Comparison of cohort smoking intensities in Denmark and the Netherlands

Jan J. Barendregt, ¹ Caspar W.N. Looman, ¹ & Henrik Brønnum-Hansen²

Objective To assess the usefulness of the general framework of the smoking epidemic.

Methods We use lung cancer mortality as an indicator for smoking intensity and employ an age—cohort model to accommodate the long-lasting and cumulative effects.

Results Dutch males have higher risks than Danish males, but the risks for the younger cohorts have been declining faster in the Netherlands than in Denmark. Danish women have about twice the risk of Dutch women, and in both countries the risks for the younger cohorts are increasing. The smoking epidemic began at about the same time in Denmark and the Netherlands. Dutch males, however, seem to have smoked more but to have given up smoking more quickly than Danish males. Danish females were quicker to take up smoking than Dutch females.

Conclusions Within the general framework of the smoking epidemic, differences in timing and levels can produce large differences between countries. For the purposes of assessing smoking-related risks, including projections, the smoking epidemic framework therefore has to be tailored to each study population.

Keywords Smoking/epidemiology; Lung neoplasms/mortality; Age factors; Sex factors; Cohort effect; Linear models; Comparative study; Denmark; Netherlands (*source: MeSH, NLM*).

Mots clés Tabagisme/épidémiologie; Tumeur poumon/mortalité; Facteur âge; Facteur sexuel; Effet cohorte; Modèle linéaire; Etude comparative; Danemark; Pays-Bas (*source: MeSH, INSERM*).

Palabras clave Tabaquismo/epidemiología; Neoplasmas pulmonares/mortalidad; Factores de edad; Factores sexuales; Efecto de cohortes; Modelos lineales; Estudio comparativo; Dinamarca; Países Bajos (*fuente: DeCS, BIREME*).

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Voir page 32 le résumé en français. En la página 32 figura un resumen en español.

Introduction

Research on the health effects of smoking has revealed not just that smoking is a risk factor for a large and still increasing number of diseases but also that its ill effects seem to be cumulative and long-lasting (1, 2). The risk of contracting at least some of the diseases associated with smoking increases with the duration of exposure. Quitting decreases the risk, but for some diseases, e.g. lung cancer and chronic obstructive pulmonary disease, it does so only very slowly. Consequently, current exposure is not a very good indicator of current and future risks, and past exposure should be taken into account as well.

A good indicator of such risks would capture lifelong exposure and, preferably, changes in the amounts smoked and the composition of cigarettes. Although for many developed countries smoking prevalences are available since the 1960s, i.e. soon after the risks were officially recognized, data on amounts smoked and on cigarette composition are much more scarce. Data on smoking exposure before 1960 are largely anecdotal.

This lack of data has prompted some authors to argue that, in developed countries, lung cancer was overwhelmingly caused by smoking, and that mortality from lung cancer was therefore a good indicator of smoking intensity, defined as the total accumulated risk. Smoking intensity, estimated in this way, was then used to estimate the risk for other smoking-related diseases and to make projections of future risks (3, 4).

In a semiquantitative analysis of data from developed countries, Lopez et al. (5) derived the typical shape of the smoking epidemic. On a time scale of 100 years, men start to smoke, reach exposures exceeding 60% after about 50 years, and stay at this high level for some 20 years. Exposure then declines gradually, stabilizing at about 30%. Women start to smoke about 20 years after men and reach exposure levels of up to about 40%. Their exposure begins declining at almost the same time as in men. Eventually, the prevalences for women and men converge at the 30% level. The mortality attributable to smoking lags its prevalence by some 40 years .

Such a general theory of the evolution of the smoking epidemic would be very useful as a contribution not only to understanding the current burden of disease caused by smoking but also to projecting the future burden. Before it can be deployed, however, it should be compared with empirical data in order to test whether it is applicable in specific circumstances.

It is appropriate to use lung cancer mortality as an indicator for past smoking because very long periods of time

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¹ Department of Public Health, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, Netherlands. Correspondence should be addressed to Dr Barendregt (email: barendregt@mgz.fgg.eur.nl).

² National Institute of Public Health, Denmark.

are under consideration (3). However, a smoking epidemic shaped as Lopez et al. (5) hypothesized would have affected subsequent birth cohorts differently. Differences between cohorts and the cumulative character of the risk for lung cancer call for an analysis of lung cancer mortality in terms of cohort smoking intensities. We report such an analysis for Denmark and the Netherlands, show the similarities and differences between the two countries, and make inferences about their respective smoking epidemics and the implications for a general theory of smoking epidemics.

Data and methods

Lung cancer mortality and population data in the Netherlands, by sex and five-year age group, for the period 1950-97 were obtained from Statistics Netherlands. For the period 1950-69 the oldest age group was ≥85 years and subsequently it was ≥95 years. Data on mortality attributable to lung cancer by sex and age in Denmark for the period 1943-96 were obtained from the National Institute of Public Health. For both countries we used deaths of persons aged ≥ 30 years.

Table 1 shows the classification systems and codes used over these periods. For International Classification of Diseases revisions 6-9 (ICD-6-9), code 162 was used; for ICD-10, code C34 was used. In the Dutch data, for ICD-6 and ICD-7 many lung cancer deaths were coded 163, whereas, starting with ICD-8 (1969), code 163 was reserved for mesothelioma. For ICD-6 and ICD-7, therefore, we took code 163 in addition to code 162. For purposes of comparability we used the same procedures for Denmark, although very few cases were coded 163 in this country.

An age-cohort model with five-year age groups was fitted to each data set. In the log-linear regression analysis the annual age-specific death rates were assumed to be composed of a basic age-specific rate multiplied by relative risks specific to birth cohorts (see Box 1). The basic rate and the cohortspecific relative risks were estimated separately for the two countries.

To make the analysis comparable between the two countries, the parameters for the 5-year age groups in Denmark were estimated on the 1-year age group data. In both countries the age groups did not fully coincide with particular birth cohorts, and interpolation was therefore used to estimate the relative contributions of adjacent birth cohorts to the death rates in particular years. The interpolation weighted the cohort-specific risk by the number of personyears in the birth cohorts.

Table 1. Classification systems and codes used for lung cancer mortality time series, Denmark and the Netherlands

Country	Years	Classification system ^a	Codes
Denmark	1943–50	Bertillon	716
	1951–68	ICD-6/7	162, 163
	1969–93	ICD-8	162
	1994–96	ICD-10	C34
Netherlands	1950–68	ICD-6/7	162, 163
	1969–95	ICD-8/9	162
	1996–97	ICD-10	C34

^a ICD = International Classification of Diseases. Denmark never used ICD-9.

Box 1. Age-cohort model fitted to data

 $\hat{y_{a,j}} = N_{a,j} \exp \left(\alpha_a + \sum_{c} \beta_c \pi_{a,j,c} \right)$; y follows a Poisson distribution.

Where:

 $\hat{y_{a,j}}$ $N_{a,j}$ is the expected number of deaths in age group a in year j;

is the number of person-years at risk in age group a in year j;

 α_a is In(risk in age group a in baseline cohort);

is In(relative risk of cohort c relative to baseline cohort); β_c

is fraction of person-years at risk in age group a in year j belonging to cohort c (baseline cohort excluded).

This log-linear model was fitted using maximum likelihood estimation with the GLIM program (6). The goodness-of-fit was assessed using the likelihood-ratio criterion (scaled deviance) based on Poisson deviates. Cohorts from before 1867 and after 1958 were combined because of small numbers.

Clayton & Schifflers observe that the parameters α and β of such a model are not identifiable because it is possible to obtain the same expected number of deaths from an infinite number of pairs of α and β values by subtracting a constant from one and adding it to the other (\nearrow). We followed the convention of resolving this parameterization problem by arbitrarily setting the relative risk of a baseline cohort (the 1918–22 cohort) at 1, and expressing the risk of all other cohorts relative to this cohort. The α values could then be interpreted as age-specific rates, and the β values as relative risks ($\overline{\lambda}$).

Results

The estimated parameter values of the regression are shown with the age-specific mortality rate of the 1918-22 baseline cohort in Table 2 and with the cohort-specific relative risks in Table 3. The goodness-of-fit criteria (scaled deviance) are also shown in Table 2. The Danish values are much higher than the Dutch because the Danish data give age at death, while the Dutch data are partitioned in five-year age groups. The degrees of freedom in the Danish analysis are correspondingly much higher than those in the Dutch analysis.

Fig. 1 and Fig. 2 show observed and fitted lung cancer mortality rates for men and women, respectively. Rates by calendar year for the period 1943-97 for six age groups are given. The mortality rates for men are much higher than those for women. For all age groups, mortality rates for Dutch males were 50-60% higher than those for Danish males throughout the period, while the rates for Danish females are two to three times higher than those of Dutch females.

For males the effect of the smoking epidemic on lung cancer has clearly peaked. Male mortality rates in Denmark are on a plateau. Among Dutch males, particularly in the younger age groups, mortality rates are declining, albeit slowly. For females the opposite is true: mortality rates are increasing sharply in both Denmark and the Netherlands, and only among Danish women aged 55-59 years is there a suggestion of stabilization during the most recent years.

Fig. 3 and Fig. 4 show the relative risks of lung cancer mortality in each birth cohort (antilogs of β , see Box 1) of men and women, respectively. The numbers are rescaled such that the 1878-82 cohort equals 1. The levels of relative risk are not comparable between Denmark and the Netherlands because the analyses were performed separately for each country. However, the shapes of the curves are comparable.

For men the increase in relative risk among the oldest cohorts is very similar, but for the cohort of 1903-07 and subsequent cohorts the relative risk stabilizes in Denmark, while in the Netherlands the relative risk begins to decline

Table 2. Goodness-of-fit criterion (scaled deviance) with degrees of freedom, estimated α values of regression model, standard errors and age-specific rates for baseline cohort 1918–22, males and females, the Netherlands and Denmark

		Netherlands						Denmark						
		Males Females					Males			Females				
Scaled deviance		1759			810			5295			4497			
Degrees of freedom		640			640			3496			3496			
Age effect (years)	α	SE ^a	Rate (per 1000)	α	SE	Rate (per 1000)	α	SE	Rate (per 1000)	α	SE	Rate (per 1000)		
30–34 35–39 40–44 45–49 50–54 55–59 60–64 65–69 70–74 75–79	-10.900 -9.699 -8.664 -7.763 -6.978 -6.312 -5.767 -5.328 -5.008 -4.772	0.0617 0.0341 0.0213 0.0150 0.0118 0.0101 0.0093 0.0090 0.0089 0.0095	0.0184 0.0613 0.1727 0.4250 0.9324 1.8138 3.1296 4.8529 6.6876 8.4597	-13.180 -11.930 -10.990 -10.060 -9.332 -8.710 -8.151 -7.688 -7.314 -6.959	0.0932 0.0615 0.0473 0.0381 0.0330 0.0299 0.0277 0.0267 0.0256 0.0279	0.0019 0.0066 0.0169 0.0426 0.0885 0.1649 0.2886 0.4582 0.6660 0.9502	-11.350 -10.200 -9.087 -8.133 -7.257 -6.544 -5.993 -5.563 -5.247 -5.055	0.1121 0.0633 0.0379 0.0256 0.0190 0.0157 0.0142 0.0135 0.0134 0.0153	0.0117 0.0372 0.1131 0.2937 0.7051 1.4387 2.4961 3.8363 5.2622 6.3753	-12.180 -11.030 -10.040 -9.039 -8.361 -7.653 -7.132 -6.615 -6.251 -5.982	0.1267 0.0765 0.0522 0.0373 0.0308 0.0261 0.0237 0.0219 0.0214 0.0250	0.0051 0.0162 0.0434 0.1186 0.2337 0.4746 0.7993 1.3406 1.9294 2.5228		
80–84 85–89 ≥ 90	-4.664 -4.651 -4.705	0.0112 0.0145 0.0244	9.4248 9.5551 9.0503	-6.717 -6.541 -6.375	0.0321 0.0369 0.0488	1.2102 1.4424 1.7033	-5.004 -5.051 -5.312	0.0186 0.0266 0.0535	6.7102 6.4055 4.9299	-5.863 -5.750 -5.857	0.0303 0.0389 0.0642	2.8428 3.1834 2.8603		

^a SE = standard error.

Table 3. Estimated β values of regression model, standard errors and relative risks for cohorts from before 1867 to after 1958, relative to baseline cohort 1918–22, males and females, the Netherlands and Denmark

	Netherlands						Denmark					
		Males		Females			Males			Females		
Cohort effect	β	SE ^a	RR ^b	β	SE	RR	β	SE	RR	β	SE	RR
1868–72 1873–77 1878–82	-2.327 -2.093 -1.730 -1.388 -1.111	0.1135 0.0703 0.0389 0.0260 0.0194	0.0976 0.1233 0.1772 0.2496 0.3292	-1.523 -1.499 -1.153 -1.124 -1.072	0.1681 0.1281 0.0807 0.0628 0.0529	0.2180 0.2234 0.3156 0.3250 0.3423	-2.979 -2.259 -1.949 -1.667 -1.227	0.1134 0.0682 0.0450 0.0340 0.0258	0.0508 0.1045 0.1425 0.1888 0.2931	-2.674 -2.302 -1.902 -1.840 -1.607	0.1312 0.1006 0.0667 0.0554 0.0451	0.0690 0.1001 0.1492 0.1589 0.2004
1893–97	-0.732 -0.318 -0.113 0.049 0.104	0.0154 0.0128 0.0116 0.0111 0.0103	0.4811 0.7278 0.8932 1.0505 1.1092	-1.014 -0.918 -0.787 -0.692 -0.552	0.0467 0.0411 0.0376 0.0357 0.0329	0.3627 0.3993 0.4552 0.5007 0.5760	-0.852 -0.510 -0.262 -0.115 -0.084	0.0213 0.0182 0.0166 0.0157 0.0153	0.4268 0.6006 0.7697 0.8918 0.9199	-1.435 -1.296 -1.118 -0.914 -0.656	0.0393 0.0348 0.0314 0.0289 0.0267	0.2382 0.2735 0.3269 0.4010 0.5191
1928–32	0.061 NA ^c -0.106 -0.080 -0.181	0.0122 NA 0.0140 0.0135 0.0177	1.0631 1.0000 0.8999 0.9230 0.8348	-0.321 NA 0.348 0.823 0.870	0.0372 NA 0.0370 0.0328 0.0398	0.7257 1.0000 1.4164 2.2776 2.3871	-0.112 NA -0.048 -0.051 -0.147	0.0163 NA 0.0185 0.0214 0.0276	0.8945 1.0000 0.9534 0.9504 0.8633	-0.378 NA 0.251 0.575 0.685	0.0266 NA 0.0272 0.0292 0.0347	0.6855 1.0000 1.2857 1.7771 1.9830
1943–47 1948–52 1953–57	-0.396 -0.354 -0.455 -0.659 -0.873	0.0237 0.0308 0.0469 0.0828 0.1352	0.6728 0.7022 0.6342 0.5175 0.4176	1.085 1.313 1.497 1.787 1.903	0.0452 0.0521 0.0667 0.0917 0.1257	2.9581 3.7158 4.4701 5.9695 6.7062	-0.328 -0.190 -0.285 -0.338 -0.523	0.0384 0.0478 0.0824 0.1460 0.2716	0.7202 0.8269 0.7523 0.7133 0.5930	0.626 0.657 0.666 0.831 0.051	0.0446 0.0557 0.0862 0.1354 0.3104	1.8707 1.9291 1.9461 2.2964 1.0522

 $^{^{\}rm a}$ SE = standard error.

^b RR = relative risk.

^c NA = not applicable.

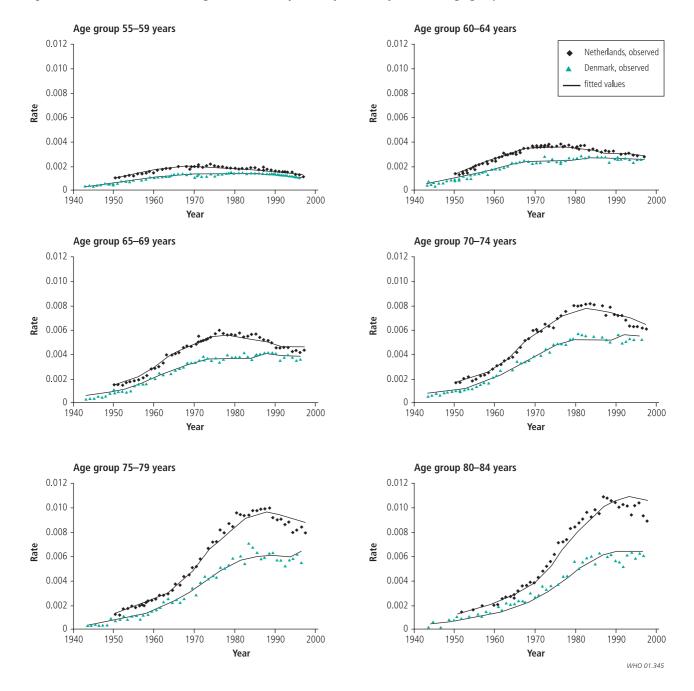


Fig. 1. Observed and fitted male lung cancer mortality rates, by calendar year, for six age groups, Denmark and the Netherlands

slowly. This happens in Denmark only with the 1933–37 cohort or the 1938–42 cohort. Consistently, Fig. 1 shows that Dutch mortality rates have clearly declined in recent years but that Danish mortality rates seem to have stabilized for the most part.

For women the picture is quite different (Fig. 4). The relative risks start to rise much later than those for men, and there is a marked difference between the two countries: the increase begins some 20 years later in Denmark and about 30 years later in the Netherlands. No declines are yet visible. The Danish relative risks seem to stabilize as from the 1933–37 cohort, the increase visible for the youngest cohorts not being statistically significant. The Dutch relative risks are rising relentlessly. Again this is consistent with the results in Fig. 2: the rates in both countries are increasing in all age groups

except for the possible recent stabilization in the youngest Danish group.

Discussion

Denmark and the Netherlands are both confronted with the late effects of a smoking epidemic that goes back many decades. There are similarities in this matter between the two countries but there are also striking differences.

For the analysis of the lung cancer data we looked at age—period models, age—cohort models, and age—period—cohort models. Age is always needed in the models because lung cancer mortality is clearly related to age. We chose an age—cohort model because lifelong smoking exposure seemed to be decisive for the level of risk. For both countries the age—cohort

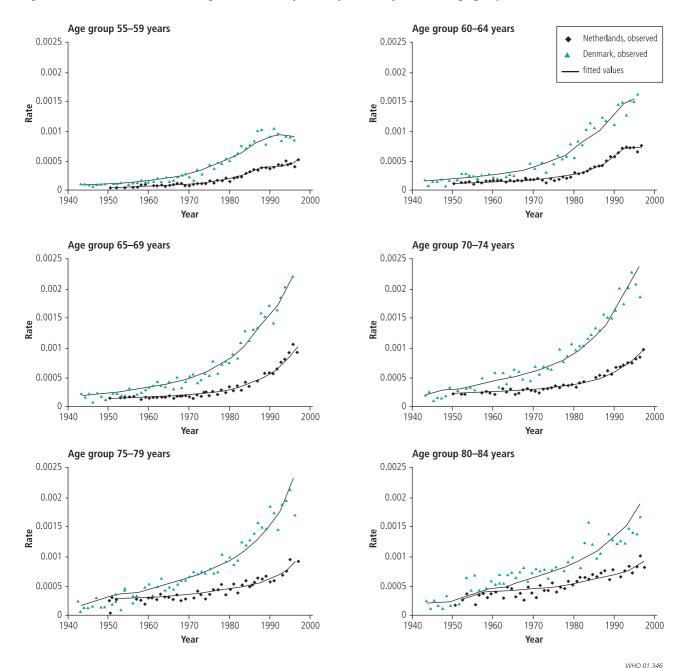


Fig. 2. Observed and fitted female lung cancer mortality rates, by calendar year, for six age groups, Denmark and the Netherlands

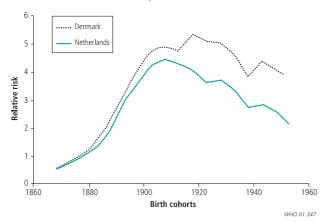
model produced a fit that was reasonable and much better than that of the age-period model. Nevertheless, for males, particularly in the Netherlands, the age-cohort model seemed to overestimate systematically for the most recent years (Fig. 1).

We explained this by the sharp declines in male smoking prevalence across age groups since 1970 which, despite the long lag times, were beginning to have a beneficial effect. We could have improved the fit of the model and lowered the scaled deviance by including a period effect so as to capture the effects of quitting smoking. We decided against this because the improvement of the fit would have been small and would not have outweighed the identification problem of a full ageperiod—cohort model, which poses fundamental difficulties in the interpretation of the parameter estimates (8).

Our results can be readily interpreted in the framework of the smoking epidemic as proposed by Lopez et al. (5). Dutch and Danish males started to smoke at about the same time, but Dutch males smoked more, per capita or as a percentage of the population, or both. However, Dutch males evidently started to quit earlier and in greater numbers than their Danish counterparts, causing the rates for the younger age groups in recent years to fall again, while the Danish rates are mostly stable.

Danish women were quicker to follow the example of the men than Dutch women, and this shows up in the much higher lung cancer mortality among the former. However, it is likely that Dutch women will eventually catch up with Danish women in this respect, given the stagnation of relative risks in recent Danish birth cohorts but not in Dutch cohorts (Fig. 4).

Fig. 3. Male relative risks for lung cancer by birth cohort (relative risks are scaled such that cohort 1878-82=1)



While time series data on smoking prevalences must be interpreted with caution, they seem to support this interpretation. The oldest Dutch data are from 1958, when 90% of Dutch males were reported to be smokers (9). The prevalence of smoking among Danish males was reported to be somewhat lower, at around 80%, in 1953–54 (10). In 1986–87, however, Dutch male smoking exposure was down to 41% while the corresponding value in Denmark was still 49%. In 1990–91 the prevalence for the Netherlands and Denmark was 39% and 47%, respectively (10, 11).

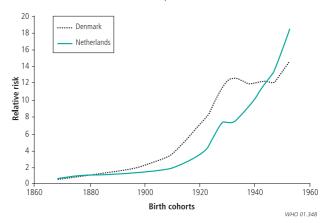
By contrast, in 1953–54 a total of 40% of Danish women smoked, while in 1958 the corresponding proportion was 29% of Dutch women The prevalence of smoking was lower among all age groups in the Netherlands, but was particularly so among women aged over 50 years. In Denmark this level remained at 40% in 1985–87 and 1990–91, although there were increases among women aged over 40 years and decreases among those younger than this. Overall exposure in the Netherlands increased to 34% in 1985–87 but fell again to 31% in 1990–91. Here too there was a shift towards older ages (9–11).

We conclude that, while both Denmark and the Netherlands fit within the concept of the smoking epidemic, there still are considerable differences. Fig. 3 shows that the part of the epidemic affecting males began at about the same time in both countries. Subsequently, much higher smoking intensities developed among Dutch males than their Danish counterparts (Fig. 1). The epidemic began to affect Danish females after a much shorter time lag than the Dutch females (Fig. 4). We interpret the difference between Dutch and Danish males as being mostly attributable to a difference in the level of the epidemic, and the difference between Dutch and Danish females as being a matter of timing and, judging by the smoking prevalence data, of level.

The age—cohort model employed in this analysis could be used for extrapolation. The extrapolation of the current fitted models could permit mortality to be determined with reference to the relative risks of the youngest cohorts in Figs. 3 and Fig. 4. The drawback is that these relative risks would be based on small numbers of deaths in the youngest age group considered.

Furthermore, predictions would be based only on lung cancer mortality, even though other data could be taken into account. Developments in the prevalence of smoking over the last 30 years or so could be considered since the decline

Fig. 4. Female relative risks for lung cancer by birth cohort (relative risks are scaled such that cohort 1878-82=1)



observed in both countries seems to be coming to an end. There is also the more general notion of the smoking epidemic, linking the current rise in female lung cancer mortality to the rise in the prevalence of smoking that occurred after the Second World War.

For the moment, however, the conceptual framework of the smoking epidemic is mostly suitable for descriptive purposes, because differences in timing and levels can produce large differences between countries. For the concept to lend itself to projection it should be tailored to particular populations. A Baysean approach might be useful here. The framework of the smoking epidemic could be regarded as the prior distribution, to be updated using cohort smoking intensities estimated through lung cancer mortality in relation to long-term exposure and developments in smoking prevalence in relation to more recent exposure.

Pending such a combined approach, certain predictions can be made. In both countries, mortality attributable to lung cancer among females is likely to rise rapidly. This can be deduced partly by extrapolating the trends of the last two decades. Moreover, it should be noted that, in the age groups 65–69 years, 70–74 years, and 75–79 years, mortality rates are virtually the same (Fig. 2). Given the age effect on lung cancer, this means that by the time women aged 65–69 years have progressed to older age groups their mortality will be higher than the current rates for these older age groups. In Denmark the first sign of stabilization in the longer term may be visible in the relative risks for the youngest cohorts and the most recent rates for the 55–59-year age group, but in the Netherlands there are no such indications.

The outlook for men is better, although it should be remembered that mortality remains far higher among males than among females. The decline in relative risks among the more recent male cohorts suggests that the fall in lung cancer mortality observed in the younger age groups will eventually extend to the older ones. For the moment this development is more pronounced in the Netherlands than in Denmark.

As more results from smoking studies become available, the smoking-related burden of disease keeps increasing, and awareness of the consequences of the smoking epidemic in the very long term becomes more acute (12).

Conflicts of interest: none declared.

Résumé

Comparaison de l'intensité du tabagisme dans des cohortes au Danemark et aux Pays-Bas

Objectif Evaluer l'utilité du schéma général de l'épidémie de tabagisme.

Méthodes Nous avons considéré la mortalité par cancer du poumon comme indicateur de l'intensité du tabagisme mais avons utilisé un modèle faisant appel aux cohortes d'âge pour tenir compte des effets durables et cumulatifs.

Résultats Parmi les sujets de sexe masculin, les Néerlandais ont un risque plus élevé que les Danois, mais le risque diminue plus rapidement dans les cohortes jeunes que dans les cohortes plus âgées. Chez les femmes, le risque est environ deux fois plus élevé chez les Danoises que chez les Néerlandaises, et dans les deux pays

le risque est en augmentation dans les cohortes jeunes. L'épidémie de tabagisme a commencé à peu près en même temps au Danemark et aux Pays-Bas. Les Néerlandais semblent toutefois avoir fumé davantage que les Danois mais avoir arrêté plus tôt. Les Danoises ont arrêté plus tôt que les Néerlandaises.

Conclusion A l'intérieur du schéma général de l'épidémie de tabagisme, des différences de chronologie et d'intensité peuvent se traduire par d'importantes divergences d'un pays à l'autre. En ce qui concerne l'évaluation des risques liés au tabagisme, et notamment les projections, le schéma général de l'épidémie doit être adapté à chaque population étudiée.

Resumen

Comparación de la intensidad del consumo de tabaco por cohortes en Dinamarca y los Países Bajos

Objetivo Evaluar la utilidad del esquema general de la epidemia de tabaquismo.

Métodos Empleamos la mortalidad por cáncer pulmonar como indicador de la intensidad del consumo de tabaco, pero utilizamos un modelo de cohortes por edades para incorporar los efectos prolongados y acumulados.

Resultados Los varones neerlandeses presentan más riesgos que los varones daneses, pero los riesgos para las cohortes jóvenes han disminuido más rápidamente que los de las de mayor edad. Las mujeres danesas presentan un riesgo equivalente aproximadamente al doble que el de las neerlandesas, y en los dos países están aumentando los riesgos para las cohortes más jóvenes. La epidemia de tabaquismo comenzó casi al mismo tiempo en

Dinamarca y en los Países Bajos. Los hombres neerlandeses, sin embargo, parecen haber fumado más, pero también haber abandonado más rápidamente el hábito, que los daneses. Las mujeres danesas adquirieron el hábito de fumar más rápidamente que las neerlandesas.

Conclusión Dentro del esquema general de la epidemia de tabaquismo, las diferencias tocantes al momento de la adquisición del hábito y a la intensidad de éste pueden dar lugar a grandes diferencias entre los países. A efectos de la evaluación de los riesgos relacionados con el tabaco, proyecciones incluidas, es preciso adaptar el esquema de la epidemia a las características de la población estudiada.

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