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QUANTITATIVE ASSESSMENT OF LUNG CANCER RISK IN MEN EMPLOYED IN THE PULP AND PAPER INDUSTRY IN POLAND

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Abstract.
Objectives: Numerous epidemiological studies have provided some evidence indicating that workers employed in the pulp and paper industry are at higher risk of death from lung cancer. The present study was undertaken to analyze lung cancer risk prediction among male workers employed in this industry. **Materials and Methods:** To estimate the probability of death from lung cancer a risk prediction model with some elements of competing risks was used. The risk assessment was based on the cohort study data collected in workers involved in pulp and paper production. **Results:** Four exposure-response relationship curves were developed adopting the age at the first occupational exposure as a criterion. The model based on the competing risk theory rendered it possible to estimate an additional risk of lung cancer related to a specific period of occupational exposure for the groups adjusted by the age of entering the cohort. For example, in the group with first exposure at the age below 29, the risk changed from $2.25 \bullet 10^{-7}$ during the first year of employment to $1.40 \bullet 10^{-5}$ after 10 years, whereas in the group of workers with first exposure at the age of 50 years, the risk changed from $6.42 \bullet 10^{-5}$ to $4.28 \bullet 10^{-4}$. In addition, the risk at first exposure at the age of 50–59 was almost two orders of magnitude higher than that in workers with first exposure at the age below 29 ($6.42 \bullet 10^{-5}$ and $2.25 \bullet 10^{-7}$, respectively). **Conclusions:** Using the additional (absolute) risk model involving elements of competing risk theory it is possible to provide a more thorough characteristics of the relationship between the exposure level and probability of death from lung cancer.

Key words:
Lung cancer, Quantitative risk assessment, Competing risk, Pulp and paper industry, Cohort study

INTRODUCTION

At present, lung cancer is the most common malignant disease. In the 1990s, the annual male mortality in Poland accounted for more than 15 000 deaths, one third of total deaths from the malignancy [1]. A certain proportion of those neoplasms was induced by occupational exposure to carcinogenic chemicals. It is assumed that occupational factors may be even responsible for 40% of the lung cancer incidence [2,3]. The Polish estimates made by Jędrychowski et al. [4] suggest that over 20% of all male, and 8% of all female deaths from lung cancer may be attributed to occupational exposure.

Pulp and paper production, involving the use of numerous chemicals, including carcinogenic ones, has not as yet been classified as a process possibly carcinogenic to humans. However, epidemiological studies have already provided some evidence indicating that workers employed in this industry are at a higher risk of death from the malignancy, including lung cancer [5]. In 1993, the Interna-

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tional Agency for Research on Cancer (IARC) assumed the responsibility to coordinate international, multicentre cohort studies of pulp and paper industry workers. In Poland, workers engaged in the production of sulfate mass, as well as paper and paperboard were covered by these studies. In production plants, the presence of over 30 different substances in the ambient air of the work environment was documented. In this number, hard wood dust, crystalline silica-containing dust and welding fumes are classified as lung carcinogens. Owing to these studies it was possible to observe an enhanced risk of death from lung cancer among male workers employed in this industry [6,7].

In the quantitative risk assessment, based on epidemiological data, a number of models are used to develop a dose-response function, starting with the simplest ones, describing linear relationship between the exposure magnitude and standardized mortality ratio (SMR) values, through more complex statistical models (Poisson and Cox models), biologic models, eg., multistage or two-stage models in particular, and completing with still more sophisticated risk prediction models, developed using some elements of competing risk theory.

The present study was undertaken to analyze lung cancer risk prediction among male workers employed in the paper and pulp mills, using a risk prediction model with some elements of competing risks.

MATERIALS AND METHODS

The risk assessment was based on the data collected during the cohort study follow-up in pulp and paper production workers.

The cohort characteristics

A thorough description of the cohort has been given in an earlier publication [6], hence only brief characteristics is presented here. In all, 8568 male workers, aged 18 years and more, employed in the mill for at least three months between 1967 and 1990 were included in the cohort. The workers were followed-up to December 31, 1995. The earliest of the following dates closed the observation period for each person:

- December 31, 1995 if the worker was still alive;
- the 80th birthday of the worker included in the cohort; and
- the date of death if the person deceased before December 31,1995 or at the age below 80 years.

Persons over 80 years of age were not eligible for the study because of substantial uncertainty as to the given cause of death. For each person included in the cohort, the following data were obtained: the date of birth, employment duration, job description, information whether a given person was alive or deceased, and the exact date together with the cause of death for those deceased. Underlying causes of death were coded according to the 9th Revision of the International Classification of Diseases (ICD-9). For mortality assessment, standardized mortality ratios (SMRs) were used. The general male and female population of Poland was adopted as the reference. The computing of death rates in the referent group was based on the number of deaths in ten-year age groups obtained from the Central Statistical Office. The data on deaths from the malignancy in 1967–1995 were provided by the National Cancer Registry, the Maria Skłodowska-Curie Memorial Cancer Center, Warsaw.

The essential results of the cohort study

The assessment of male mortality from selected malignancies is summarized in Table 1.

Excess mortality (over 20%) from lung cancer, close to statistical significance and a relatively high absolute number of deaths from the disease of interest, have motivated an attempt to look for an appropriate model that could facilitate the risk prediction. A small number of deaths observed for the majority of sites in several small groups of workers with varied magnitude of exposure hinders the estimation of dose-response relationship.

Classification of factors included in the model

Duration of occupational exposure, calendar period and workers' age, which may be considered as indirect exposure indicators, and tumor latency period were recognized

Table 1. Male mortality from selected malignancies in the cohort of pulp and paper workers*. The general male population of Poland was adopted as a reference population [6,7]

Causes of death (ICD-9)	Death**		SMR	95% CI ***
	Observed	Expected		
Malignant neoplasms (140-208)	189	201.5	94	81–108
Malignant neoplasm of				
pharynx (146-148)	4	2.8	141	38–361
retroperitoneum (158)	3	0.6	485	100–1417
respiratory system (160-165)	88	78.9	112	90–138
lung (162)	80	68,1	117	93–146
melanoma of skin (172)	4	2.3	178	48–456
other neoplasm of skin (173)	3	0.8	383	79–1119
prostate (185)	5	4.7	107	35–250
bladder (188)	7	5.3	131	53–270
brain (191)	10	8.0	126	60–232

* The table includes only these cancer sites for which at least three deaths were observed.
** The data presented in this table differ from those given in the publications by Szadkowska-Stańczyk et al. [6,7] because of a slightly different criterion used in selecting the cohort members. In the study carried out by the authors, persons with at least one year of employment were eligible for the cohort, whereas for the purpose of risk assessment at least three months of employment was adopted as a criterion.
*** CI – confidence interval.

Table 2. Standardized mortality ratios for lung cancer in pulp and paper workers by risk factors

Risk factor	Death		SMR	95% CI *
	Observed	Expected		
Duration of employment (years)				
<1 in production or administration departments	8	8.82	91	39–179
[1, 5]	24	17.04	141	90–210
(5, 10]	20	11.90	168	103–259
(10, 20]	18	17.41	103	61–163
20>	10	12.93	77	37–142
Latency period (years)				
0–9	11	11.03	100	50–179
10–19	35	28.77	122	85–170
20–29	34	27.60	123	85–172
30–39	0	0.69	0	–
40-49	0	0.00	0	–
Calendar period				
1965–1970	0	0.54	0	–
1971–1980	9	7.91	114	52–216
1981–1990	30	31.18	96	65–137
1991–1995	41	28.47	144	103–195
Age (years)				
< 29	0	0.28	0	–
30–39	3	2.49	120	25–351
40–49	11	14.09	78	39–140
50–59	34	27.04	126	87–176
60–69	19	19.45	98	59–153
70–79	13	4.75	274	146–469

* CI – confidence interval.

as potential factors able to modify the probability of death from lung cancer. As smoking histories of all workers included in the cohort were not available, this variable was not analyzed directly. Nevertheless, in order to eliminate potential for confounding by this factor, an internal reference group, described below, was selected for the risk modeling.

The cohort was stratified, i.e., divided into separable strata corresponding with the categories of the aforementioned factors.

The workers were divided into five groups according to employment duration: group 1 – workers employed under one year in production departments and administration workers never involved in production, regardless of the employment duration; group 2 – those employed in the production departments for 1–5 years; group 3 – employed for 5–10 years; group 4 – employed for 10–20 years; and group 5 – workers employed for more than 20 years.

In addition, five latency periods: 0–9; 10–19; 20–29; 30–39; and 40–49 years, four calendar periods: 1965–1970; 1971–1980; 1981–1990; and 1991–1995, and six age groups: below 29 years; 30–39; 40–49; 50–59; 60–69 and 70–79 years, were distinguished.

Mortality from lung cancer in the study cohort by variables singled out above is characterized in Table 2.

Following the data given in Table 2, two conclusions may be drawn:

1. Mortality rates did not increase significantly along with prolonged latency;

2. A significant increase in mortality rates during the calendar period of 1991–1995 was more likely caused by the cohort aging than by possible changes in exposure parameters, since consecutive calendar periods were rather characterized by improvement than by degradation of working conditions.

Bearing the following in mind, neither latency nor calendar periods were recognized as confounding variables, thus the workers' age was the only confounding variable included in the model, and employment duration was adopted as an exposure variable. The workers' age and duration of employment were made a base of the risk modeling.

Quantitative risk analysis methods

The method involving elements of competing risk (cause) theory was used in estimating additional risk of death from lung cancer. Computing lifetime risks of occupational exposures based on the results of the cohort study was performed according to the following formula [8,9]:

$$R(d) = \sum_{i=20}^{74} [RR_i(d) - 1]\, q_d(i) \bullet \exp\left\{-\sum_{j=20}^{i} [(RR_j(d) - 1) q_d(j) + q_a(j)]\right\} \qquad (1)$$

where:

RR_i is the rate ratio estimate from the model for exposure d achieved at age i;

$q_d(i)$ represents the background age-specific lung cancer rate;

$q_a(i)$ represents the background age-specific mortality for all cases; and

i – age indices.

As exposure in pulp and paper mills is very complex, and practically it is not feasible to determine the proportion of its individual components, duration of employment "d" in the mill was adopted as an indicator of the exposure level.

The term "exposure-response" will be henceforth used to define the relationship between the level of exposure and lung cancer risk.

Estimates of relative risk (RR) were based on the results of the cohort studies and employed the Poisson regression model (for the subgroup data) or the Cox model (for non-grouped data). If the exposure effects can be modified by specific covariate variables, RR values are adjusted in this formula to eliminate in a way the effect of covariance on the risk values.

In the modeling of relative risk associated with occupational exposure in the pulp and paper mill (RR in formula (1)), both the Poisson model and the Cox proportional hazards model were used. The data on which the calculations of relative risk were based are given in Table 3.

In employment duration group 1 was adopted as a reference group (internal reference group), providing that a short period of employment in the production department (under 1 year) should not increase the number of deaths from lung cancer induced by this exposure. Deaths

Table 3. Male mortality from lung cancer in the cohort of pulp and paper workers: data used as a basis for risk modeling

Duration of employment (years)	Duration of exposure (median)	Workers' age (midpoint)	No. of death from lung cancer	Person-years
<1 in production or administration departments	0.55	27	0	19 750
		45	1	5780
		55	3	1861
		65	2	549
		75	2	102
[1, 5] in production departments	2.34	27	1	33 045
		45	2	9366
		55	13	3521
		65	3	1285
		75	5	292
(5, 10] in production departments	7.13	27	1	16 324
		45	3	4620
		55	6	2429
		65	8	1145
		75	2	314
(10, 20] in production departments	14.63	27	1	22 074
		45	3	6739
		55	7	3782
		65	4	1670
		75	3	312
>20 in production departments	24.10	27	0	17 357
		45	2	8951
		55	5	3313
		65	2	594
		75	1	17

observed in this group should be considered as a background hazard. Adopting such a group as a reference level in estimating RR values, to some degree eliminated confounding which resulted from the lack of smoking histories of the mill workers. Since the reference group also consisted of workers of the same department, there was no ground for assuming that the distribution of smokers in this group differed from that in other groups.

The Poisson and Cox models were adjusted, taking account of only first three groups of exposure duration, for risk enhanced along with increased period of exposure only in the employment below 10 years. The decreased lung cancer risk, expressed by SMRs observed in groups of workers employed in the production department for more than 10 years, may be related to somewhat positive selection of workers (individuals not healthy enough to

Table 4. Standardized mortality ratios for lung cancer, ischemic heart disease and cerebrovascular disease in the cohort of pulp and paper workers by duration of exposure

Duration of employment (years)	Lung cancer			Ischaemic heart disease			Cerebrovascular diseases		
	Death		SMR	Death		SMR	Death		SMR
	Observed	Exposed		Observed	Exposed		Observed	Exposed	
<1 in production or administration departments	8	8.82	91	8	20.00	40	9	6.25	144
[1, 5]	24	17.04	141	41	36.88	111	15	12.00	125
(5, 10]	20	11.90	168	28	23.80	118	7	8.29	84
(10, 20]	18	17.41	103	52	34.60	150	15	11.59	129
> 20	10	12.93	77	18	27.94	64	2	8.08	25

work dropped out earlier) or with the occurrence of other causes of death, competing with lung cancer. The positive selection of workers so called "health worker effect" is observed in the group of workers employed for more than 20 years; in this group, SMR values for all causes of death are below 100. The presence of possible competing causes of death in groups of workers employed for over 10 years is illustrated in Table 4.

As depicted in this table, the high rates of mortality from ischemic heart disease and cerebrovascular diseases were observed.

RESULTS

The results of the Poisson and Cox models adjustment to the data given in Table 3 are summarized in Table 5.

The coefficient present at the employment duration variable in the Poisson model was adjusted by the workers' age. In the Cox model, the age of workers is automatically included in calculations, and thus the coefficient is already adjusted.

Using the estimated coefficients of the Poisson and Cox regression models (Table 5) the relative risk of death from lung cancer, depending on exposure duration, was computed. The results are shown in Table 6.

Beside RR values, the rates of death from relevant causes in the general population of Poland were indispensable to estimate the additional risk of death from lung cancer associated with the employment in the pulp and paper mill (Formula (1)). For further calculations, the averaged rates for the years 1961–1995 were used (Table 7).

The data summarized in Tables 6 and 7 were the basis for estimating additional risk of death from lung cancer in male workers, dependent on employment duration in the production departments of the pulp and paper mill.

Table 6. The relative risk of lung cancer based on male mortality in pulp and paper workers, depending on the duration of occupational exposure, obtained from the Poisson and Cox models

Duration of occupational exposure (years)	Relative risk values	
	Poisson model	Cox model
Internal reference group	1.000	1.000
1	1.045	1.076
2	1.092	1.157
3	1.141	1.244
4	1.192	1.338
5	1.246	1.440
6	1.302	1.548
7	1.361	1.666
8	1.422	1.791
9	1.486	1.927
10	1.553	2.073

Table 7. The mean rates of mortality from lung cancer and all causes of male deaths in Poland, 1961–1995

Age group (years)	Mean rates of mortality per 100 000 men	
	All causes	Lung cancer
>29	176	0.5
30–39	287	4
40–49	624	34
50–59	1465	145
60–69	3275	300
70–79	7439	375

The rates of mortality from lung cancer in the cohort did not increase with the employment duration over 10 years, whereas mortality rates for Poland increase with age. Therefore, four exposure-response relationship curves were developed with the age at the first occupational exposure as a criterion. Additional risk of lung cancer related to a specific period of occupational exposure for the groups adjusted by the age of entering the cohort in both models is presented in Table 8.

Table 5. The results of the Poisson and Cox models adjustment to the data on male mortality from lung cancer in pulp and paper workers

Model	Model variable	Regression coefficient	Standard error of coefficient	Z-statistic	Probability	95 %Cl	
Poisson	Duration of employment	0.0440	0.0523	0.842	0.4000	-0.058	0.146
	Age	0.1182	0.0104	11.329	0.0005	0.098	0.139
	Constant	-13.137	0.6275	-20.935	0.0005	-14.37	-11.91
Cox	Duration of employment	1.0756	0.0504	1.556	0.120	0.981	1.179

Table 8. Additional risk of death from lung cancer induced by occupational exposure based on the Poisson and Cox models data together with background risk, depending on the age at the cohort entrance. The workers employed below one year in the production or administration departments served as a background

Period of occupational exposure (years)	Age at first exposure (years)			
	>29	30–39	40–49	50–59
Poisson model				
1	$2.25 \bullet 10^{-7}$	$1.84 \bullet 10^{-6}$	$1.53 \bullet 10^{-5}$	$6.42 \bullet 10^{-5}$
2	$6.83 \bullet 10^{-7}$	$5.59 \bullet 10^{-6}$	$1.84 \bullet 10^{-5}$	$7.71 \bullet 10^{-5}$
3	$1.38 \bullet 10^{-6}$	$1.13 \bullet 10^{-5}$	$2.32 \bullet 10^{-5}$	$9.67 \bullet 10^{-5}$
4	$2.34 \bullet 10^{-6}$	$1.91 \bullet 10^{-5}$	$2.96 \bullet 10^{-5}$	$1.23 \bullet 10^{-4}$
5	$3.56 \bullet 10^{-6}$	$2.91 \bullet 10^{-5}$	$3.78 \bullet 10^{-5}$	$1.56 \bullet 10^{-4}$
6	$5.05 \bullet 10^{-6}$	$4.12 \bullet 10^{-5}$	$4.78 \bullet 10^{-5}$	$1.96 \bullet 10^{-4}$
7	$6.84 \bullet 10^{-6}$	$5.57 \bullet 10^{-5}$	$5.96 \bullet 10^{-5}$	$2.43 \bullet 10^{-4}$
8	$8.92 \bullet 10^{-6}$	$7.26 \bullet 10^{-5}$	$7.34 \bullet 10^{-5}$	$2.97 \bullet 10^{-4}$
9	$1.13 \bullet 10^{-5}$	$9.21 \bullet 10^{-5}$	$8.91 \bullet 10^{-5}$	$3.59 \bullet 10^{-4}$
10	$1.40 \bullet 10^{-5}$	$1.14 \bullet 10^{-4}$	$1.07 \bullet 10^{-4}$	$4.28 \bullet 10^{-4}$
Increase in lung cancer risk after 10 years of the employment	0.000011	0.000112	0.000092	0.000364
Multiplicity of the initial risk after 10 years of the employment	62.2	62.0	7.0	6.7
Cox model				
1	$3.77 \bullet 10^{-7}$	$3.09 \bullet 10^{-6}$	$2.58 \bullet 10^{-5}$	$1.08 \bullet 10^{-4}$
2	$1.16 \bullet 10^{-6}$	$9.49 \bullet 10^{-6}$	$3.11 \bullet 10^{-5}$	$1.30 \bullet 10^{-4}$
3	$2.37 \bullet 10^{-6}$	$1.94 \bullet 10^{-5}$	$3.93 \bullet 10^{-5}$	$1.64 \bullet 10^{-4}$
4	$4.06 \bullet 10^{-6}$	$3.31 \bullet 10^{-5}$	$5.06 \bullet 10^{-5}$	$2.10 \bullet 10^{-4}$
5	$6.23 \bullet 10^{-6}$	$5.09 \bullet 10^{-5}$	$6.52 \bullet 10^{-5}$	$2.69 \bullet 10^{-4}$
6	$8.95 \bullet 10^{-6}$	$7.30 \bullet 10^{-5}$	$8.33 \bullet 10^{-5}$	$3.42 \bullet 10^{-4}$
7	$1.22 \bullet 10^{-5}$	$9.98 \bullet 10^{-5}$	$1.05 \bullet 10^{-4}$	$4.28 \bullet 10^{-4}$
8	$1.61 \bullet 10^{-5}$	$1.31 \bullet 10^{-4}$	$1.31 \bullet 10^{-4}$	$5.30 \bullet 10^{-4}$
9	$2.07 \bullet 10^{-5}$	$1.68 \bullet 10^{-4}$	$1.61 \bullet 10^{-4}$	$6.47 \bullet 10^{-4}$
10	$2.60 \bullet 10^{-5}$	$2.11 \bullet 10^{-4}$	$1.95 \bullet 10^{-4}$	$7.80 \bullet 10^{-4}$
Increase in lung cancer risk after 10 years of the employment	0.000026	0.000180	0.000169	0.000672
Multiplicity of the initial risk after 10 years of the employment	69.0	68.3	7.6	7.2

In the group of workers who had started their employment in the pulp and paper mill at the age of 29 years and 30–39 years, an increase in lung cancer risk of about two orders of magnitude during one decade of employment was observed, whereas in the 40–49 and 50–59 age groups the increase fell below one order of magnitude. However, the whole range of risk variability during a 10-year period of employment in the youngest group of workers was by

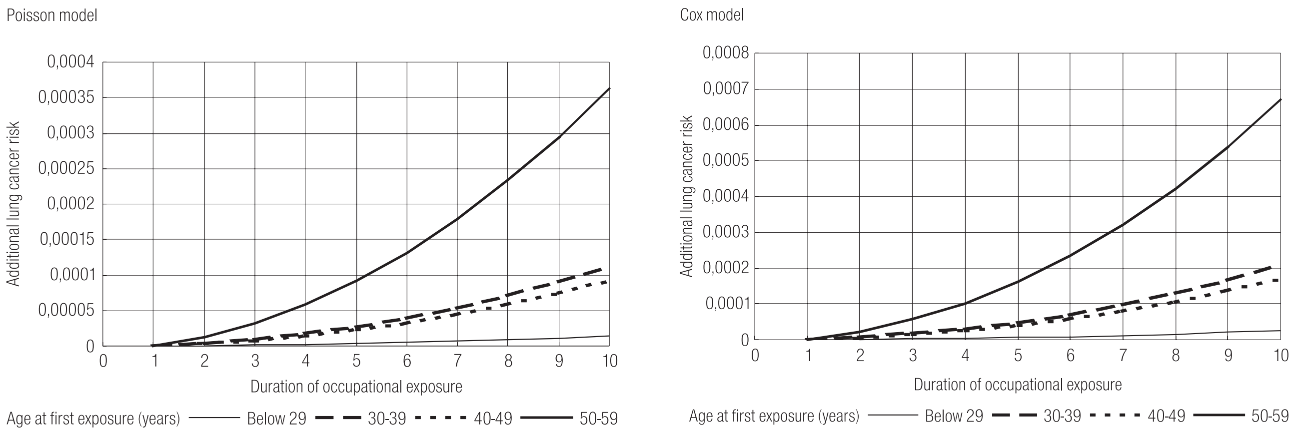

Fig. 1. Relationships between duration of employment in the pulp and paper mill production departments and additional cancer risk among male workers, depending on age at first exposure. The use of the Poisson and Cox models was an intermediate stage of risk assessment.

at least one order of magnitude lower than in the other groups while the oldest group of workers began their employment with a burden of the highest risk.

The results of lung cancer risk assessment in workers of the pulp and paper mill may also be viewed from a slightly different perspective. It was earlier assumed that possible cases of lung cancer in workers employed for no less than one year in the production or administration were to be considered as background hazard, namely not related to occupational exposure. Therefore, after eliminating the background hazard, all exposure-response curves would begin with the null risk value and illustrate only the risk increased due to the exposure present in the departments in question. Figure 1 shows the results yielded after such modification.

The comparison of exposure-response curves obtained from the Poisson and Cox models showed that their shapes were practically the same (Fig. 1), but the risk in the Cox model was slightly higher than that in the Poisson model. It is most likely that the difference resulted from the different way of eliminating the workers' age effect.

DISCUSSION

The use of the additional (absolute) risk model described by formula (1) rendered it possible to provide a more thorough characteristics of the relationship between the exposure level and probability of death from lung cancer. A classic analysis of the cohort study yields standardized mortality rates and relative risk indices, showing how many times the risk of death from lung cancer in the group exposed is higher than that in the reference group (frequently regarded as non-exposed group). Making use of the cohort study results in the modeling of the exposure-response relationship, it is possible to estimate additional risk (absolute risk) associated with the exposure to a particular substance or with a hazardous occupation.

The classic analysis of the results obtained in the cohort study of the pulp and paper mill workers showed increased SMRs in subsequent periods of employment (but only up to 10 years) and their somewhat upward trend in successive age groups (Table 2). Relative risk of death from lung cancer in those employed in the production and administration departments for less than one year was equal to 0.91 as compared to the risk in the reference group (population of Poland). Among workers employed for 1–5 and 5–10 years, this risk was, respectively 1.41 and 1.68 times higher than in the reference population. But using the Poisson and Cox models in estimating relative risk and the model described by formula (1) in estimating additional risk, it was possible to observe different dynamics of changes in the risk as a function of employment duration in harmful conditions in different age groups adjusted by the age at first exposure. The analysis of the results indicated that the changes in risk of death from lung cancer in the two oldest age groups varied considerably from those observed in the younger groups (Table 8). In the former groups, the increase in risk resulting from occupational exposure in the pulp and paper production mill was much slower than in the younger age groups. For example, in the Poisson model, in the group with first exposure at the age below 29 years, the risk changed from $2.25 \cdot 10^{-7}$ during the first year of employment to $1.40 \cdot 10^{-5}$ after 10 years of employment (62-fold increase, 0.000011 absolute growth), whereas in the group of workers with first exposure at the age of 50–59 years, the risk changed from $6.42 \cdot 10^{-5}$ to $4.28 \cdot 10^{-4}$ (about 7-fold increase, and 0.000364 absolute growth).

In addition, the model based on the competing risk theory rendered it possible to infer that the risk at first exposure at the age of 50–59 was almost two orders of magnitude higher than that in workers with first exposure at the age below 29. The values of this risk were $6.42 \cdot 10^{-5}$ and $2.25 \cdot 10^{-7}$, respectively. The difference between the risk levels at starting the employment caused different dynamics of change in the risks during 10 years although work conditions in those two groups of workers were the same. Such a relationship could not be observed in the classic analysis of the cohort study.

Relative risks obtained from the Poisson and Cox models on the basis of data obtained from the cohort study of workers employed in the pulp and paper mill differed slightly.

The Cox model values were somewhat higher than those obtained from the Poisson model. Obviously, the question arises as to which of these models should be used to obtain the values as close to reality as possible. As a matter of fact, this question has no answer as there is no criterion that could provide the basis for explicit choice of the model. Of course, each of these models should meet certain assumptions on which they are grounded, but it should be remembered that all of them are equipped with their own sets of premises. Some approaches take account of data on biological mechanisms, others of statistical data, the goodness of fit of the model and the ability to properly predict the risk in other similar situations. As to the goodness of fit, most frequently this measure has no property of model discrimination, if viewed from the statistical perspective, each of these models may provide a reasonable fit to the data.

A very common habit of cigarette smoking among cohort workers should be highlighted here as an essential problem. The lack of smoking histories may be disadvantageous in the studies of cohorts exposed to carcinogenic chemicals because of frequent synergetic effect of exposure to chemicals and smoking on the lung cancer incidence.

As noted by Axelson and Steenland [10], if smoking histories are not available, the assessment of possible effects of smoking on the results of the epidemiological study should be based on theoretical considerations. Such an assessment is of particular importance in case of positive relationship between exposure and diseases whose incidence strongly depends on smoking habit as is the case of lung cancer. The question of smoking effect on the results of the epidemiological study is considered not only in terms of smokers themselves [11–14], but also in terms of attempts made to assess lung cancer risk induced by passive smoking known also as environmental tobacco smoke [15].

The authors of this paper have presented in one of their earlier publications the results of the classic cohort analysis [7] in which they used Axelson's method, modified to include the effect of cigarette smoking. SMR values for cancer risk in pulp and paper workers reached then a 20%decrease in the starting risk value. But in this study, an internal reference group was adopted in risk modeling by means of the Poisson and Cox models, providing that the percentage of smokers should be similar in this group and in the group of remaining cohort workers, as both groups were composed of workers employed in the same plant. This approach should minimize the problem resulting from the lack of direct data on smoking habits in the cohort.

Risk assessment methods described in this paper have also been used by other authors. For example, Steenland et al. [16] using these methods modeled the relationship between lung cancer risk and exposure to Diesel exhaust, and Stayner et al. [17,18] defined in quantitative risk assessment the probability of lung cancer incidence due to cadmium exposure. Those authors, taking as a basis the results of epidemiological studies, extended the classic epidemiological analysis to include quantitative risk assessment. Despite numerous limitations associated with use of such models for epidemiological studies and a number of uncertainties concerning the obtained results [9], risk modeling methods gain a still growing number of adherents among epidemiologists. Not only models of competing risks, but also various types of regression [19–22] and mathematical models, involving biological mechanisms responsible for the incidence of malignancies such as multistage models, are used [23].

It should be stressed that owing to the methods of risk modeling, the analysis of the results of epidemiological studies can be more thorough and complementary. In individual strata indicated by the levels of risk factors it is possible to assess the exposure-response relationship. Owing to this assessment, a different dynamics of risk changes in different age groups can be observed. In addition, the value of the risk of death from a given cancer, or the risk of development of a given cancer can be calculated for any level of human exposure to a specified chemical (sometimes the level of exposure may be replaced for example, by the employment duration).

A classic analysis of the results yielded by cohort studies allows to estimate relative risk with regard to the reference population whereas the model of competing risk renders it possible to estimate the absolute risk. The values of the absolute risk are free from the effect of confounders as the Poisson and Cox models allow to estimate the adjusted relative risk.

CONCLUSIONS

The method of risk assessment, discussed in this paper, involves more work than the classic analysis of the cohort study results, because of required intermediate modeling of relative risk, nevertheless it seems that the benefits gained due its application easily recompensate the effort put into the job.

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