ORIGINAL ARTICLE

Expected number of asbestos-related lung cancers in the Netherlands in the next two decades: a comparison of methods

Sjoukje Van der Bij,[1,2] Roel C H Vermeulen,[1,3] Lützen Portengen,[3] Karel G M Moons,[1] Hendrik Koffijberg[1]

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/oemed-2014-102614).

[1]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands
[2]NIVEL, Netherlands Institute for Health Services Research, Utrecht, The Netherlands
[3]Division of Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands

Correspondence to
Professor Karel G M Moons, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, P.O. Box 85500, Utrecht 3508 GA, The Netherlands; k.g.m.moons@umcutrecht.nl

Received 30 September 2014
Revised 11 December 2015
Accepted 20 January 2016
Published Online First 8 February 2016

ABSTRACT

Objectives Exposure to asbestos fibres increases the risk of mesothelioma and lung cancer. Although the vast majority of mesothelioma cases are caused by asbestos exposure, the number of asbestos-related lung cancers is less clear. This number cannot be determined directly as lung cancer causes are not clinically distinguishable but may be estimated using varying modelling methods.

Methods We applied three different modelling methods to the Dutch population supplemented with uncertainty ranges (UR) due to uncertainty in model input values. The first method estimated asbestos-related lung cancer cases directly from observed and predicted mesothelioma cases in an age-period-cohort analysis. The second method used evidence on the fraction of lung cancer cases attributable (population attributable risk (PAR)) to asbestos exposure. The third method incorporated risk estimates and population exposure estimates to perform a life table analysis.

Results The three methods varied substantially in incorporated evidence. Moreover, the estimated number of asbestos-related lung cancer cases in the Netherlands between 2011 and 2030 depended crucially on the actual method applied, as the mesothelioma method predicts 17 500 expected cases (UR 7000–57 000), the PAR method predicts 12 150 cases (UR 6700–19 000), and the life table analysis predicts 6800 cases (UR 6800–33 850).

Conclusions The three different methods described resulted in absolute estimates varying by a factor of ~2.5. These results show that accurate estimation of the impact of asbestos exposure on the lung cancer burden remains a challenge.

What this paper adds

- Many studies have estimated the historical burden of asbestos-related lung cancer cases but information on the expected future lung cancer cases is still limited.
- We show that using three different plausible modelling methods results in different absolute estimates of future asbestos-related lung cancers varying by a factor of 2.5.
- Although information on the relation between asbestos and lung cancer is substantial, accurate and robust estimation of the impact of asbestos exposure on the future lung cancer burden remains challenging.

INTRODUCTION

Exposure to asbestos is known to increase the risk of developing mesothelioma and lung cancer.[1] While the vast majority of mesothelioma cases are generally accepted as being caused by asbestos, the proportion of all lung cancers that is asbestos-related is less clear. This proportion cannot be determined directly because asbestos-related lung cancer is not clinically distinguishable from lung cancer due to other causes.[2] Consequently, the historical number of asbestos-related lung cancers is unknown and cannot be used to forecast the future number of asbestos-related lung cancers. Estimates of the disease burden are an important input to healthcare decision-making and planning. Prediction of the future number of asbestos-related lung cancers in any population is therefore necessarily based on mathematical models using a variety of other sources of evidence.

To estimate the future number of asbestos-related lung cancers in the general population, various modelling methods might be applied, such as, for example, life table analysis of the lung cancer risk in exposed individuals.[3] However, owing to the limited availability of estimates of asbestos exposure in the general population, this method of analysis is often limited to cohorts of workers exposed in a specific industry.[4] An alternative modelling method uses the population attributable risk (PAR), which can be derived from lung cancer case–control or cohort studies.[5–7] Yet another modelling method focuses on forecasting the number of mesothelioma cases and converting these estimates in a prediction of future lung cancer cases based on the observed ratios of these two cancers in asbestos-exposed populations.[2 8–10]

Any modelling method that is applied may provide estimates of uncertainty surrounding the predicted number of asbestos-related lung cancer cases. However, this indicates only how the predicted number may vary given the uncertainty in the input values for the model, assuming that the model structure itself is correctly specified. In general, this assumption cannot be verified. When the correct model structure is unknown, structural uncertainty therefore can and should be assessed by comparing the results from different model structures.

To cite: Van der Bij S, Vermeulen RCH, Portengen L, *et al*. *Occup Environ Med* 2016;**73**:342–349.

When estimating the number of lung cancer cases associated with asbestos, the three commonly used models differ substantially in model structure. Estimating the number of lung cancers attributable to asbestos exposure directly from mesothelioma cases typically requires evidence on the association between these diseases. The PAR method depends on estimates of studies about the proportion exposed and associated relative risk (RR). The life table method projects the probability of lung cancer among individuals and, in comparison with the PAR method, typically allows the incorporation of additional evidence influencing the future number of asbestos-related lung cancers, such as the effect of competing causes of death, changes in risk levels and different exposure scenarios.

In this paper, we compare these three modelling methods with different structures for the prediction of the expected asbestos-related lung cancers in the Netherlands from 2011 to 2030. In the first model, we estimate the asbestos-related lung cancer cases directly from predicted mesothelioma cases; in the second model, we make use of the PAR method, and in the third model we use exposure information and the asbestos-related lung cancer risk as a direct function of exposure in a life table analysis. The three models were constructed on the basis of the best available evidence. We discuss their advantages and disadvantages, the evidence they incorporate, and compare their results.

METHODS

Three model types were applied to predict the number of future asbestos-related lung cancers in the Netherlands from 2011 to 2030. All methods were applied separately to men and women and results were aggregated. Model specifications were limited to the level of information that was available in the Dutch context.

Model 1: mesothelioma model

Estimates of historical and future cases of asbestos-related lung cancer can be derived directly from observed and predicted mesothelioma cases through a conversion factor.[10] To predict the future number of mesothelioma cases, an age-period-cohort (APC) analysis was used.[11] The required data were provided by Statistics Netherlands (CBS) and included the observed number of mesothelioma deaths in 1969–2010, annual observed demographic distributions of the Dutch population in 1969–2010, and annual expected demographic distributions for 2011–2030.[12] For the years 1969–1995, deaths due to mesothelioma were identified by International Classification of Diseases, Eighth/Ninth Revision (ICD-8/9) code 163.0 (pleural cancer). Since this category did not include death due to non-pleural mesothelioma, we divided the number of deaths by 0.95 as the number of non-pleural mesothelioma deaths is estimated to be around 5% of all mesothelioma deaths.[13–15] For the years 1996–2010, the number of deaths due to mesothelioma was identified by ICD-10 code C45 and included pleural and non-pleural mesothelioma. All data were tabulated into 13 age groups (31–35, 36–40,…, 86–90, and 91–95) and eight 5-year periods following the years 1969–1970 (1971–1975, 1976–1980,…, 2006–2010). This resulted in 20 partially overlapping 10-year birth cohorts (1876–1885,…, 1966–1975, 1971–1980) and 1 of 6 years (1874–1880), which were identified by mid-point year (thus, the birth cohort of 1965 comprised those born between 1961 and 1970). Using the number of mesothelioma deaths observed in 1969–2010, the age-specific mortality rates and cohort RRs by year of birth were calculated using the APC method separately for men and women. Since pleural mesothelioma under the age of 40 years was very rare, the birth cohort of 1965 was the youngest cohort for which a reliable risk estimate could be obtained. Given that in the Netherlands asbestos use after 1984 was very limited and an asbestos ban was implemented in 1993,[16 17] birth cohorts beyond 1965 were assigned zero risk of mesothelioma and lung cancer due to asbestos exposure. Estimated age-specific rates of mesothelioma per birth cohort were projected on the expected future demographic distributions to predict the future number of mesothelioma deaths (see online supplementary material for information about the estimated age-specific mortality rates and birth cohort risk). A sensitivity analysis was performed in which the birth cohort of 1970 was assigned the risk of the birth cohort of 1965 instead of zero risk and birth cohorts beyond 1970 were assigned zero risk, to simulate longer propagation of risk over time. To estimate the future number of asbestos-related lung cancers, an estimated smoking-adjusted ratio between mesothelioma and lung cancer from a published meta-analysis was applied.[10] In the Netherlands, different types of asbestos have been used; therefore, the ratio reported for mixed asbestos fibres was used: a ratio of 1.5 (95% CI 1.1 to 2.0) asbestos-related lung cancers per mesothelioma death.[10]

Model 2: PAR model

This model uses the number of lung cancers observed in 2010, and the estimated PAR by age categories. In a Dutch study, it was estimated that 11.6% of the lung cancer cases that occurred in men aged 55–73 years in the period 1986–1990 were related to asbestos exposure.[7] This PAR was assumed to be fixed and applicable to the total number of lung cancers in men >40 years of age in 2010 and later years. All younger individuals, born after 1970, were assumed to be never exposed to asbestos and had zero PAR.

For men, the distribution of lung cancer cases over age was derived as the average of the observed distributions over age in the years 2008–2010. When the age categories under consideration contained both individuals born before and after 1970, a linear interpolation of the PAR was used. The estimated PAR values over time were then applied to the expected future number of lung cancer cases which were calculated from the observed lung cancer incidence in 2008–2010 and the expected male demographic distribution in 2011–2030.[12]

Since no reliable PAR estimates were available for Dutch women, first the ratio of the expected number of asbestos-related lung cancers based on the PAR model to the observed number of mesotheliomas among men in 2010 was estimated. Then this ratio of 1.77 asbestos-related lung cancers per one mesothelioma was applied to the observed number of mesotheliomas among women in 2010 to derive the number of asbestos-related lung cancers in women in 2010. This resulted in a PAR of 2.5% for women, which is only slightly less than the PAR of 3.8% found in a French study applying the same procedure.[5]

Model 3: life table model

In this model, the future number of asbestos-related lung cancers was estimated on the basis of exposure information and the asbestos-related lung cancer risk as a direct function of exposure. To estimate the number of individuals exposed to asbestos, data from the Netherlands cohort study (NLCS) were used.[18] The NLCS is a prospective cohort study started in 1986 among men and women aged 55–69 years (n=120 852). At baseline, a comprehensive lifetime job history up to the year 1986 was collected for all participants, but only information from a randomly drawn subcohort (n=5000) was entered

Table 1 Characteristics of the applied models to estimate lung cancer cases in the future

Model	1. Mesothelioma	2. PAR	3. Life table
Model type	Ratio of lung cancer to mesothelioma cases	PAR	Life table
Evidence available and used in the Dutch context*	▶ Demographics ▶ Mesothelioma cases ▶ Ratio of mesothelioma to asbestos-related lung cancer	▶ Demographics ▶ PAR ▶ Number of lung cancers (single point in time)	▶ Demographics ▶ Detailed information about asbestos exposure levels ▶ Incidence of non-asbestos-related lung cancer ▶ (Relative) risk of lung cancer from asbestos exposure
Underlying assumptions	▶ Mesothelioma is proxy for asbestos exposure ▶ A single constant ratio can describe the relation between mesothelioma and lung cancer ▶ Risk of adjacent birth cohorts can be well determined ▶ Accurate recording of mesothelioma cases	▶ The PAR (from a single well-designed study) is representative of the total population ▶ The PAR is representative for future years ▶ Lung cancer risk does not change over time	▶ Asbestos exposure is representative of the total population ▶ Exposure response relation is known ▶ Lung cancer risk does not change over time
Advantages	▶ Simple to construct ▶ Evidence commonly available ▶ Integrates the timing and level of cumulative exposure	▶ Simple to construct ▶ Evidence commonly available from case–control or case–cohort studies	▶ Gives detailed outcomes and allows for estimation of other statistics (eg, life expectancies)
Disadvantages	▶ Ratio between mesothelioma and lung cancer depends heavily on fibre type which decreases robustness of results ▶ It is likely that the ratio is not constant but depends on asbestos exposure levels ▶ It is likely that ratio changes in forecasting are due to differences in the dynamics of the diseases	▶ Does not take into account competing risks ▶ Is a single indicator and does not easily take into account changes in asbestos-related and non-asbestos-related lung cancer risk (eg, it does not easily take into account the effect of changes in smoking behaviour)	▶ Requires evidence that may not be (readily) available ▶ Can easily result in input that may be uncertain as assumptions about the input have to be made

*In other contexts, these models may be applied with either more or less detailed information, depending on availability.
PAR, population attributable risk.

digitally. Complete job histories were available for 4568 (91.4%) participants in the subcohort. Job titles were linked to a general Finnish job-exposure matrix (FINJEM) for asbestos exposure. FINJEM is a quantitative-exposure matrix that assigns probabilities and mean levels of asbestos exposure to probably exposed individuals based on International Standard Classification of Occupations (ISCO) 68 coded occupation and time period (see online supplementary material II).[19] Subsequently, the cumulative exposure in fibre years (f-y/mL) was calculated for each participant by multiplying the exposure probability by the mean level of exposure and the duration for each recorded job period, then aggregating the exposure estimates over all job periods.

The age-specific job distribution of the NLCS cohort was taken to be representative of the Dutch population for all workers born during 1916–1931 (ie, aged 55–69 years in 1986) and all those born subsequently, regardless of the calendar time they worked. Asbestos exposure was assigned to these jobs if held prior to 1990.

Finally, the proportions of probably exposed participants, estimated from the NLCS cohort by age and gender, were multiplied by the corresponding age-specific and gender-specific Dutch population in 1990. Results were extrapolated to the year 2010 and cumulative exposures were then averaged by age and gender.

To estimate the asbestos-related lung cancer risk, we estimated age-specific lung cancer rates for men and women in the general population. These rates were assessed by Poisson regression using the number of observed lung cancer deaths in 2001–2010.[12] The asbestos-related lung cancer risk was determined by multiplying lung cancer rates by the RR associated with asbestos exposure. This RR was determined as $RR=1+K_L \times$cumulative exposure, where $K_L(\times 100)=15.5$. We used this K_L value as it was estimated from a population-based cohort of individuals using FINJEM exposure estimates.[20 21] To estimate the future number of asbestos-related lung cancers, a standard life table analysis of lung cancer was conducted.[22]

RESULTS

The specifications of the three applied models, in terms of incorporated evidence, complexity, underlying assumptions, advantages and disadvantages in the context of making future projections, are summarised in table 1. This table allows an informal comparison of the models and may be used to check the incorporated evidence, and thereby feasibility, of each of the models for application in other settings and countries.

Model 1: mesothelioma model

Figure 1 shows the number of future asbestos-related lung cancers as estimated by the mesothelioma model. The left panel shows the expected absolute number of asbestos-related lung cancers per year. The right panel shows the corresponding cumulative number of cases per year. On the basis of the smoking-adjusted ratio of 1:1.5, the number of lung cancers between 2011 and 2030 was estimated to be around 17 500. The sensitivity analyses in which the birth cohort of 1970 was assigned the risk of the birth cohort of 1965 yielded similar results (data not shown). Figure 1 indicates that the annual

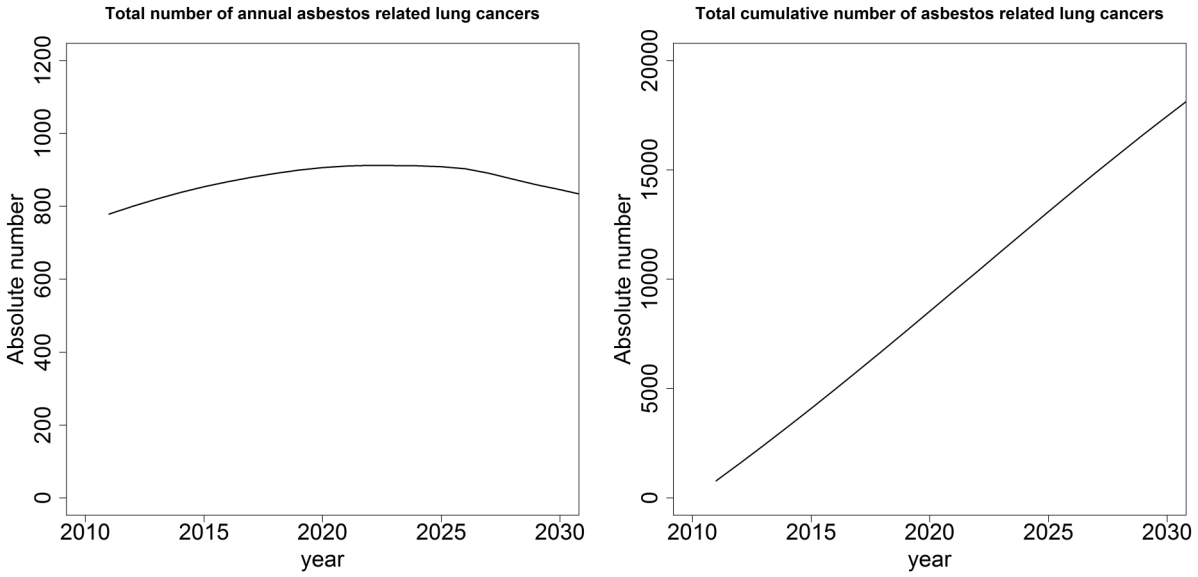

Figure 1 Total number of asbestos-related lung cancer cases in 2011–2030 as estimated by the mesothelioma model, that is, based on the estimated number of mesothelioma cases between 2011 and 2030.

number of asbestos-related lung cancers is expected to increase up to year 2022 and to decrease thereafter.

Model 2: PAR model

Figure 2 has a layout similar to figure 1, and shows the number of future asbestos-related lung cancers as estimated by the PAR model. In this figure, the annual number of asbestos-related lung cancers decreased consistently over time, from 826 in 2011 to 371 in 2030. The cumulative number of asbestos-related lung cancers between 2011 and 2030 was estimated to be around 12 150.

Model 3: life table model

On the basis of available exposure information, it was estimated that in 2010 about 25% of all men aged 50 years or older, and <1% of all women aged 50 years or older, might have been exposed to asbestos. Among these probably exposed individuals, the average cumulative exposure ranged from 0.1 to 3.6 f-y/mL in men and from 0.1 to 0.9 f-y/mL in women (table 2).

Figure 3 has a layout similar to figures 1 and 2, and shows the number of future asbestos-related lung cancers as estimated by the life table model. Here, the annual number of asbestos-related lung cancers decreased consistently over time, from 459 in 2011 to 207 in 2030. Finally, the total number of lung cancers due to asbestos exposure between 2011 and 2030 was estimated to be about 6800.

DISCUSSION

In this study, we compared different modelling methods to estimate the number of future asbestos-related lung cancers. Instead of applying just a single model, our analysis provides insight into the uncertainty associated with model choice and specification. The first model was relatively simple and estimated asbestos-related lung cancer cases directly from observed and

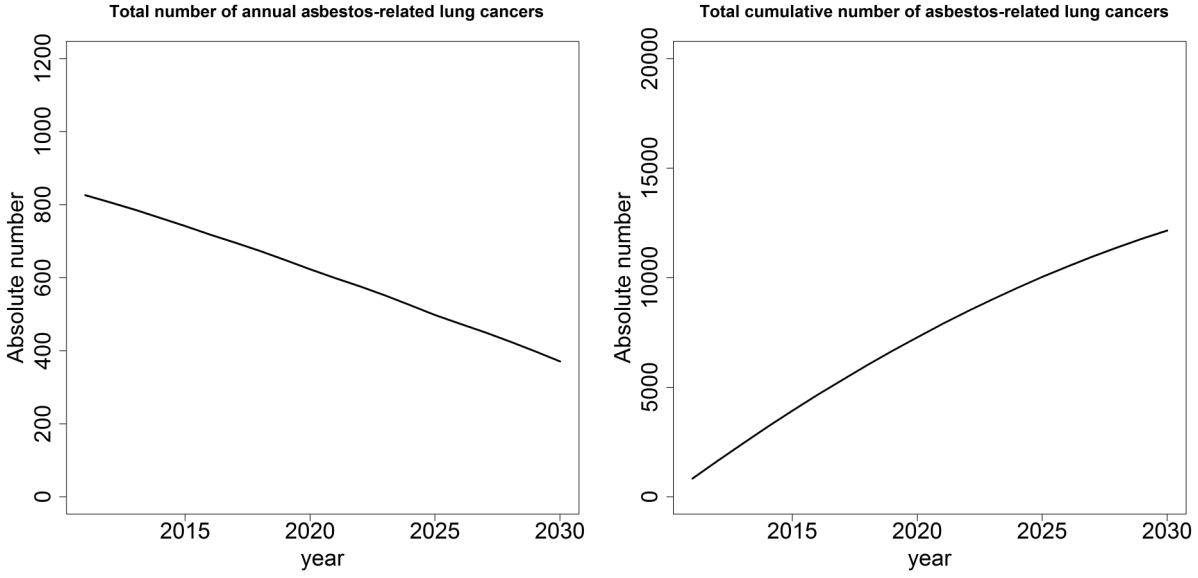

Figure 2 Total number of asbestos-related lung cancer cases in 2011–2030 as estimated by the population attributable risk (PAR) model.

Table 2 Estimated population with probable exposure and cumulative exposures among probably exposed persons in 2010*

	Proportion of population with probable exposure (%)	Average cumulative asbestos exposure level among probably exposed persons (f-y/mL)
Men aged, years		
<20	0	–
20–40	3.8	0.0
40–49	14.6	0.1
50–59	21.9	0.6
60–69	25.6	1.4
70–79	26.9	2.3
80–89	26.3	3.1
90–94	21.4	3.6
Women aged, years		
<20	0	–
20–40	0.2	0.0
40–49	0.4	0.1
50–59	0.8	0.4
60–69	0.9	0.7
70–79	1.0	0.6
80–89	0.8	0.6
90–94	0.2	0.9

*The cumulative exposure in fibre years (f-y/mL) was calculated for each participant by multiplying the exposure probability by the mean level of exposure and the duration for each recorded job period. These levels are on average quite low due to our choice of asbestos assessment in which the level of exposure reflects the level of exposure among all persons with probable exposure (as opposed to the level of exposure among only those persons who were actually exposed). For further information, see online supplementary material II.

predicted mesothelioma cases in an APC analysis. The second model incorporated evidence on the fraction of lung cancer cases attributable to asbestos exposure. The third model in our study was the most comprehensive, incorporating exposure information and exposure response functions for mesothelioma and lung cancer, in a life table analysis on all individuals in the Dutch population. In our setting, the third model was the most comprehensive one. However, for each model approach, the complexity may vary from very simple to highly complex, depending on the evidence available in a particular setting.

Given the results of the three models applied, the expected number of asbestos-related lung cancer cases in the Netherlands in the period 2011–2030 varies from 6800 to 17 500. The highest number of cases was estimated when the number of asbestos-related lung cancers was related to the number of mesothelioma cases (model 1), whereas the lowest number of cases was estimated by the life table method (model 3). In all three models, we assumed that persons born after 1970 were at negligible risk of asbestos-related lung cancer. There is very little information on asbestos exposure after 1990, but in very rare cases exposure could have occurred during demolition or maintenance. Hence, the actual number of future cases may be marginally higher than we predict for all three models.

It is not straightforward to determine which model is likely to provide the best estimation of the future number of asbestos-related lung cancers. Each model has its own advantages, yet all three are based on assumptions and suffer from uncertainty in input values, which substantially decreases the robustness of their results (table 1). We can, however, identify the main uncertainties for each of the three models (see online supplementary material III).

The main uncertainties in model 1 relate to the choices in the APC analysis, most notably the necessary constraints imposed for identifiability of the model, expectations about future developments of birth cohort risks and the ratio between mesothelioma and asbestos-related lung cancer. In our analysis, we linearly projected estimated age-specific rates per birth cohort on the expected future demographic distributions. Other types of analysis have suggested that the peak of mesothelioma might be earlier with a more rapid decline thereafter.[23 24] In these other analyses, current mortality is related to past asbestos exposure and the age distribution of mortality is allowed to vary for the different birth cohorts.[23 24] We chose to use the same method as a previous Dutch study performed 12 years ago,[25] as their derived predictions appear to closely match actual observations over the period 2000–2011. Compared with that previous study, our future annual number of mesothelioma cases was about 20% higher. However, these previous predictions comprised only pleural mesothelioma cases in individuals up to age

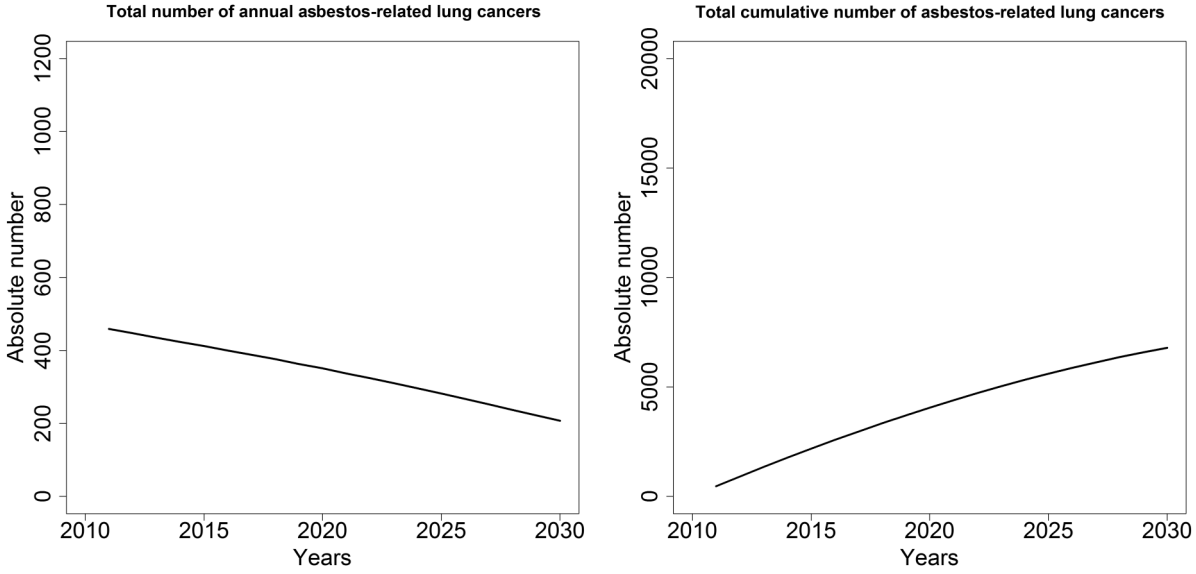

Figure 3 Total number of asbestos-related lung cancer cases in 2011–2030 as estimated by the life table model.

85 years, which may have resulted in lower estimates. If we assume that our predictions might be overestimated by at most 20%, our expected number of asbestos-related lung cancers would be lowered by about 5000. The assumption that birth cohorts beyond 1965 had zero risk appeared to be reasonable as the estimated risk for the male birth cohort of 1965 was indeed very low (we estimated for the birth cohort of 1960 a 65% lower risk compared with the birth cohort of 1940). Therefore, our sensitivity analysis in which the birth cohort of 1970 was assigned the risk of the birth cohort of 1965 yielded results very similar to our base analysis. Another source of uncertainty could be the number of recorded mesothelioma cases, given the inadequate coding scheme for mesothelioma prior to ICD-10.[26] However, the Dutch mesothelioma deaths registry is believed to be quite complete.[15 25] The greatest uncertainty in model 1 is likely to be in the ratio between mesothelioma and lung cancer, which depends strongly on asbestos fibre type.[10] Different types of asbestos have been used in the past in the Netherlands. For example, asbestos sprays contained amosite, whereas asbestos cement products typically contained chrysotile but may have also contained crocidolite (J Tempelman, Dutch asbestos expert, personal communication 2011). Therefore, it is hard to define a single ratio that can be applied universally to the general Dutch population. Using the smoking-adjusted ratio estimated for chrysotile (1:3) or amosite (1: 4.9) instead of mixed fibres would have more than doubled the estimated number of asbestos-related lung cancers.[10] If the smoking-adjusted ratio for crocidolite (1:0.6) had been applied, estimates would have decreased by >50%. Moreover, the authors of the meta-analysis from which we extracted the smoking-adjusted ratios stated that these ratios are likely to be underestimates. This is due to the fact that they applied a potentially exaggerated correction to reduce ratio estimates from studies if smoking had not been taken into account.[10] If we used the unadjusted ratio for mixed fibres (1:1.9), which is assumed to be an overestimate, we would have estimated 22 100 cases. One could also argue that a ratio of 1:1 might be more appropriate. This ratio has been observed and used for estimations in the UK.[2 27 28] Since the numbers of mesotheliomas are comparable between the Netherlands and the UK, it has been suggested that these countries are also comparable regarding asbestos exposure. Moreover, in the published meta-analysis about the cancer ratios, there was a large amount of unexplained variability between studies even after stratification on fibre type; the IQR of the ratio for studies with mixed asbestos fibres was 1.1–4.4.[10] Discrepancies in the ratios might be explained by the fact that mesothelioma has another asbestos exposure–response relationship than lung cancer. When comparing the exposure–response relationships, the ratio is likely to be affected by follow-up time, (mean) age at time of exposure and exposure intensity.[10] Other reasons for the discrepancies may be found in potential confounding, different background of lung cancer rates and smoking levels and misclassification of mesothelioma cases.[10 29] The majority of the studies included in the meta-analyses comprised cohorts of highly exposed individuals from which the ratio between mesothelioma and lung cancer was estimated. However, asbestos exposures at the population level are likely to be lower. Hence, it might be inappropriate to apply the mean meta-analysed ratio to the number of mesothelioma cases as observed in the general population. Moreover, since latency time is shorter for lung cancer than for mesothelioma[30] (ie, current lung cancer cases are associated with later exposure periods than current mesothelioma cases), one may expect the ratio between mesothelioma and lung cancer to decrease over time. In addition, declining smoking trends may reduce the ratio over time, as asbestos has a stronger effect on lung cancer in smokers than in non-smokers, whereas smoking has little or no effect on mesothelioma.[31] These large uncertainties in the ratio present significant challenges in estimating the number of asbestos-related lung cancer from mesothelioma diagnoses. If we assume the true ratio is between 1:0.6 and 1:4.9, then our estimates of the total number of asbestos-related lung cancer in the period between 2011 and 2030 would vary from around 7000 to 57 000 cases in the mesothelioma model.

The main uncertainty in model 2 relates to the applied PAR. We used a PAR of 11.6% estimated from a Dutch case–cohort study.[7] Although this estimate appears to be reasonable compared with other studies, higher and lower PARs have also been reported.[5 6 32 33] A systematic review of asbestos-related cancer in Europe estimated the PAR to be between 5.7% and 19%.[32] A very recent study estimated a PAR of 18% among men in Lombardy.[34] In the UK, a PAR of 8.9% among men was estimated, which was based on an applied ratio of 1 asbestos-related lung cancer per mesothelioma case.[27] These differences in estimates of the PAR are likely to be related to the methods applied, as well as the actual amount of asbestos use in the past. Moreover, we assumed that the estimated PAR in 1986–1990 for men aged 55–73 years was also applicable to all men above the age of 40 years in 2010. However, this assumption may be questionable as asbestos exposures are likely to have been lower for younger men, resulting in a lower PAR. Another source of uncertainty is related to the applied lung cancer rates. We assumed observed age-specific lung cancer rates for 2008–2010 to be representative for the years 2010–2030. However, lung cancer rates in future years may be 10–15% lower due to declining smoking rates.[35] Owing to the large uncertainties in the PAR estimates, results from model 2 are also uncertain. If we assume that the overall PAR could range from 5.7% to 19%, then our estimates of the total number of asbestos-related lung cancer in the period 2011–2030 would vary from around 6700 to 19 000 cases in the PAR model.

The main uncertainties in model 3 relate to the exposure–response relationship between asbestos and lung cancer risk, the expected lung cancer rates, the estimated number of asbestos-exposed individuals and their estimated cumulative exposure levels. In a recent meta-regression analysis, a $K_L(\times 100)$ value of 0.33–0.75 was estimated.[20 21 36] This summary K_L value was primarily based on highly exposed industrial populations and as such may not be directly applicable to the general population. We therefore used a $K_L(\times 100)$ value of 15.5, which was observed in a population-based study that applied FINJEM for the primary exposure estimates.[21] Given the similarities in our study populations, we assumed this K_L value to be the most appropriate. Still, using a very high K_L value, the results of model 3 were much lower than the numbers predicted by model 1 and model 2. Therefore, the results of model 3 imply that the other two methods tend to overestimate the burden or that we might have underestimated the exposed population in model 3. Results from the model may be biased due to inaccuracies in occupational history data and estimated cumulative exposure. In a sensitivity analysis, exposure estimates from the NLCS cohort were calibrated using predicted mesothelioma cases. For this, mesothelioma incidence was calculated similar to the US Environmental Protection Agency model with an estimated cumulative exposure potency factor (K_m) of 2.53e-8 for mixed fibre types.[37] However, our calibration procedure indicated that either cumulative exposures or mesothelioma risks needed to be about three times higher in

order to predict the same number of mesothelioma cases as was observed on average in 2006–2010. If we assume that the underestimation is more likely in the cumulative exposure, exposure estimates should be increased by a factor 3. When we repeated the analysis with the calibrated exposure data, the estimate increased to 33 850 asbestos-related lung cancer cases. Further assessment of the extent and direction of potential bias, however, was not possible with available data. Assuming asbestos exposure ranges from lower estimates that we calculated originally to higher levels that we observed after the calibration, the total number of asbestos-related lung cancer cases in the period 2011–2030 would vary from around 6800 to 33 850 in the life table analysis.

Having raised these concerns, the question remains as to which model is most suitable for predicting the number of asbestos-related lung cancers. Overall, our comparisons indicate that none of the investigated models is a clear winner based on all modelling aspects. Although the lifetime approach might be intuitively preferable, high-quality exposure data are required and the approach depends crucially on the adopted exposure-response model, which is associated with considerable uncertainty. The other two models offer pragmatic alternatives but have their own limitations.[38 40] While the starting point for the mesothelioma model approach (ie, the mesothelioma projections) might be quite solid in many situations, particular attention needs to be paid to the various factors that may affect how the ratio might change over time when making future predictions. The PAR approach can be used if one wants to estimate the number of cases in a specific year due to exposures over a number of years in the past.[38] However, the PAR approach is potentially problematic, given that the validity of extrapolating past PARs to the future is questionable. In addition, sex-specific and age-specific PARs will most likely outperform generic sex-specific PARs.[39] Hence, the model to prefer is highly guided by the available data and context.

In conclusion, the preferred method for estimating the number of asbestos-related lung cancer cases in the general population necessarily depends on the available evidence and context. In addition, the robustness of results from any method depends highly on the quality of evidence used as input. Therefore, a more comprehensive method is not necessarily better than a simple one. Results obtained by any one specific method should always be interpreted with caution unless both data collection and analysis are of undeniably high quality. In the Netherlands, the available information on asbestos exposure and lung cancer is extensive in comparison to other exposures. Given the different assumptions and uncertainties present in all three methods considered, there is considerable value in applying different methods and comparing their results. Only then is insight gained into the robustness of the estimated number of cases. We show that using three different methods results in different absolute estimates of the asbestos-related lung cancers varying by a factor of 2.5.

Acknowledgements The authors would like to thank Dr P van de Brandt for use of NLCS data. They would also like to thank N Offermans and Dr T Kauppinen for the use of FINJEM.

Funding Institute for Asbestos Victims, the Netherlands.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Straif K, Benbrahim-Tallaa L, Baan R, *et al*. A review of human carcinogens—part C: metals, arsenic, dusts, and fibres. *Lancet Oncol* 2009;10:453–4.
2 Darnton AJ, McElvenny DM, Hodgson JT. Estimating the number of asbestos-related lung cancer deaths in Great Britain from 1980 to 2000. *Ann Occup Hyg* 2006;50:29–38.
3 Nicholson WJ, Perkel G, Selikoff IJ. Occupational exposure to asbestos: population at risk and projected mortality—1980–2030. *Am J Ind Med* 1982;3:259–311.
4 Gasparrini A, Pizzo AM, Gorini G, *et al*. Prediction of mesothelioma and lung cancer in a cohort of asbestos exposed workers. *Eur J Epidemiol* 2008;23:541–6.
5 Boffetta P, Autier P, Boniol M, *et al*. An estimate of cancers attributable to occupational exposures in France. *J Occup Environ Med* 2010;52:399–406.
6 Gustavsson P, Ahlbom A, Andersson T, *et al*. Calculation of fractions of lung cancer incidence attributable to occupational exposure to asbestos and combustion products in Stockholm, Sweden. *Eur J Epidemiol* 2002;18:937–40.
7 van Loon AJ, Kant IJ, Swaen GM, *et al*. Occupational exposure to carcinogens and risk of lung cancer: results from the Netherlands cohort study. *Occup Environ Med* 1997;54:817–24.
8 Lilienfeld DE, Mandel JS, Coin P, *et al*. Projection of asbestos related diseases in the United States, 1985–2009. I. Cancer. *Br J Ind Med* 1988;45:283–91.
9 Marinaccio A, Scarselli A, Binazzi A, *et al*. Magnitude of asbestos-related lung cancer mortality in Italy. *Br J Cancer* 2008;99:173–5.
10 McCormack V, Peto J, Byrnes G, *et al*. Estimating the asbestos-related lung cancer burden from mesothelioma mortality. *Br J Cancer* 2012;106:575–84.
11 Carstensen B. Age-period-cohort models for the Lexis diagram. *Stat Med* 2007;26:3018–45.
12 CBS Statline (database). Voorburg: Centraal Bureau voor de Statistiek (Statistics Netherlands). 2012. [electronic resource: http://statline.cbs.nl].
13 van der Bij S, Koffijberg H, Burgers JA, *et al*. Prognosis and prognostic factors of patients with mesothelioma: a population-based study. *Br J Cancer* 2012;107:161–4.
14 Nesti M, Marinaccio A, Gennaro V, *et al*. Epidemiologic surveillance for primary prevention of malignant mesothelioma: the Italian experience. *Med Lav* 2005;96:338–46.
15 Damhuis RAM. *Lung cancer and mesothelioma in the Netherlands 1989–1997*. Utrecht: Association of Comprehensive Cancer Centers, 2000.
16 Burdorf L, Swuste PH, Heederik D. A history of awareness of asbestos disease and the control of occupational asbestos exposures in the Netherlands. *Am J Ind Med* 1991;20:547–55.
17 Virta RL. *Mineral commodity profiles-Asbestos*. Virginia: U.S. Geological Survey, 2005:56.
18 van den Brandt PA, Goldbohm RA, van 't Veer V, *et al*. A large-scale prospective cohort study on diet and cancer in the Netherlands. *J Clin Epidemiol* 1990;43:285–95.
19 Kauppinen T, Uuksulainen S, Saalo A, *et al*. Use of the Finnish Information System on Occupational Exposure (FINJEM) in epidemiologic, surveillance, and other applications. *Ann Occup Hyg* 2014;58:380–96.
20 Lenters V, Vermeulen R, Dogger S, *et al*. A meta-analysis of asbestos and lung cancer: is better quality exposure assessment associated with steeper slopes of the exposure-response relationships? *Environ Health Perspect* 2011;119:1547–55.
21 Gustavsson P, Nyberg F, Pershagen G, *et al*. Low-dose exposure to asbestos and lung cancer: dose-response relations and interaction with smoking in a population-based case-referent study in Stockholm, Sweden. *Am J Epidemiol* 2002;155:1016–22.
22 Cox D, Oakes D. *Analysis of survival data*. London: Chapman and Hall, 1984.
23 Hodgson JT, McElvenny DM, Darnton AJ, *et al*. The expected burden of mesothelioma mortality in Great Britain from 2002 to 2050. *Br J Cancer* 2005;92:587–93.
24 Tan E, Warren N, Darnton AJ, *et al*. Projection of mesothelioma mortality in Britain using Bayesian methods. *Br J Cancer* 2010;103:430–6.
25 Segura O, Burdorf A, Looman C. Update of predictions of mortality from pleural mesothelioma in the Netherlands. *Occup Environ Med* 2003;60:50–5.
26 Delgermaa V, Takahashi K, Park EK, *et al*. Global mesothelioma deaths reported to the World Health Organization between 1994 and 2008. *Bull World Health Organ* 2011;89:716–24.
27 Brown T, Darnton A, Fortunato L, *et al*. Occupational cancer in Britain. Respiratory cancer sites: larynx, lung and mesothelioma. *Br J Cancer* 2012;107(Suppl 1):S56–70.
28 Rushton L, Hutchings S, Brown T. The burden of cancer at work: estimation as the first step to prevention. *Occup Environ Med* 2008;65:789–800.
29 Lemen RA, Frank AL, Soskolne CL, *et al*. Comment on 'estimating the asbestos-related lung cancer burden from mesothelioma mortality'—IARC and chrysotile risks. *Br J Cancer* 2013;109:823–5.
30 Selikoff IJ, Hammond EC, Seidman H. Latency of asbestos disease among insulation workers in the United States and Canada. *Cancer* 1980;46:2736–40.
31 Henderson DW, Rödelsperger K, Woitowitz HJ, *et al*. After Helsinki: a multidisciplinary review of the relationship between asbestos exposure and lung

cancer, with emphasis on studies published during 1997–2004. *Pathology* 2004;36:517–50.
32 Albin M, Magnani C, Krstev S, *et al*. Asbestos and cancer: an overview of current trends in Europe. *Environ Health Perspect* 1999;107(Suppl 2):289–98.
33 Li P, Deng SS, Wang JB, *et al*. Occupational and environmental cancer incidence and mortality in China. *Occup Med (Lond)* 2012;62:281–7.
34 De Matteis S, Consonni D, Lubin JH, *et al*. Impact of occupational carcinogens on lung cancer risk in a general population. *Int J Epidemiol* 2012;41:711–21.
35 Cancer research UK. Lung cancer incidence projections to 2024: future rates and numbers of new cases in Great Britain and the UK. 2009: http://publications.cancerresearchuk.org/downloads/product/CSCPLC.pdf
36 van der Bij S, Koffijberg H, Lenters V, *et al*. Lung cancer risk at low cumulative asbestos exposure: meta-regression of the exposure-response relationship. *Cancer Causes Control* 2013;24:1–12.
37 Health council of the Netherlands. *Asbest. Risico's van milieu- en beroepsmatige blootstelling*. Voorburg: Health council of the Netherlands, 2010.
38 Fritschi L, Carey R, Peters S, *et al*. The lifetime risk approach to estimating the burden of occupational cancer. *Occup Environ Med* 2014;71(Suppl 1):A44.
39 Hutchings S, Rushton L, Driscoll T. Estimating the burden of occupational cancer taking into account age. *Occup Environ Med* 2014;71(Suppl 1):A34.
40 Driscoll T, Hutchings S, Rushton L. Holes in the burden estimates—some can be filled, some maybe not. *Occup Environ Med* 2014;71(Suppl 1):A33.

Expected number of asbestos-related lung cancers in the Netherlands in the next two decades: a comparison of methods

Sjoukje Van der Bij, Roel C H Vermeulen, Lützen Portengen, Karel G M Moons and Hendrik Koffijberg

Occup Environ Med 2016 73: 342-349 originally published online February 8, 2016
doi: 10.1136/oemed-2014-102614