

MORTALITY FROM MALIGNANT NEOPLASMS AMONG WORKERS OF AN ASBESTOS PROCESSING PLANT IN POLAND: RESULTS OF PROLONGED OBSERVATION

URSZULA WILCZYŃSKA, WIESŁAW SZYMCZAK, and NEONILA SZESZENIA-DĄBROWSKA

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

Abstract

Objectives: The study on mortality from cancer among workers of an asbestos plant manufacturing asbestos yarn, cloth, cords, packings, stuffing, brake linings and asbestos-rubber sheets was launched in the 1980s. The present paper discusses the results of further tracing of asbestos workers of the same plant. **Materials and Methods:** The study cohort covered 4497 workers employed at the asbestos plant in 1945–1980. The follow-up of the cohort continued until 31 December 1999. Deaths by causes were analyzed using standardized mortality ratio (SMR) calculated by the person-years method. The mortality pattern of the general population of Poland was used as reference. **Results:** The availability of the cohort was 93.1% (2805 men and 1382 women were traced). Mortality from malignant neoplasms in total (281 deaths among men, SMR = 118, 95%CI: 105–133 and 135 deaths among women, SMR = 159, 95%CI: 133–188) as well as that from lung cancer (102 deaths among men, SMR = 126, 95%CI: 103–153 and 18 deaths among women, SMR = 259, 95%CI: 153–409) were significantly higher than in the general population. Unlike earlier stages of analysis, the present study revealed an increased risk of pleural mesothelioma (2 deaths among men, SMR = 510, 95%CI: 62–1842 and 3 deaths among women, SMR = 2033, 95%CI: 419–5941). Mortality analysis among workers with asbestosis and in those without diagnosed asbestosis, did not reveal direct association between the risk of asbestos-induced lung cancer and previously diagnosed asbestosis. **Conclusions:** The prolonged cohort tracing showed an increased risk of asbestos-related cancers. It concerned mainly workers hired by the plant between 1945–1955, when the working condition were most strenuous.

Key words:

Asbestos, Cohort study, Lung cancer, Mortality, Pleural mesothelioma, Smoking

INTRODUCTION

The study on mortality from cancer among workers of the asbestos plant manufacturing asbestos yarn, cloth, cords, packings, stuffing, brake linings, and asbestos-natural rubber sheets was launched in the 1980s. In view of the project specificity, namely the cohort definition, tracing time and long latency period of asbestos-induced cancers, which for mesotheliomas can be of more than 30 years, the previous stages of the study could not yield a comprehensive assess-

ment of cancer risk in this cohort. The present paper discusses the results of further tracing of an enlarged initial cohort of asbestos workers of the same plant.

MATERIALS AND METHODS

The cohort comprised all workers employed at the study plant for at least three months and hired within the period of 1945–1980. This period can be divided into three

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Address reprint requests to Dr. Ź. Wilczyńska, Department of Environmental Epidemiology, Nofer Institute of Occupational Medicine, św. Teresy 8, 91-348 Łódź (e-mail: wies@imp.lodz.pl).

intervals: from 1945 to 1955, from 1956 to 1973, and from 1974–1980. The first interval marks the period when the working conditions in the plant were most strenuous. In 1956, the plant was thoroughly modernized due to installing a ventilation system. Accordingly, the workers who were employed in 1956 or later were exposed to lower levels of asbestos dust than those who joined the plant before that year. The workers employed during the first two intervals were the subject to cohort tracing at the two earlier stages of the project [1–4]. The present stage includes the observation of the cohort enlarged by including workers who joined the plant workforce in the period of 1974–1980.

The cohort was traced until 31 December 1999. For the deceased workers, the date and place of death were recorded and then verified against the documentation collected from different sources to ascertain the cause of death given in the death certificate. The latter was coded according to the International Classification of Diseases, Injuries and Causes of Death (ICD-9).

The analysis of deaths by causes was based on standardized mortality ratios calculated using the person-years method [5]. The reference group was the general population of Poland, including the data on deaths by causes, gender and age during 1945–1999. The person-years for the cohort members were calculated for the period between starting the employment and “exit” from the cohort because of death or reaching the age of 80 years. The remaining cohort members had their person-years calculated until 31 December 1999, when the tracing was terminated. The 95% confidence intervals (CI) for SMRs were calculated by applying Poisson distribution, with the use of the PYRS software provided by the International Agency for Research on Cancer (IARC) [6]. Separate analysis was made for male and female workers.

Based on the employment data at the asbestos plant, sub-cohorts by exposure duration were distinguished. The exposed workers were those working at the production and auxiliary departments and the non-exposed were administration workers. Additional analysis was made for workers at particular departments and those with diagnosed/non-diagnosed asbestosis.

For mortality analysis, the data on the smoking habit were also collected. This information derived from the medical records of prophylactic examinations and consultations conducted by the Out-patient Clinic of Occupational Diseases, Nofer Institute of Occupational Medicine, Łódź. Each cohort member reporting for such an examination was interviewed whether he or she had been smoking at least one cigarette a day for a period of more than three months. The findings made it possible to estimate the proportion of smokers in the study population and then to assess lung cancer risk with the use of Axelson’s correction for the control of the tobacco smoking parameter [7,8].

RESULTS

The cohort tracing concerned 4497 workers (3027 males and 1470 females) employed at the asbestos plant for at least three months within the period of 1945–1980. Life status was established for 4187 workers (2805 males and 1382 females). Thus, the availability of the cohort was 93.1%; 1854 deaths of workers aged below 80 years were recorded and 91.7% of cases had their cause of death ascertained (Table 1).

The cohort characteristics, by selected parameters, is summarized in Table 2. Most (55.2%) of the cohort members had their history of work in the plant shorter than five years. The percentage of workers with such a short period of employment was higher among male (60.7%) than female (41.5%) workers. In the cohort, the majority (72.6%) of workers were below 40 years of age at starting their work at the plant. Almost 50% of workers were involved in the production of insulation materials (20.6%), asbestos yarn and cloth (17.9%) and friction materials (7.9%). Over 50% of workers were employed at auxiliary (mechanical, electricity, maintenance and repair works) and administration departments (Table 2). A total of 371 workers in the cohort (8.9%) had asbestosis diagnosed as an occupational disease.

The smoking status was determined for 1096 (26.2%) workers. Generally speaking, almost two third of the sub-cohort smoked or used to smoke cigarettes. The propor-

Table 1. Vital status of the cohort of asbestos plant workers

Subjects	Men	Women	Total
Included in the study	3027	1470	4497
Traced	2805 (92.7%)	1382 (94.0%)	4187 (93.1%)
Alive	1386	947	2333
Deceased	1419	435	1854
Cause of death identified	1302 (91.8%)*	398 (91.5%)*	1700 (91.7%)*
Lost to follow-up	222 (7.3%)	88 (6.0%)	310 (6.9%)

* 100% = number of deceased workers.

Table 2. Distribution of the cohort by selected characteristics

Characteristics	Men		Women		
	n	%	n	%	
Year of birth					
–1920	628	22.4	291	21.1	
1921–1930	667	23.7	396	28.6	
1931–1940	605	21.6	286	20.7	
1941–1950	543	19.4	243	17.6	
1951–	362	12.9	166	12.0	
Year of starting employment in the asbestos plant					
–1950	293	10.4	181	13.1	
1951–1960	805	28.7	366	26.5	
1961–1970	792	28.2	432	31.2	
1971–1980	915	32.7	403	29.2	
Duration of employment					
<1	780	27.8	197	14.3	
1–4	922	32.9	377	27.2	
5–9	318	11.3	211	15.3	
10–19	442	15.8	368	26.6	
20–	343	12.2	229	16.6	
Age at starting employment in the to asbestos plant					
–39	2 039	72.7	999	72.3	
40–	766	27.3	383	27.7	
Departments					
Yarn and cloth	356	12.7	394	28.5	
Friction materials	294	10.5	38	2.7	
Insulating materials	420	15.0	441	32.0	
Auxiliary depts.	1 587	56.5	328	23.7	
Administration	148	5.3	181	13.1	
Total	Persons	2 805	100	1 382	100
	Person-years	76 574		42 168	

tion of smokers was much higher in the male (84.2%) than in the female (39.6%) population.

Mortality in the male cohort

The general mortality in the cohort was found to be significantly higher (1419 deaths, SMR = 138, 95%CI: 131–145) than in the reference population. An excess of cancer mortality was also noted (281 deaths, SMR = 118, 95%CI: 105–133), including lung cancer (102 deaths, SMR = 126, 95%CI: 103–153). Moreover, two cases of pleural mesothelioma and a five-fold increased risk of this pathology were found. A significant excess in general and cancer-related mortality was observed among male workers classified as “exposed to asbestos dust”. A higher than expected (1353 cases, SMR = 141, 95%CI: 134–149) total number

of deaths was recorded. Mortality from cancer (272 deaths, SMR = 122, 95%CI: 108–137) was 20% higher in the cohort than in the reference population, and approximately every third cancer death among male workers was due to lung cancer (97 cases, SMR = 128, 95%CI: 104–156). In this group, the risk of pleural mesothelioma was over five times as high as in the general population (2 deaths, SMR = 545, 95%CI: 66–1969) (Table 3).

Excess mortality from cancer applied to workers at all the departments, but it was statistically significant among those employed at the production of insulating materials (49 deaths, SMR = 137, 95%CI: 101–181) and auxiliary departments (157 deaths, SMR = 120, 95%CI: 102–140). The former presented a significantly increased risk of gallbladder cancer (3 deaths, SMR = 931, 95%CI: 192–2721), while the

Table 3. Mortality from malignant neoplasms (number of observed deaths, SMR and 95%CI) by exposure status in the male subcohort of asbestos workers

Cause of death (coded according to ICD-9)	Non-exposed			Exposed			Total		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001–999)	66	100	77–127	1353	141	134–149	1419	138	131–145
Malignant neoplasms (140–208)	9	58	27–110	272	122	108–137	281	118	105–133
Lip, oral cavity and pharynx (140–149)	–	0		3	45	9–132	3	42	9–123
Digestive organs and peritoneum (150–159)	1	19		101	131	107–159	102	123	100–149
Oesophagus (150)	–	0		10	173	83–318	10	162	78–298
Stomach (151)	1	43		43	127	92–171	44	121	88–162
Colon (153)	–	0		12	184	95–321	12	172	89–300
Rectum and anus (154)	–	0		10	118	57–217	11	110	55–197
Liver (155)	–	0		10	124	59–228	10	116	56–213
Gallbladder (156)	–	0		4	197	54–504	4	184	50–471
Pancreas (157)	–	0		10	114	55–210	10	106	51–195
Respiratory and intrathoracic organs (160–165)	5	83	27–194	112	130	107–156	117	127	105–152
Larynx (161)	–	0		12	151	78–264	12	141	73–246
Lung (162)	5	95	31–222	97	128	104–156	102	126	103–153
Pleura (163)	–	0		2	545	66–1969	2	510	62–1842
Bone and articular cartilage (170)	–	0		2	107	13–387	2	100	12–361
Melanoma of skin (172)	–	0		2	137	17–495	2	128	16–462
Prostate (185)	1	154		6	70	26–152	7	76	31–157
Bladder (188)	1	181		3	39	8–114	4	49	13–125
Kidney (189)	–	0		3	53	11–155	3	50	10–146
Brain (191)	–	0		7	129	52–266	7	122	49–251
Lymphatic and hematopoietic tissue (200–208)	–	0		11	96	48–172	11	90	45–161

Obs. – observed deaths;

SMR – standardized mortality ratio;

95%CI – 95% confidence interval.

Table 4. Mortality from malignant neoplasms (obs., SMR and 95%CI) by plant departments in the male subcohort of workers exposed to asbestos dust

Cause of death (coded according to ICD-9)	Departments											
	Yarn and cloth				Friction materials				Insulating materials			
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001-999)	198	144	125-166	151	148	125-174	219	145	126-166	785	138	129-148
Malignant neoplasms (140-208)	34	105	73-147	32	132	90-186	49	137	101-181	157	120	102-140
Lip, oral cavity and pharynx (140-149)	-	0		-	0		2	189	23-683	1	26	
Digestive organs and peritoneum (150-159)	11	97	48-174	12	146	75-255	15	123	69-203	63	138	106-177
Oesophagus (150)	1	120		2	324	39-1170	-	0		7	205	82-422
Stomach (151)	6	120	44-261	4	114	31-292	7	132	53-272	26	129	84-189
Colon (153)	-	0		1	141		2	191	23-690	9	236	108-448
Rectum and anus (154)	-	0		2	216	26-780	1	73		7	141	57-291
Liver (155)	3	254	52-742	-	0		2	157	19-567	5	105	34-245
Gallbladder (156)	-	0		-	0		3	931	192-2721	1	83	
Pancreas (157)	1	79		3	311	64-909	-	0		6	116	226-1341
Respiratory and intrathoracic organs (160-165)	16	129	74-209	14	148	81-248	20	145	89-224	62	123	94-158
Larynx (161)	2	177	21-639	2	228	28-824	1	78		7	150	60-309
Lung (162)	14	129	71-216	12	145	75-253	19	156	94-244	52	117	87-153
Pleura (163)	-	0		-	0		-	0		2	932	113-3367
Bone and articular cartilage (170)	1	373		-	0		-	0		1	90	
Melanoma of skin (172)	-	0		1	608		1	424		-	0	
Prostate (185)	1	80		-	0		2	147	18-531	3	59	12-172
Bladder (188)	-	0		-	0		1	83		2	45	5-163
Kidney (189)	-	0		-	0		-	0		3	91	19-266
Brain (191)	1	132		-	0		2	229	28-827	4	126	34-323
Lymphatic and hematopoietic tissue (200-208)	2	123	15-444	1	80		2	108	13-390	6	89	33-194

Abbreviations as in Table 3.

latter of pancreas cancer (6 deaths, SMR = 116, 95%CI: 226–1341) and pleural mesothelioma (2 deaths, SMR = 932, 95%CI: 113–3367). The risk of lung cancer was found to concern all the plant departments, but the SMR values ranging from 117 (for 52 deaths) to 156 (for 19 deaths) did not reach the level of statistical significance (Table 4).

The analysis by duration of employment under exposure revealed excess mortality from the same causes as those found for the whole cohort, but statistically significant findings for total cancers and lung cancer applied only to the workers with exposure below five years (155 deaths, SMR = 125, 95%CI: 106–146 and 59 deaths, SMR = 140, 95%CI: 107–181, respectively). In the group working for more than five years, the risk of death from these two causes was also increased, but its level was not statistically significant (SMR = 110 and 111, respectively). In all the groups classified by exposure duration, one case of pleural mesothelioma was recorded, which indicated about a five-fold increase, but death risk was not statistically significant compared to the level observed in the general population (Table 5). Mortality analysis with respect to the year of employment revealed that the highest risk of death from asbestos-related cancer concerned the workers hired by the plant between 1945 and 1955. They were characterized

by significant excess mortality from cancer (117 deaths, SMR = 139, 95%CI: 115–167), including lung cancer (42 deaths, SMR = 155, 95%CI: 112–210) and pleural mesothelioma (2 deaths, SMR = 1587, 95%CI: 192–5733). In workers employed in a later period of the plant's activity, the number of cancer deaths only slightly exceeded that in the general population (Table 6).

Mortality in the female cohort

Under the period of cohort tracing, 435 deaths cases were recorded among female workers compared to the expected 320.9 (SMR = 136, 95%CI: 124–149), which indicates a significantly higher mortality in the cohort than in the reference population. The main causes of this high mortality were malignant neoplasms (135 deaths, SMR = 159, 95%CI: 133–188), including gallbladder cancer (10 deaths, SMR = 257, 95%CI: 123–473), lung cancer (18 deaths, SMR = 259, 95%CI: 153–409), pleural mesothelioma (3 deaths, SMR = 2033, 95%CI: 419–5941), and cervical cancer (13 deaths, SMR = 196, 95%CI: 104–335) (Table 7).

Significant excess mortality from cancer was mostly found among female workers exposed to asbestos dust. This finding referred to total cancer cases (124 deaths, SMR = 162, 95%CI: 135–193), gallbladder cancer (9 deaths,

Table 5. Mortality from selected causes by duration of employment in the male subcohort of asbestos workers

Cause of death (coded according to ICD-9)	< 5 years			≥ 5 years		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001–999)	894	167	156–178	525	107	98–117
Malignant neoplasms (140–208)	155	125	106–146	126	110	92–131
Lung (162)	59	140	107–181	43	111	80–150
Pleura (163)	1	476		1	556	

Abbreviations as in Table 3.

Table 6. Mortality from selected causes by the year of starting employment in the plant in the male subcohort of asbestos workers

Cause of death (coded according to ICD-9)	1945–1955			1956–1973			1974–1980		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001–999)	468	125	114–137	779	140	130–150	172	182	156–211
Malignant neoplasms (140–208)	117	139	115–167	142	106	89–125	22	105	66–159
Lung (162)	42	155	112–210	52	112	84–147	8	110	47–217
Pleura (163)	2	1587	192–5733	–	0		–	0	

Abbreviations as in Table 3.

Table 7. Mortality from malignant neoplasms (obs., SMR and 95%CI) by exposure status in the female subcohort of asbestos workers

Cause of death (coded according to ICD-9)	Non-exposed			Exposed			Total	
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	95%CI
All causes (001-999)	21	68	42-104	414	143	130-157	435	136
Malignant neoplasms (140-208)	11	126	63-25	124	162	135-193	135	159
Digestive organs and peritoneum (150-159)	4	134	37-343	42	147	106-199	46	146
Oesophagus (150)	-	0		1	167		1	152
Stomach (151)	1	130		4	51	14-131	5	58
Colon (153)	1	285		5	159	52-371	6	171
Rectum and anus (154)	-	0		7	191	77-394	7	172
Liver (155)	1	236		8	187	81-368	9	192
Gallbladder (156)	1	269		9	256	117-486	10	257
Pancreas (157)	-	0		3	90	19-263	3	81
Respiratory and intrathoracic organs (160-165)	5	594	193-1386	17	240	140-384	22	278
Larynx (161)	-	0		1	320		1	285
Lung (162)	5	678	220-1582	13	209	111-357	18	259
Pleura (163)	-	0		3	2267	468-6625	3	2033
Bone and articular cartilage (170)	-	0		1	179		1	160
Melanoma of skin (172)	-	0		1	154		1	135
Breast (174)	1	76		18	170	101-269	19	159
Cervix uteri (180)	1	136		12	204	105-356	13	196
Ovary (183)	-	0		8	176	76-347	8	156
Bladder (188)	-	0		1	141		1	128
Kidney (189)	-	0		2	126	15-455	2	112
Brain (191)	-	0		3	161	3-471	3	142
Lymphatic and hematopoietic tissue (200-208)	-	0		1	25		1	22

Abbreviations as in Table 3.

Table 8. Mortality from malignant neoplasms (obs., SMR and 95% CI) by plant departments in the female subcohort of workers exposed to asbestos dust

Cause of death (coded according to ICD-9)	Departments											
	Yarn and cloth				Friction materials				Insulating materials			
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001-999)	157	153	130-179	21	185	115-283	119	118	98-141	117	156	129-187
Malignant neoplasms (140-208)	43	159	115-214	7	245	99-505	35	130	91-181	39	200	142-273
Digestive organs and peritoneum (150-159)	17	168	98-269	2	179	22-647	12	121	63-211	11	150	75-268
Oesophagus (150)	1	469		-	0		-	0		-	0	
Stomach (151)	2	71	9-256	-	0		-	0		2	98	12-354
Colon (153)	1	91		-	0		3	267	55-780	1	125	
Rectum and anus (154)	2	156	19-564	-	0		3	229	47-669	2	216	26-780
Liver (155)	5	327	106-763	-	0		2	136	16-491	1	90	
Gallbladder (156)	3	241	50-704	1	727		2	162	20-585	3	334	69-976
Pancreas (157)	1	86		-	0		1	84		1	119	
Respiratory and intrathoracic organs (160-165)	3	121	25-354	2	770	93-2782	7	274	110-565	5	278	90-649
Larynx (161)	-	0		-	0		-	0		1	1248	
Lung (162)	3	138	28-403	1	439		5	223	72-520	4	254	69-650
Pleura (163)	-	0		1	20 024*		2	4218	511-15 237	-	0	
Bone and articular cartilage (170)	-	0		-	0		-	0		1	696	
Melanoma of skin (172)	1	451		-	0		-	0		-	0	
Breast (174)	5	134	44-313	2	530	64-1915	5	131	43-306	6	222	81-483
Cervix uteri (180)	2	96	12-347	1	476		5	238	77-555	4	268	73-686
Ovary (183)	6	376	138-818	-	0		-	0		2	172	21-621
Bladder (188)	-	0		-	0		-	0		1	555	
Kidney (189)	-	0		-	0		1	174		1	249	
Brain (191)	1	155		-	0		1	147		1	210	
Lymphatic and hematopoietic tissue (200-208)	1	71		-	0		-	0		-	0	

* p < 0.01;

Abbreviations as in Table 3.

Table 9. Mortality from selected causes by duration of employment in the female subcohort of asbestos workers

Cause of death (coded according to ICD-9)	< 5 years			≥ 5 years		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001-999)	193	158	136-182	242	122	107-138
Malignant neoplasms (140-208)	57	178	135-231	78	147	116-183
Lung (162)	8	311	134-613	10	228	109-419
Pleura (163)	1	1667		2	2222	269-8027

Abbreviations as in Table 3.

Table 10. Mortality from selected causes by the year of starting employment in the plant in the female subcohort of asbestos workers

Cause of death (coded according to ICD-9)	1945-1955			1956-1973			1974-1980		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001-999)	193	145	125-167	195	115	99-132	47	267	196-355
Malignant neoplasms (140-208)	59	184	140-237	57	120	91-155	19	338	203-528
Lung (162)	8	332	143-654	5	123	40-287	5	1014	329-2366
Pleura (163)	2	3782	458-13 662	1	1250		-	0	

Abbreviations as in Table 3.

SMR = 256, 95%CI: 117-486), lung cancer (13 deaths, SMR = 209, 95%CI: 111-357), and pleural mesothelioma (3 deaths, SMR = 2267, 95%CI: 468-6625). The site of cancer, for which an increased risk could be found regardless of asbestos exposure was the lung. Among the exposed workers, the risk of lung cancer was doubled (13 deaths, SMR = 209, 95%CI: 111-357) and in the non-exposed population, six times higher (5 deaths, SMR = 678, 95%CI: 220-1582) compared with the reference population (Table 7).

An analysis by departments revealed in general an increased cancer risk for all the departments and significantly increased for asbestos yarn and cloth production (43 deaths, SMR = 159, 95%CI: 115-214) and auxiliary departments (39 deaths, SMR = 200, 95%CI: 142-273). An analysis by cancer site indicated a significant excess mortality from liver cancer in women working in the asbestos yarn and cloth production (5 deaths, SMR = 327, 95%CI: 106-763), pleural mesothelioma in those involved in the production of friction (1 case, SMR = 20024, $p < 0.01$) and insulation materials (2 cases, SMR = 4218, 95%CI: 511-15237), and ovarian cancer in women employed in the department of asbestos yarn and cloth production (6 deaths, SMR = 376, 95%CI: 138-818). In the departments under study, a non-

significant increase in the number of lung cancer cases among workers could be noted (Table 8).

A significant excess in general mortality and that from malignant neoplasms, including lung cancer, was found in the workers with both short and long period of employment under exposure. Among workers with a short exposure duration, the risk of lung cancer was found to be about three times higher (8 deaths, SMR = 311, 95%CI: 134-613) than in the reference population, while in those exposed for a longer period, this risk was more than twice as high (10 deaths, SMR = 228, 95%CI: 109-419). The latter group was also characterized by a significantly increased risk of pleural mesothelioma (2 deaths, SMR = 2222, 95%CI: 269-8027) (Table 9).

SMRs calculated for subcohorts distinguished by the year of employment pointed to a significant excess of all cancer cases (59 deaths, SMR = 184, 95%CI: 140-237), lung cancer (8 deaths, SMR = 332, 95%CI: 143-654) and pleural mesothelioma cases (2 deaths, SMR = 3782, 95%CI: 458-13662) among female workers hired by the plant between 1945 and 1955. However, the excess in all cancer cases and lung cancer in particular appeared to be still higher for workers who began their employment in 1974-1980 (19 deaths, SMR = 338, 95%CI: 203-528 and 5 deaths, SMR = 1014, 95%CI: 329-2366, respectively) (Table 10).

Asbestosis and asbestos-related cancer

An analysis of mortality among workers with and without diagnosed asbestosis, did not reveal direct association between the risk of asbestos-induced lung cancer and previously diagnosed asbestosis. Asbestosis concerned 371 cohort members (231 males and 140 females). In the group of workers with this disease, a higher than expected number of deaths from lung cancer could be noted (13 cases among males, SMR = 111, 2 cases among females, SMR = 210), but the excess was not statistically significant. An increased risk was also found for pleural mesothelioma (1 death in males, SMR = 1783 and 1 death in females, SMR = 5130, the latter at a statistically significant level, $p < 0.05$). However, the increased risk also applied to the workers without diagnosed asbestosis. The excess in lung cancer as well as pleural mesothelioma cases in female workers turned out to be statistically significant (Tables 11 and 12). These seemingly surprising values of cancer risk in the group of workers with and without asbestosis, become less “out of place” if you take into account the fact that the workers with asbestosis were characterized by a relatively longer period of employment under exposure. In the group of male workers with asbestosis, an average period of employment was over 22 years and in the female

group it was over 21 years. For comparison, other male and female workers had an average employment period of six and almost nine years, respectively. As mentioned above, an excess risk of lung cancer pertains mostly to workers with a shorter period of exposure (Tables 5 and 9).

Tobacco smoking

The data from medical records of the cohort members were used to estimate the proportion of smokers in the study population. It was found that 84.2% of male and 39.6% of female workers smoked. The findings indicate that the proportion of smokers in the male cohort exceeded that in the general population (84.2% vs. 75%), while in female workers the proportion of smokers was very close to the value found for the Polish female population (39.6% vs. 39.5%) [9]. When the SMRs for lung cancer were recalculated using Axelson's correction [7,8] that accounts for the smoking rate, the SMR_{cor} was 114 (95%CI: 93–138) for males and 259 (95%CI: 153–409) for females.

Pleural mesothelioma

Considering a very long latency period of pleural mesothelioma it is not surprising that a significant excess of this cancer could not be noted until the present study.

Table 11. Mortality from selected causes (obs., SMR, 95%CI) by diagnosis of asbestosis in the male subcohort of asbestos workers

Cause of death (coded according to ICD-9)	Asbestosis			No asbestosis diagnosed		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001–999)	113	84	69–101	1306	147	139–155
Malignant neoplasms (140–208)	35	105	73–146	246	120	105–136
Lung (162)	13	111	59–190	89	129	104–159
Pleura (163)	1	1783		1	298	

Abbreviations as in Table 3.

Table 12. Mortality from selected causes (obs., SMR, 95%CI) by diagnosis of asbestosis in the female subcohort of asbestos workers

Cause of death (coded according to ICD-9)	Asbestosis			No asbestosis diagnosed		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI
All causes (001–999)	49	123	91–163	386	137	124–151
Malignant neoplasms (140–208)	12	108	56–189	123	166	138–198
Lung (162)	2	210	25–759	16	267	153–434
Pleura (163)	1	5130*		2	1562	189–5642

* $p < 0.05$;

Abbreviations as in Table 3.

Table 13. Characteristics of workers (n = 5) who died from malignant pleural mesothelioma

Characteristics	Min-Max	$\bar{x} \pm SD^*$	Variation coefficient
Age at starting employment in the plant	16 – 46	26.8 $\pm$ 11.7	4.4
Duration of employment	1 – 34	17.6 $\pm$ 16.0	90.9
Concentration of asbestos dust (mg/m ³)	0.1 – 3.0	1.58 $\pm$ 1.17	74.1
Age at death	54 – 79	66.0 $\pm$ 9.0	13.6
Latency period	33 – 52	39.2 $\pm$ 8.3	21.2

* $\bar{x}$ – arithmetic mean;

SD – standard deviation.

Five deaths were recorded, including three of female workers. Of all five deaths, four were found in the workers employed in the plant before 1955 (the year when the ventilation system was installed). A significantly increased risk of this cancer was observed in the whole female cohort (3 deaths, SMR = 2033, 95%CI: 419–5941), and in female workers employed in the friction (1 death, SMR = 20024, $p < 0.01$) and insulation materials departments (2 deaths, SMR = 4218, 95%CI: 511–15237). This related to exposure for more than five years (2 deaths, SMR = 2222, 95%CI: 269–8027) and employment in the period of 1945–1955 (2 deaths, SMR = 3782, 95%CI: 458–13662).

In the male workers, an excess mortality from pleural mesothelioma was observed in the subcohort working in auxiliary departments; one technician and one mechanic died (2 deaths, SMR = 932, 95%CI: 113–3367). The risk of this cancer concerned only those workers who joined the plant before 1955 (2 deaths, SMR = 1587, 95%CI: 192–5733). The characteristics of workers who died from pleural mesothelioma is given in Table 13. As depicted, the mean age at which the deceased began their employment under exposure to asbestos dust was 27 years, their duration of employment was 18 years on average, they died at the mean age of 66 years after 39 years since the onset of exposure.

DISCUSSION AND CONCLUSIONS

The cohort of asbestos plant workers was formed about 20 years ago and comprised workers who began their employment between 1945 and 1973. Mortality analysis was performed three times: in 1981, 1985 and 1990. The present study concerns an enlarged cohort, including the workers

employed in the period of 1974–1980 and reports data on mortality in the cohort between 1945–1999.

The first analysis of mortality ratio carried out in 1981, revealed excess in cancer-related mortality, but the findings mostly applied to workers employed in the early years of the plant operation. A significantly increased number of cancer cases (18 deaths, SMR = 187, 95%CI: 111–296) among male workers and only a single case of death among females (SMR = 125) were recorded at that time. Since the number of deaths from lung cancer was increasing with the cohort enlargement and prolonged duration of tracing, one can deduce that the risk of this cancer was significantly increased in both the male (102 deaths, SMR = 126, 95%CI: 103–153) and female (18 deaths, SMR = 259, 95%CI: 153–409) populations. The findings are then consistent with a commonly expressed and well-documented view that exposure to asbestos dust increases the risk for lung cancer [10,11]. While in male workers the elevated risk was observed only among the exposed workers, in female workers it could be noted in the non-exposed group as well. The “non-exposed” were the administration workers whose workposts were outside the production departments and no measurements of asbestos dust concentrations were made. However, it should be noted that the office facilities were located in the same building practically next to production halls. Accordingly, one can hardly assume that the office workers would be completely free from asbestos dust exposure. This has been confirmed by 12 cases of asbestosis recorded among 329 workers classified under the “non-exposed” category.

It is worth noting that in the cohort, the risk of lung cancer in the female workers was twice as high as in the male

workers, while in the general population a reverse tendency can be noted: lung cancer risk among males was found to be six times higher than in females. This result of our study would thus indicate that women may be more sensitive to asbestos dust than men. Similar unfavorable result obtained in the females for pleural mesothelioma can be explained by different anatomic (e.g., body size) and physiologic (e.g., breathing mode) characteristics between male and female patients. The female characteristics enhances asbestos fiber retention in the lungs and facilitates cancer development [12].

The increased risk of lung cancer was noted in the workers at all the departments under study, but it was not statistically significant.

As revealed in the analysis by exposure duration, the excess risk of lung cancer applied to male workers employed for less than 5 years. In the female cohort the risk of lung cancer was increased, regardless of exposure duration. This finding also concerned the general and cancer-related mortality. One may expect that in the group of workers with a short duration of employment, the effects of other undefined occupational exposures at previous workplaces will become evident. This group may also be characterized by a larger number of hazardous lifestyle factors than the workers with longer employment.

These aspects may affect the results of an analysis that takes account of the asbestosis diagnosed in the cohort. The views on a possible association between asbestosis and the risk of lung cancer in workers exposed to asbestos dust vary among the researchers [13–22]. In the study cohort, an excess mortality from lung cancer could be noted in both groups of workers with and without diagnosed asbestosis. Moreover, a statistically significant risk of lung cancer was found only in the group of workers without asbestosis. This might be due to the confounding variable of “employment duration” since the workers with asbestosis naturally worked for a longer period under exposure. One should add that the absence of a significant lung cancer risk in the asbestosis-affected population, which seems contradictory to the findings of other cohort studies on workers with asbestosis [13–24], is actually far from being realistic. In other studies, the cohort tracing started from

the date of diagnosed asbestosis, while in the present project it started from the date of the worker’s employment in the asbestos plant.

The problem of tobacco smoking as a factor modifying the risk of lung cancer has been investigated from the beginning of the cause-effect epidemiological studies on populations exposed to asbestos dust [25–27]. The outcomes of numerous analyses have definitely confirmed that smoking contributes to an increased risk of lung cancer. However, it remains to be investigated whether the combined effect of both causal agents: smoking and asbestos dust, is of additive or multiplicative nature [28–38]. Since it was extremely difficult to obtain individual data on the smoking habit in the retrospective cohort, which is a common methodological obstacle, we decided to apply Axelson’s correction [7,8] that makes it possible to assess lung cancer risk once the impact of tobacco smoking is eliminated. For this purpose we used, medical records of prophylactic examinations and medical consultations of asbestos plant workers who were referred to the Nofer Institute of Occupational Medicine for check-ups. Like in other studies on asbestos dust exposure, current and ex-smokers prevailed in the cohort [8,39–41], making 84.2% of the male and 39.6% of the female populations. The respective values for the general population of Poland are 75.0% and 39.6%. Considering that the percentage of smoking women in the study cohort and in the general population was the same, Axelson’s correction did not affect the risk of death from lung cancer ($SMR_{cor} = SMR = 259$). The proportion of male smokers in the study cohort was significantly higher than in the general population of Poland (84.2% vs. 75.0%) and after applying Axelson’s correction ($SMR_{cor} = 114$) it points to a statistically insignificant increase in the risk of lung cancer development. However, considering the proven synergistic effect of tobacco smoking and asbestos exposure, we are aware that the corrected value does not reflect the risk in the real carcinogen-exposed population. The value of the true risk of cancer development in the male cohort was $SMR = 126$.

Unlike the earlier stages of the analysis, the present study revealed a significantly increased risk for pleural mesothelioma that is specific for asbestos exposure. The increased

incidence of mesothelioma could be detected only as late as at this stage of our study because of very long latency period of this neoplasm. Prolonged observation of the cohort revealed five cases of this cancer, with an average latency period of more than 39 years.

In other cohort studies on workers exposed to asbestos dust, excess mortality from other cancer sites [28,42–44] could also be noted. In the female population this finding applied to gallbladder, cervical and breast cancers, and in men to gallbladder and large intestine cancers. The increased risk for large intestine cancer is consistent with the outcomes of the meta-analysis [45] concerning 31 reports on workers' exposure to asbestos dust.

The results of the present prolonged cohort tracing of asbestos workers revealed a significant health hazard from exposure, manifested by an increased risk of lung cancer and pleural mesothelioma. This refers particularly to female workers for whom the mortality ratio was found to be 2.5 times as high as for the female general population.

Further report will be devoted to the risk of lung cancer in relation to the exposure level in terms of an absorbed dose of asbestos dust.

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