International Journal of Occupational Medicine and Environmental Health, Vol. 15, No. 3, 267—278, 2002

MORTALITY STUDY OF WORKERS COMPENSATED FOR ASBESTOSIS IN POLAND, 1970–1997

NEONILA SZESZENIA-DĄBROWSKA, URSZULA WILCZYŃSKA, WIESŁAW SZYMCZAK and ALICJA STRZELECKA

Department of Occupational and Environmental Epidemiology
Nofer Institute of Occupational Medicine
Łódź, Poland

Abstract. The aim of the study was to assess the risk of asbestos-related malignancies among persons with diagnosed asbestosis. The study covered a cohort composed of 907 men and 490 women afflicted by asbestosis, diagnosed in 1970–1997. The follow-up of the cohort continued until 31 December 1999. In all, 421 deaths were registered and causes of death were retrieved for 93.3% of the deceased. A significantly increased mortality was observed both in the male (300 deaths; SMR = 127; 95%CI: 113–142) and female (121 deaths, SMR = 150; 95%CI: 124–179) cohorts. The elevated number of deaths in the male and female cohorts were noted mainly due to respiratory diseases (men: 42 deaths; SMR = 344; 95%CI: 248–465; women: 20 deaths, SMR = 789; 95%CI: 482–1219) malignant neoplasms (men: 91 deaths, SMR = 146; 95%CI: 118–179; women: 34 deaths, SMR = 159; 95%CI: 110–222), including lung cancer (men: 39 deaths, SMR = 168; 95%Cl: 119–230; women: 13 deaths, SMR = 621; 95%CI: 331–1062) and pleural mesothelioma (men: 3 deaths, SMR = 2680; 95%CI: 553–7832; women: 3 deaths, SMR = 7207; 95%CI: 1031–14612). Taking into account a cumulative dose of fibers, it was found that a significantly increased mortality from lung cancer and pleural mesothelioma applied to persons exposed to a dose above 25 f-y/ml. The results indicate that persons with asbestosis are at higher risk of developing malignant neoplasms, especially lung cancer and mesothelioma.

Key words:
Asbestosis, Lung cancer, Pleural mesothelioma, Cohort study, Mortality

INTRODUCTION

Over many years, health effects of occupational exposure to asbestos dust have been the subject of intensive epidemiological studies. In 1955, Doll, in the first study recognized as epidemiologically correct, proved the relationship between asbestos dust exposure and lung cancer. In this study, he found that lung cancer risk in persons employed in the asbestos industry for more than 20 years was 20 times higher than in the general population. In the 15 of 18 lung cancer cases coincident asbestosis was diagnosed [1]. This finding laid the basis for the belief, which has persisted for many years, that asbestos-induced lung cancer is preceded by lung fibrosis. Scarring were regarded as a pre-neoplastic condition conducive to the development of malignancies. Despite very rich literature devoted to this issue, the problem of the concurrence of asbestosis and lung cancer still needs to be clarified [2–18]. A hypothesis that in occupational exposure to asbestos dust, the occurrence of lung cancer is associated with a high dose of dust able to induce asbestosis is still topical. A question also arises whether fibrosis lesions in the form of asbestosis predispose to more frequent incidence of lung cancer.

The following two criteria for diagnosing asbestosis are usually used in Poland: (1) a job history confirming occupational exposure to asbestos; and (2) positive radiographic findings of asbestosis of the lungs (profusion on small opacities of at least 1/0 according to the ILO

This work was performed under the Nofer Institute Research Program (No. IMP 10.5) "Risk of asbestosis and asbestos-related cancers among workers exposed to asbestos dust".
Address reprint requests to Prof. N. Szeszenia-Dąbrowska, Department of Occupational and Environmental Epidemiology, Nofer Institute of Occupational Medicine, P.O. Box 199, 90-950 Łódź, Poland (e-mail: wies@imp.lodz.pl).

Classification of Pneumoconiosis). In 1970–1997, 1397 cases of asbestosis were registered. The follow-up of death causes in this group aimed at assessing the risk of asbestos-related malignancies, taking at the same time account of variables characteristic of a given exposure.

MATERIALS AND METHODS

The assessment of the health effects of occupational exposure to asbestos dust was based on the cohort study. The cohort was enumerated from the file of the National Register of Occupational Diseases and composed of 1397 persons with asbestosis diagnosed in 1970–1997. The data obtained from offices of civil statistics helped to find out whether persons included in the cohort were alive or deceased. The follow-up continued until 31 December 1999. For the deceased subjects, exact dates and places of death were elicited in order to obtain from registry offices information on the underlying causes of death recorded in death certificates. The underlying causes of death were coded following the 9th Revision of the International Classification of Disease (ICD-9).

The analysis of deaths by causes was based on standardized mortality ratio (SMR) calculated by the person-years (PYRS) method. The person-years of the cohort members were calculated for the period between the asbestosis detection and ”exit” from the cohort, i.e. death or reaching the age of 80 years. For the people remaining in the cohort, the person-years were calculated until the end of follow-up (31 December 1999). The general population of Poland served as the reference. The Poisson distribution test was used to assess the statistical significance of SMR and their 95% confidence intervals (95% CI) were also calculated. The data were analyzed using the PYRS program made available to the authors by the International Agency for Research on Cancer (IARC). The data were analyzed separately for men and women in subcohorts identified by types of workplaces and cumulative doses of asbestos fibers.

In order to select from all the analyzed risk factors the ones that potentially induce the development of specific types of cancer, the univariate modeling according to Cox proportional hazards model [19] was applied. In the model, the time parameter was measured from the date that asbestosis was diagnosed.

Data from the history of job performed in exposure to asbestos were included in the occupational disease certificates. The information on the duration of asbestos exposure was supplemented by the date at first employment in exposure. It was then possible to determine the age of workers at first exposure. In the forms of 33 persons (2.4%), the data on the number of exposure years were missing, thus the age at hire remained unknown. Nevertheless, these persons remained in the cohort, but they were excluded from some of the analyses.

In asbestos processing plants and in those using asbestos-containing materials for various production processes, up to 1981 only weighted asbestos concentrations, expressed in mg/m^3 of air were usually the basis for assessing the exposure. This information was given in 77% of occupational disease certificates.

In order to determine individual cumulative dose of asbestos fibers, a questionnaire was mailed to work safety and hygiene sections of the plants at which the cohort members were employed. The questionnaire contained a detailed description of workposts and jobs, as well as the characteristics of technology and hygiene conditions in the plant, including the results of individual dosimetry (in f/ml) if it was performed in a given plant. These data together with the information on the duration of employment rendered it possible to estimate individual doses of fibers for 76.6% of study subjects. In the remaining group, a reliable estimation was not possible because of scant information, so it was excluded from further analyses, depending on the size of the dose.

RESULTS

The cohort was composed of 1397 persons (907 men and 490 women). The follow-up continued until 31 December 1999; 1391 (99.6%) persons were traced. This number included 421 deceased persons. The information on the underlying cause of death was retrieved for 93.3% of persons (Table 1).

Table 1. Vital status of the cohort

Workers	Males	Females
Potential study cohort	907	490
- Traced	902 (99.4%)	489 (99.8%)
- Alive	602	368
- Dead	300	121
- Known cause of death	276 (92.0%)	117 (96.7%)
- Lost to follow-up	5	1
- Emigrated	1	–

The majority of the cohort members (60.1% of men and 76.5% of women) were employed in asbestos processing plants. This was followed by foundry (16.1% men and 11.7% of women) and shipyard (14.7% of men and 9.6% of women) workers (Table 2). Fitters of thermal insulation (19 men) and masons of industrial furnaces (18 men) predominated in other occupational groups.

The age of the cohort members widely varied at the time of asbestosis detection (Table 2). The mean age at the diagnosis was 55 years. The youngest man was 28 years old. He worked for 8 years as a fitter-maintenance technician in the asbestos cement plant, being involved in the machine repair and maintenance, and exposed to the concentration of asbestos dust at a dose of 3.7 f/ml on average (cumulative dose, 29.6 f-y/ml). The youngest women, a spinner, was

Table 2. Distribution of the cohort by workplace and age at the diagnosis of asbestosis

	Males		Females	
	No.	%	No.	%
Type of plant				
Asbestos-cement plants	229	25.4	70	14.3
Other asbestos processing plants	313	34.7	304	62.2
Foundries	145	16.1	57	11.7
Shipyards	133	14.7	47	9.6
Other plants	82	9.1	11	2.2
Age at diagnosis				
>39	46	5.1	19	3.9
40–49	202	22.4	111	22.7
50–59	387	42.9	214	43.8
60–69	219	24.3	114	23.3
70<	48	5.3	31	6.3
Total	902	100.0	489	100.0

Table 3. Distribution of the cohort* by age at first employment in exposure to asbestos dust and duration of exposure

	Males		Females	
	No.	%	No.	%
Age at first employment in exposure (yr)				
≤ 29	443	49.8	171	36.5
30–39	287	32.3	192	40.9
≥ 40	159	17.9	106	22.6
Duration of exposure (yrs)				
≤ 14	182	20.5	126	26.9
15–19	164	18.4	122	26.0
20–24	196	22.1	120	25.6
≥ 25	347	39.0	101	21.5
Total	889	100.0	469	100.0

* 33 persons with unknown data are not included in the Table.

Table 4. Distribution of the cohort* by cumulative dose of asbestos fibers

Cumulative dose of asbestos fibers (f-y/ml)	Males		Females	
	No.	%	No.	%
≤ 25	29	4.3	18	4.5
26–65	230	34.5	134	33.2
66–105	214	32.0	123	30.5
≥ 106	195	29.2	128	31.8
Total	668	100.0	403	100.0

* 320 persons with unknown data are not included in the Table.

33 years old. She was employed for 15 years in a plant, manufacturing asbestos packings and other asbestos products. The mean concentration of asbestos at her workpost was estimated at 5.5 f/ml (cumulative dose, 82.5 f-y/ml).

The dates on which the employment in asbestos exposure began and ceased were traced for 889 men (98.6%) and 469 women (95.9%); only these persons were included in the analysis of cancer risk, depending on the age at first exposure and duration of employment in exposure. The distribution of these variables is given in Table 3.

The questionnaire data made available by industrial hygienists in individual plants provided the grounds for estimating cumulative doses of asbestos fibers for 668 men (74.0%) and 403 women (82.4%) employed in plants manufacturing asbestos products, asbestos-cement plants and shipyards (Table 4). The highest doses were received by shipbuilders, and the lowest by employees of asbestos-cement plants (Table 5).

of Poland (300 deaths; SMR = 127; 95%CI: 113–142) (Table 6). The registered deaths were mostly due to respiratory diseases (42 deaths, SMR = 344; 95%CI: 248–465) and malignant neoplasms (91 deaths, SMR = 146; 95%CI: 118–179). Asbestosis as an underlying cause of death was most frequently recorded in death certificates of men who died from respiratory diseases (26 cases). Taking into account the cancer site, a significant excess of asbestos-related malignancies, namely lung cancer (39 deaths, SMR = 168; 95%CI: 119–230) and mesothelioma (3 deaths, SMR = 2680; 95%CI: 553–7832) was revealed. In addition, over five-fold increase in bladder cancer (3 deaths, SMR = 523; 95%CI: 108–1528), and almost three-fold excess of prostate cancer (8 deaths, SMR = 291; 95%CI: 126–573) were observed.

The female total mortality was one and a half times higher than that in the general population (121 deaths, SMR = 150; 95%CI: 124–179). The analysis of deaths according to major groups of diseases showed a significantly larger number of observed than expected deaths from respiratory diseases (20 deaths, SMR = 789; 95%CI: 482–1219) and malignant neoplasms (34 deaths, SMR = 159; 95%CI: 110–222), including pleural mesothelioma (3 deaths, SMR = 7207; 95%CI: 1031–14612), lung cancer (13 deaths, SMR = 621; 95%CI: 331–1062), and pancreas cancer (4 deaths, SMR = 376; 95%CI: 102–963). Among respiratory diseases, asbestosis was most frequently recorded as an underlying cause of death (15 cases of 20) (Table 7).

Table 5. Cumulative dose of asbestos fibers by workplaces

Workplace	Males			Females		
	No.	Dose (f-y/ml)		No.	Dose (f-y/ml)	
		Median	Range		Median	Range
Asbestos-cement plants	223	64.8	5.4–262.5	69	56.7	8.1–187.5
Other asbestos processing plants	315	71.5	3.7–247.5	290	82.5	12.0–262.5
Shipyards	130	127.5	22.0–300.0	44	135.0	45.0–277.5
Total	668	75.6	3.7–300.0	403	82.5	8.1–277.5

Mortality

A significantly increased mortality was observed in the male cohort, as compared to the general male population

As depicted in Table 8, the group of persons deceased from lung cancer, both men and women, was vastly differentiated in the time elapsed since asbestosis detection and

Table 6. Mortality (number of deaths, SMR and 95% CI) in the cohort of men with asbestosis

Causes of death (ICD-9)	Observed deaths	SMR	95% CI
All causes (001–999)	300	127	113–142
Infectious and parasitic diseases (001–139)	1	39	
Malignant neoplasms (140–208)	91	146	118–179
- Digestive organs and peritoneum (150–159)	16	83	47–135
- - Oesophagus (150)	1	65	
- - Stomach (151)	5	70	23–163
- - Colon (153)	1	51	
- - Rectum and anus (154)	2	77	9–278
- - Liver (155)	1	49	
- - Gallbladder (156)	3	523	108–1528
- - Pancreas (157)	3	118	24–345
- Respiratory and intrathoracic organs (160–165)	44	168	122–226
- - Larynx (161)	1	43	
- - Lung (162)	39	168	119–230
- - Pleura (163)	3	2680	553–7832
- Prostate (185)	8	291	126–573
- Bladder (188)	2	85	10–307
- Kidney (189)	2	113	14–408
- Brain (191)	2	150	18–542
- Thyroid gland (193)	1	829	
- Lymphatic and haematopoietic tissue (200–208)	6	222	81–483
Endocrine and metabolic diseases (240–279)	2	63	8–228
Mental disorders (290–319)	1	81	
Nervous system diseases (320–389)	1	63	
Circulatory system diseases (390–459)	107	93	76–112
Respiratory system diseases (460–519)	42	344	248–465
Digestive system diseases (520–579)	10	115	55–211
Ill-defined conditions (780–799)	7	68	27–140
Injury and poisoning (800–999)	14	98	54–164

death, and the magnitude of exposure to asbestos dust. The cases of pleural mesothelioma are listed in Table 9, all but one were noted among asbestos processing workers.

Taking into account the level of exposure to asbestos dust measured by a cumulative dose of fibers, it was found that statistically significant excess mortality from all malignant neoplasms, lung cancer, pleural mesothelioma and respiratory diseases was relevant to workers exposed to doses above 25 f-y/ml. All deaths from mesothelioma were concentrated in this group of persons (Table 10).

An increased total male mortality was observed in all types of plants except for shipyards. In asbestos processing plants and in "other plants", a significantly larger number of observed than expected deaths were noted (148 deaths, SMR = 135; 95%CI: 114–159 and 28 deaths, SMR = 169; 95%CI: 112–244, respectively). An enhanced mortality from all malignant neoplasms was observed, regardless of the type of plant, and in asbestos processing plants, the excess was statistically significant (48 deaths, SMR = 168; 95%CI: 124–223). Except for "other plants", an increased lung cancer risk was also found in all plants. In asbestos-cement plants and in those manufacturing asbestos products, this risk was statistically significant (11 deaths, SMR = 234; 95%CI: 117–419 *v* 19 deaths, SMR = 181; 95%CI:

Table 7. Mortality (number of deaths, SMR and 95% CI) in the cohort of women with asbestosis

Causes of death (ICD-9)	Observed deaths	SMR	95% CI
All causes (001–999)	121	150	124–179
Malignant neoplasms (140–208)	34	159	110–222
- Digestive organs and peritoneum (150–159)	9	118	54–224
- - Colon (153)	2	199	24–719
- - Rectum and anus (154)	1	86	
- - Gallbladder (156)	1	96	
- - Pancreas (157)	4	376	102–963
- Respiratory and intrathoracic organs (160–165)	16	689	394–1119
- - Lung (162)	13	621	331–1062
- - Pleura (163)	3	7207	1031–14612
- Bone (170)	1	747	
- Skin, melanoma (172)	1	553	
- Breast (174)	3	103	21–301
- Ovary (183)	1	79	
- Kidney (189)	1	131	
Endocrine and metabolic diseases (240–279)	2	74	9–267
Circulatory system diseases (390–459)	46	109	80–145
Respiratory system diseases (460–519)	20	789	482–1219
Digestive system diseases (520–579)	6	192	70–418
Genitourinary system diseases (580–629)	2	146	18–527
Musculoskeletal system diseases (710–739)	1	212	
Ill–defined conditions (780–799)	1	38	
Injury and poisoning (800–999)	4	160	44–410

109–283, respectively). In the three subcohorts, workers of asbestos-cement plants, shipyard and asbestos processing plants, the occurrence of single cases of mesothelioma was observed, which revealed, an increased risk of this cancer. In the two former types of plants, the risk increase was statistically significant (SMR = 4406 and SMR = 6540; $p < 0.05$, respectively). In all plants, except for shipyards, mortality from respiratory diseases was significantly increased. In asbestos cement plants and in those of asbestos processing, the excess mortality was about three times higher (8 deaths, SMR = 356; 95%CI: 154–701 and 17 deaths, SMR = 280; 95%CI: 163–448, respectively) and in foundries and "other plants" it was even more than five times higher (11 deaths, SMR = 664; 95%CI: 331–1188 and 5 deaths, SMR = 532; 95%CI: 173–1242, respectively) (Table 11).

The differentiation of the female subcohort by the place of employment revealed significant total mortality excess in asbestos processing plants (87 deaths, SMR = 154; 95%CI: 123–190) and steel mills (16 deaths, SMR = 186; 95%CI: 106–302). The observed number of deaths from malignant neoplasms, especially from lung cancer, significantly exceeded the expected number in asbestos processing plants (23 deaths, SMR = 159; 95%CI: 101–239 and 11 deaths, SMR = 769; 95%CI: 384–1376, respectively). Among female workers of asbestos cement plants, 2 cases of pleural mesothelioma were found indicating high risk of this disease (SMR = 50945; 95%CI: 606–18062).

Mortality from respiratory diseases was significantly higher in the female subcohort employed in asbestos processing plants (12 deaths, SMR = 668; 95%CI: 345–1167) and foundries (5 deaths, SMR = 1906; 95%CI: 619-4448) (Table 12).

The analysis of male mortality, depending on a lapse of time since the diagnosis of occupational disease, revealed that during the first 10 years, the risk of all deaths (202

Table 8. Characteristics of deaths from lung cancer in the cohort (39 males, 13 females)

Characteristics	Gender	$\bar{x} \pm SD$	Me	Range	$v = \frac{SD}{\bar{x}} \cdot 100\%$
Age at first employment in exposure to asbestos dust	M	32.1 ± 9.7	30	17–55	30.2
	F	32.1 ± 8.6	32.5	16–45	26.8
Duration of employment	M	22.2 ± 7.6	24	8–36	34.2
	F	20.2 ± 8.3	21	5–34	41.1
Cumulative dose of asbestos fibres (f-y/ml)	M	92.5 ± 52.1	80.1	21.6–247.6	56.3
	F	101.7 ± 46.5	96.2	13.5–187.0	45.7
Age at diagnosis of asbestosis	M	58.7 ± 8.8	60	37–79	15.0
	F	54.5 ± 9.4	52	37–75	17.2
Time since first exposure	M	33.1 ± 9.1	35	7–45	27.5
	F	29.8 ± 7.2	32	14–39	24.2
Time since diagnosis of asbestosis	M	6.5 ± 5.3	6	0–20	81.5
	F	8.1 ± 4.9	9	0–15	60.5
Age at death	M	65.2 ± 7.8	65	46–79	12.0
	F	62.5 ± 7.3	63	49–76	11.7

M – males; F – females.

Table 9. Cases of deaths from pleural mesothelioma

Identification number	Gender	Age at			Duration of exposure to asbestos	Cumulative dose of asbestos fibres f-y/ml	Type of plant
		First employment	Diagnosis of asbestosis	Death			
898	M	41	53	66	12	32.4	Asbestos-cement
109	M	27	54	59	27	148.5	Shipyard
681	M	23	55	65	31	85.0	Asbestos products
962	F	37	52	69	16	43.2	Asbestos-cement
794	F	42	60	79	18	66.5	Asbestos products
1187	F	31	52	58	20	74.0	Asbestos-cement

Table 10. Mortality (observed deaths – O, SMR, 95% CI) from selected causes among workers with asbestosis by cumulative dose of asbestos fibers and gender

Causes of death (ICD–9)	Males						Females					
	Dose (f-y/ml)						Dose (f-y/ml)					
	>25			26<			>25			26<		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes (001–999)	13	185	99–316	211	121	105–138	4	158	43–405	88	143	115–176
Malignant neoplasms (140–280)	4	221	60–566	72	153	120–193	1	167		27	163	107–237
- Lung (162)	2	307	37–1109	32	182	124–257	1	1707		11	667	333–1193
- Pleura (163)	–	0		3	3551	732–10378	–	0		3	9187	2508–23700
Respiratory system diseases (460–519)	2	539	65–1947	23	260	165–390	1	1219		10	513	246–943

deaths, SMR = 272; 95%CI: 236–312), malignant neoplasms (67 deaths, SMR = 336; 95%CI: 260–427), lung cancer (31 deaths, SMR = 416; 95%CI: 283–599) and mesothelioma (2 deaths, SMR = 5450; 95%CI:

Table 11. Mortality (observed deaths – O, SMR, 95% CI) from selected causes among male workers with asbestosis by workplaces

Causes of death (ICD–9)	Asbestos-cement plants			Other asbestos processing plants			Foundries			Shipyards			Other plants		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes (001–999)	55	118	89–154	148	135	114–159	45	134	98–179	24	80	51–119	28	169	112–244
Malignant neoplasms (140–208)	18	145	86–229	48	168	124–223	9	100	46–190	10	123	59–226	6	140	51–305
- Lung (162)	11	234	117–419	19	181	109–283	4	117	32–300	4	127	35–325	1	64	
- Pleura (163)	1	4406		1	1995		–			1	6540		–		
Respiratory system diseases (460–519)	8	356	154–701	17	280	163–448	11	664	331–1188	1	77		5	532	173–1242

Table 12. Mortality (observed deaths – O, SMR, 95% CI) from selected causes among female workers with asbestosis by workplaces

Causes of death (ICD–9)	Asbestos-cement plants			Other asbestos processing plants			Foundries			Shipyards			Other plants		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes (001–999)	7	95	38–196	87	154	123–190	16	186	106–302	7	119	48–245	4	195	53–499
Malignant neoplasms (140–208)	4	203	55–520	23	159	101–239	3	127	26–371	3	173	36–506	1	192	
- Lung (162)	–			11	769	384–1376	–			1	583		1	2000	
- Pleura (163)	2	50945	606–18062	1	3507		–			–			–		
Respiratory system diseases (460-519)	1	434		12	668	345–1167	5	1906	619–4448	1	554		1	1666	

Table 13. Mortality (observed deaths – O, SMR, 95% CI) from selected causes among male workers with asbestosis by period after diagnosis of occupational disease

Causes of death (ICD–9)	>4 yrs			5–9 yrs			10–14 yrs			15< yrs		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes (001–999)	102	523	426–635	100	183	149–223	70	101	79–128	28	31	21–45
Malignant neoplasms (140–208)	29	564	378–810	38	256	181–351	18	96	57–152	6	25	9–54
- Lung (162)	17	904	527–1447	14	251	137–421	5	71	23–166	3	34	7–99
- Pleura (163)	–	0		2	7481	899–27041	1	2932		–	0	
Respiratory system disease (460–519)	20	2028	1239–3132	10	381	183–701	8	248	107–489	4	89	24–228

564–19637) increased significantly. The larger number of observed than expected deaths from respiratory diseases maintained up to 15 years since asbestosis detection (38 deaths, SMR = 556; 95%CI: 393–763).

In the female cohort the increased risk of death could be observed during the period of 15 years following the asbestosis detection, and this applies to all causes (100 deaths, SMR = 257; 95%CI: 194–411), all malignant neoplasms (30 deaths, SMR = 288; 95%CI: 194–411), lung cancer (12 deaths, SMR = 1143; 95%CI: 591–1997) and respiratory diseases (17 deaths, SMR = 1453; 95%CI: 846–2326). All deaths from mesothelioma occurred by the end of 10 years since the diagnosis of occupational disease (3 deaths, SMR = 28846; 95%CI: 5962–84327). Almost every third person (32.6%) among those who died before a lapse of 5 years since the diagnosis of occupational disease had started their employment in exposure to asbestos before 1960 and worked for at least 20 years. The proportion of those who died from lung cancer during

Table 14. Mortality (observed deaths – O, SMR, 95% CI) from selected causes among female workers with asbestosis by period after diagnosis of occupational disease

Causes of death (ICD–9)	≤ 4 yr			5–9 yr			10–14 yr			15 ≥ yr		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes (001–999)	32	691	473–975	40	264	189–359	28	146	97–211	21	54	33–83
Malignant neoplasms (140–208)	12	1118	578–1953	9	217	99–412	9	173	79–328	4	38	10–97
- Lung (162)	3	2859	590–8355	5	1188	386–2772	4	760	207–1946	1	98	
- Pleura (163)	2	95923	11429–343810	1	12075		–	0		–	0	
Respiratory system disease (460–519)	2	1367	166–4938	8	1754	757–3456	7	1232	495–2538	3	251	52–734

such a short period of time was even higher, over 50% (11 of the 20 persons). The data summarized in Tables 13 and 14 show the tendency of decreasing risk with time flow.

The results of Cox modeling are displayed in Tables 15 and 16. With regard to the male subcohort, only the worker's age at diagnosis of asbestosis was proved to be of significance. As the worker's age on diagnosing asbestosis increased, the risk of lung cancer rose (hazard ratio: 1.085, $p < 0.0005$) and so was the risk of cancers of all respiratory and intrathoracic organs (hazard ratio: 1.076, $p < 0.0005$). None of the analyzed parameters had a significant influence on the risk of pleural mesothelioma. With respect to the female subcohort a significant relationship was found only between the worker's age at the time when asbestosis was diagnosed and the risk of pleural mesothelioma. The older the worker with a diagnosed occupational disease, the higher the risk of developing pleural mesothelioma. However, when modeling was applied to investigate the relationship between the risk of lung cancer in males, as well as pleural mesothelioma in females, and the patient's age at diagnosing abestosis, this rela-

Table 15. Risk factors of selected malignant neoplasms in male cohort. Results of univariate modeling according to Cox proportional hazard model (origin time: date of diagnosis of occupational disease)

Risk factor	Hazard ratio	Standard error	P	95% CI	
Lung cancer					
Duration of exposure	1.015	0.023	0.652	0.971	1.060
Concentration of asbestos fibers	0.950	0.080	0.540	0.805	1.120
Cumulative dose of asbestos	1.000	0.003	0.911	0.993	1.006
Age at diagnosis of asbestosis	1.085	0.022	<0.0005	1.043	1.129
Age at employment in exposure	1.011	0.020	0.583	0.972	1.051
Malignant neoplasm of pleura					
Duration of exposure	1.047	0.079	0.609	0.903	1.215
Concentration of asbestos fibers	0.782	0.260	0.459	0.408	1.500
Cumulative dose of asbestos	0.998	0.011	0.888	0.977	1.020
Age at diagnosis of asbestosis	1.045	0.071	0.523	0.914	1.195
Age at employment in exposure	0.999	0.069	0.991	0.873	1.143
Malignant neoplasm of respiratory and intrathoracic organs					
Duration of exposure	1.014	0.021	0.509	0.973	1.056
Concentration of asbestos fibers	0.945	0.074	0.475	0.810	1.103
Cumulative dose of asbestos	0.999	0.003	0.832	0.993	1.005
Age at diagnosis of asbestosis	1.076	0.020	<0.0005	1.037	1.117
Age at employment in exposure	1.011	0.019	0.568	0.975	1.048

Table 16. Risk factors of selected malignant neoplasms in female cohort. Results of univariate modeling according to Cox proportional hazard model (origin time: date of diagnosis of occupational disease)

Risk factor	Hazard ratio	Standard error	P	95% CI	
Lung cancer					
Duration of exposure	1.051	0.047	0.273	0.962	1.148
Concentration of asbestos fibers	0.994	0.168	0.972	0.714	1.384
Cumulative dose of asbestos	1.006	0.006	0.367	0.993	1.018
Age at diagnosis of asbestosis	1.015	0.040	0.704	0.940	1.096
Age at employment in exposure	0.970	0.038	0.441	0.899	1.048
Malignant neoplasm of pleura					
Duration of exposure	0.980	0.083	0.811	0.830	1.157
Concentration of asbestos fibers	0.575	0.261	0.223	0.236	1.401
Cumulative dose of asbestos	0.982	0.017	0.296	0.949	1.016
Age at diagnosis of asbestosis	1.187	0.093	0.028	1.018	1.384
Age at employment in exposure	1.082	0.080	0.283	0.937	1.251
Malignant neoplasm of respiratory and intrathoracic organs					
Duration of exposure	1.034	0.041	0.394	0.957	1.118
Concentration of asbestos fibers	0.905	0.139	0.516	0.670	1.223
Cumulative dose of asbestos	1.001	0.006	0.770	0.990	1.013
Age at diagnosis of asbestosis	1.053	0.036	0.131	0.985	1.125
Age at employment in exposure	0.994	0.034	0.865	0.930	1.063

Table 17. Age at diagnosis of asbestosis as a risk factor of selected malignant neoplasms in male and female cohort. Results of univariate modeling according to Cox proportional hazard model (origin time: date of birth)

Risk factor: age at diagnosis of asbestosis	Hazard ratio	Standard error	P	95% CI	
Males					
Lung cancer	1.056	0.041	0.159	0.979	1.138
Malignant neoplasm of pleura	0.972	0.129	0.827	0.749	1.259
Malignant neoplasm of respiratory and intrathoracic organs	1.037	0.037	0.310	0.967	1.112
Females					
Lung cancer	0.961	0.059	0.522	0.852	1.085
Malignant neoplasm of pleura	1.318	0.244	0.136	0.917	1.895
Malignant neoplasm of respiratory and intrathoracic organs	1.012	0.056	0.829	0.908	1.129

tionship was found to be only the effect of the subject's age in general. If we assume that one's date of birth is the origin time in the Cox model, then one's age at the moment that asbestosis was diagnosed will not be a significant cancer risk factor (Table 17).

DISCUSSION

The workers with diagnosed asbestosis, and thus exposed to asbestos dust at a considerable level were followed-up. The basic source of information on workers included in the cohort were the files with reported cases of asbestosis, provided by the National Register of Occupational Diseases.

The results of the cohort follow-up showed a significant increase in the total mortality attributed mainly to the enhanced number of deaths from respiratory diseases and malignant neoplasms, especially lung cancer and pleural mesothelioma. Such a mortality pattern is in agreement

with findings of similar studies carried out in Australia, Finland, Italy and the United Kingdom [9,14–18,20,21]. Taking into account the workplaces of the cohort members, it could be stated that the manufacture of asbestos-cement products and asbestos processing were responsible for the highest risk of the aforesaid diseases. It is worth to note the significantly raised total mortality and that from respiratory diseases in steel mill female workers.
An unfortunate draw back of the present study was the lack of the analysis of smoking – a well known confounding factor. But in the adopted way of forming the cohort including all cases of asbestosis diagnosed in all regions of Poland over a period of 26 years, the collection of reliable data on smoking was not feasible. However, the lack of these data gives rise to the question whether a significantly increased risk of death from asbestos-related diseases, observed in our study, cannot be rather attributed to the more common smoking habit in the cohort than in the general population. Although smoking is a factor increasing the lung cancer risk especially if combined with exposure to asbestos, it is not associated with the risk for mesothelioma, which was very high in the study cohort. This generally adopted view contradicts the former assumption.
The analysis of the risk of death from other diseases, including cardiovascular diseases, whose incidence is also related with smoking, is one of the indirect methods for assessing the effect of suspected enhanced number of smokers in a study group. In the male cohort, the observed number of deaths from the circulatory system diseases was smaller than the expected one (SMR = 93), while in women the risk of death from this cause was slightly higher albeit insignificant (SMR = 109; 95% CI: 80–145). In addition, statistically significant excess of lung cancer, pleural mesothelioma and respiratory diseases was observed in the group of workers exposed to high doses of asbestos fibers, which proves the relationship between the risk and asbestos exposure. Another finding that indirectly supports a view concerning a dominant role of asbestos exposure and not of smoking is a consistent effect in cause-specific SMR both in males and females and apparently larger in the latter group, whereas – in general – women smoke less then men.
Like in the UK study [15], the highest risk of death, particularly from asbestos-related diseases, was observed soon after the detection of asbestosis. This in turn suggests that occupational disease was certified only at a very advanced stage of pathology.
A significantly increased risk of death from diseases listed above was observed in workers employed in asbestos-cement plants and in those manufacturing asbestos products. A considerable excess of risk, in relatively small group of shipyard workers, did not reach statistical significance, except for pleural mesothelioma in men, because of a small number of observed deaths.
It should also be mentioned that a significant female risk of pancreas cancer, as well as male risk of bladder and prostate cancers were observed in the cohort. The relationship between these neoplasms and exposure to asbestos dust has not been proved, and the authors of other studies of persons with asbestosis do not mention these sites among excess of deaths.
The risk of lung cancer among men and the risk of pleural mesothelioma among women was significantly associated with worker's age at the moment the asbestosis was diagnosed. The older the worker at diagnosis, the higher the risk of malignant neoplasms, but in fact it was simply the effect of worker's age.
To sum up, the results of this study showed the increased risk of malignancies, especially lung cancer and pleural mesothelioma, in persons with asbestosis.

REFERENCES

1. Doll R. *Mortality from lung cancer in asbestos workers*. Br J Ind Med 1955; 12, 81–6.
2. Abraham JL. *Asbestos inhalation, not asbestosis, causes lung cancer.* Am J Ind Med 1994; 26: 839–42.
3. Browne K. *Do silica and asbestosis cause lung cancer?* Arch Pathol Lab Med 1992; 116: 1103–14.
4. Case BW, Dufrense A. *Asbestos, asbestosis and lung cancer observations in Quebec chrysotile workers.* Environ Health Perspect 1997; 105: 1113–9.

5. Edelman SA. *Does asbestosis increase the risk of lung cancer?* Int Arch Occup Environ Health 1990; 62: 345–9.
6. Egilman D, Reinert A. *Lung cancer and asbestos exposure: asbestosis is not necessary.* Am J Ind Med 1996; 30: 398–406.
7. Finkelstein MM. *Radiographic asbestosis is not a prerequisite for asbestos-associated lung cancer in Ontario asbestos-cement workers.* Am J Ind Med 1997; 32: 341–8.
8. Hillerdal G, Henderson DW. *Asbestos, asbestosis, pleural plaques and lung cancer.* Scand J Work Environ Helath 1997; 23: 93–103.
9. Hughes JM, Weil H. *Asbestosis as a precursor of asbestos-related lung cancer: results of a prospective mortality study.* Br J Ind Med 1991; 48: 229–33.
10. Oksa P, Klockars M, Karjalainen A, Huuskonen MS, Valtulainen K, Pukkala E, et al. *Progresion of asbestosis predicts lung cancer.* Chest 1998; 113: 1517–21.
11. Roggli VL, Hammar SP, Pratt PC, Maddox JC, Legier J, Mark EJ, et al. *Does asbestos or asbestosis cause carcinoma of the lung?* Am J Ind Med 1994; 26: 835–8.
12. Sluis-Cremer GK, Bezuidenhout BN. *Relation between asbestosis and bronchial cancer in amphibole asbestos miners.* Br J Ind Med 1989; 46: 537–40.
13. Weiss W. *Asbestosis: a marker for the increased risk of lung cancer among workers exposed to asbestos.* Chest 1999; 115: 536–49.
14. Belli S, Bruno C, Comba P, Grignoli M. *Cause-specific mortality of asbestos-cement workers compensated for asbestosis in the city of Bari (in Italian)*. Epiedemiol Prev 1998; 22: 8–11.
15. Berry G. *Mortality of workers certified by pneumoconiosis medical panels as having asbestosis.* Br J Ind Med 1981; 38; 130–7.
16. Cookson WO, Musk AW, Glancy JJ, de Klerka NH, Yin R, Carr NG, et al. *Compensation, radiographic changes, and survival in applicants for asbestosis compensation.* Br J Ind Med 1985, 42 (7): 461–8.
17. Coults II, Gilson JC, Kerr IH, Parkes WR, Turner-Warwick M. *Mortality in cases of asbestosis diagnosed by a pneumoconiosis medical panel*. Thorax 1987; 42: 111–6.
18. Germani D, Belli S, Bruno C, Grignoli M, Nesti M, Pirastu R, et al. *Cohort mortality study of women compensated for asbestosis in Italy.* Am J Ind Med 1999; 36: 129–34.
19. Lee ET. *Statistical methods for survival data analysis*. New York: John Wiley and Sons Inc. 1992; p. 243–80.
20. Germani D, Grignoli M, Belli S, Bruno C, Maiozzi P, Anibaldi L, et al. *A mortality study of recipients of compensation for asbestosis in Italy (1980-1990) (in Italian).* Med Lav 1996; 87: 371–85.
21. Huuskonen MS. *Clinical features, mortality and survival of patients with asbestosis.* Scand J Work Environ Health 1978; 4: 265–74.

Received for publication: May 23, 2002
Approved for publication: July 5, 2002