addition, results may depend on the SES indicator

(income, education or occupation) considered [38] or vary over time [42]. Finally, more comprehensive tobacco control policies have been shown to be more effective in increasing the number of smokers who attempt quitting, and who are successful in these attempts [39].

Denmark has gradually implemented a number of tobacco control policies. Most have been implemented during the 2000s: smoking ban in school in 2001, ban on smoking advertising in 2002, sell of tobacco prohibited to people younger than 16 in 2004 and changed to 18 in 2008, a more general smoking ban in 2007, and a 10% increase in cigarette prices twice in 2010. These policies may be more efficient in decreasing smoking prevalence among young subjects, and more so among low SES groups. These policies have yet to affect lung cancer rates and we can thus expect larger decrease in smoking prevalence, and consequently larger decrease in inequalities in lung cancer rates in future years.

Despite large decrease in lung cancer incidence rates, we observed that relative inequalities between educational groups would be stable or even increasing during the period 2005-2050. This trend fits the general pattern that relative inequalities tend to increase when the occurrence of a health problem in the population decreases [43]. Nonetheless, under all smoking reduction scenarios, a substantial absolute number of lung cancer cases would be avoided, among both lower and higher educated people. The lack of decrease in inequalities is also partly due to the definition of the scenarios. The levelling-up scenario, however, showed that relative inequalities in lung cancer incidence would decrease only if special efforts were to be made to reduce the gap in smoking between high and low educated groups. This scenario however also showed that reducing this gap alone does not bring down absolute levels of lung cancer incidence to a great extent, and only at a longer run.

Cancer prevention works on a long-time scale. The incidence rates in the next decade are nearly completely determined by past smoking exposure. Even though this result may be easily predictable on the basis of the epidemiology of lung cancer, this great inertia is easily

forgotten in public health policies. We need scenarios based on population health models like Prevent to demonstrate that some actions take much time to have their full effect. With regards to smoking, because any change in smoking prevalence is likely to be gradual, any effect of alternative smoking policies on lung cancer incidence is not expected to be noticeable before the year 2030. As shown by our results, the levelling-up scenario will level out educational differences in smoking prevalence in 2050 only and it will take 20 to 30 more years before it fully impacts lung cancer rates. Increasing smoking cessation rates among adults will be the most effective way to decrease lung cancer rates within a few decades. Even though lowering initiation rates may be the most effective way to prevent high smoking prevalence among young generations, the effect on change in smoking prevalence in the population at large will be visible only on a long time scale. Therefore the success of antismoking policies in decreasing overall levels and socio-economic inequalities in lung cancer incidence will be evident only on a very long time scale. These policies are however likely to show an earlier impact on other diseases such as cardiovascular diseases that have a much shorter latency period.

#### Conclusion

Decreasing socioeconomic inequalities in lung cancer incidence is a major public health challenge. This paper illustrates what could be achieved under different realistic scenarios for smoking reduction. The decrease in socioeconomic inequalities may be modest even after several decades. However, we observed a substantial decrease in lung cancer rates for all educational groups, which means a significant number of lung cancer cases avoided. Our results also underline the need for implementing anti-smoking policies focused both on cessation rates (to bring important benefits to older generations at shorter run) and initiation rates (to bring even greater benefits to younger generations at longer run).

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## **CONFLICT OF INTEREST STATEMENT**

All authors declare that they do not have any conflict of interest.

Figure 1: Age-specific lung cancer incidence rate (per 100,000 person years) in Denmark in 2004 by sex and education level [7]



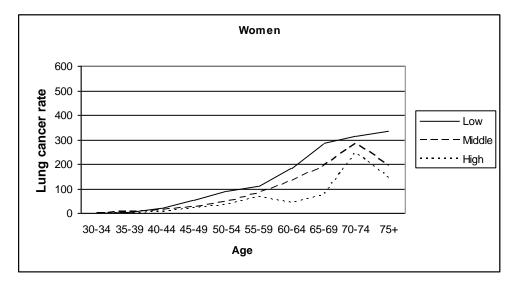
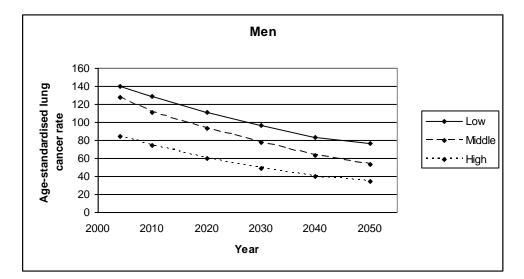


Figure 2: Age-standardised lung cancer incidence rates (per 100,000 person years) in 2004, 2010, 2020, 2030, 2040 and 2050 by sex and education level. Baseline scenario



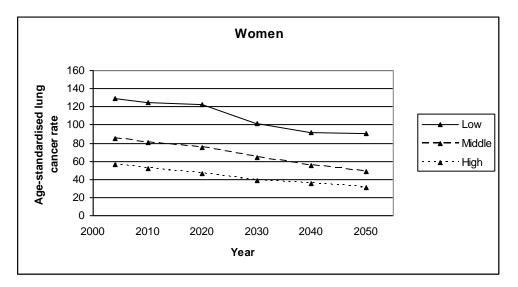


Table 1: Age-specific smoking prevalence by education, gender, and calendar year between1987 and 2005 in Denmark

			MEN			WOMEN				
Year	Age group	Low	Middle	High	Low	Middle	High			
1987	20-24	59	49	44	69	57	42			
	25-44	67	52	45	57	52	43			
	45-66	60	59	52	50	46	46			
	67+	44	44	38	28	29	41			
1994	20-24	45	39	35	64	46	29			
	25-44	37	51	36	68	54	40			
	45-66	59	56	43	49	42	28			
	67+	34	47	42	26	31	36			
2000	20-24	69	46	28	76	38	27			
	25-44	60	47	33	62	51	32			
	45-66	53	46	37	44	40	32			
	67+	36	34	32	24	27	26			
2005	20-24	70	43	39	67	52	38			
	25-44	61	48	36	63	48	32			
	45-66	50	42	33	47	41	29			
	67+	30	31	32	32	28	21			

Table 2: Cessation rates by education, gender, and age group applied to the baseline scenario\*

20-30	20 50	
	30-50	50+
0.0253	0.0258	0.0425
0.0328	0.0301	0.0411
0.0403	0.0344	0.0397
	0.0328	0.0328 0.0301

\*: These cessation rates were used to project smoking prevalence between 2006 and 2050.

(Federico 2009)

Table 3: Age-standardised smoking prevalence by education, gender, calendar year according to different smoking scenarios between 2010 and 2050 in Denmark MEN WOMEN Scenario Education Baseline High Middle Low Initiation High Middle Low Cessation High Middle Low Combined High Middle Low 

2020; Combined: combines initiation and cessation scenarios; Levelling-up: convergence towards the 2005 initiation and cessation rates of highly educated by 2020

Initiation: 50% decrease in initiation rate by 2020; Cessation: 50% in cessation rates by

Levelling-up

High

Low

Middle

Scenario	Education _	MEN							WOMEN								
		2020		2030		2040		2050		2020		2030		2040		2050	
		IR	RR	IR	RR	IR	RR	IR	RR	IR	RR	IR	RR	IR	RR	IR	RR
Baseline	High	60	1	49	1	40	1	35	1	46	1	39	1	35	1	31	1
	Middle	93	1.55	78	1.59	63	1.56	53	1.52	75	1.63	64	1.65	55	1.59	49	1.58
	Low	111	1.85	97	1.98	83	2.06	77	2.24	123	2.67	102	2.65	92	2.67	90	2.89
Initiation	High	60	1	49	1	40	1	33	1	46	1	38	1	34	1	29	1
	Middle	93	1.55	78	1.59	62	1.55	49	1.50	75	1.63	63	1.65	54	1.59	46	1.57
	Low	111	1.85	96	1.97	82	2.04	71	2.16	123	2.67	102	2.65	90	2.65	84	2.84
Cessation	High	60	1	46	1	35	1	28	1	46	1	37	1	31	1	27	1
	Middle	93	1.55	73	1.60	55	1.57	44	1.57	74	1.63	60	1.64	48	1.59	42	1.58
	Low	110	1.85	90	1.98	71	2.06	62	2.19	122	2.67	96	2.62	80	2.63	73	2.76
Combined	High	60	1	45	1	34	1	27	1	46	1	36	1	30	1	25	1
	Middle	93	1.55	73	1.60	54	1.56	41	1.51	74	1.63	60	1.64	47	1.58	39	1.55
	Low	110	1.85	90	1.97	70	2.04	57	2.09	122	2.67	96	2.62	78	2.60	68	2.69
Levelling-up	High	60	1	49	1	40	1	35	1	46	1	39	1	35	1	31	1
	Middle	93	1.55	78	1.59	62	1.53	50	1.46	75	1.63	63	1.64	54	1.55	46	1.48
	Low	111	1.85	96	1.95	78	1.94	66	1.90	123	2.67	99	2.62	87	2.53	79	2.53

Table 4: Age-adjusted lung cancer incidence rates\* (IR) and rate ratios (RR) by scenarios, calendar year, sex and education level.

\* per 100,000 person years, 2005 Danish population was used as standard. Sex-specific weights were used.

Initiation: 50% decrease in initiation rate by 2020; Cessation: 50% increase in cessation rates by 2020; Combined: combines initiation and

cessation scenarios; Levelling-up: convergence of initiation and cessation rates towards to the 2005 characteristics of highly educated by 2020

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