Scand J Work Environ Health 1986;12(6):538-544

<https://doi.org/10.5271/sjweh.2103>

Issue date: Dec 1986

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The following article refers to this text: [2011;37\(4\):316-324](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/3823802

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Mortality and incidence of cancer among Swedish rubber workers, 1952–1981

by Per Gustavsson, MD,¹ Christer Hogstedt, MD,^{1,2} Bo Holmberg, PhD³

GUSTAVSSON P, HOGSTEDT C, HOLMBERG B. Mortality and incidence of cancer among Swedish rubber workers, 1952–1981. *Scand J Work Environ Health* 12 (1986) 538–544. The mortality and incidence of cancer was studied among 8 734 workers from two Swedish rubber manufacturing companies. Mortality was investigated from 1952 to 1981 and cancer incidence from 1959 to 1980. The expected numbers of deaths were calculated from national statistics. No significant risk excesses were detected when the cohort was analyzed without consideration of employment time or latency period. However, the mortality from coronary heart disease and the incidence of lung cancer were increased when the study period was limited to ≥ 40 years since first employment. The standardized mortality ratio for coronary heart disease correlated positively with employment duration. The mortality from asthma, bronchitis, and emphysema was nonsignificantly increased. The incidence of bladder cancer was increased among individuals with heavy and long-term exposure in the weighing and mixing departments. Twenty-five percent of the individuals in the cohort were not Swedish citizens at the time of employment, and an analysis of the mortality and cancer incidence in this group showed a markedly increased lung cancer incidence for certain immigrant groups, probably mainly due to ethnic factors. The results indicate that ethnic factors must be considered in the analysis of occupational groups when a high proportion of the workers are immigrants.

Key terms: bladder cancer, coronary heart disease, epidemiology, lung cancer, rubber chemicals.

Workers in the rubber industry may be exposed to a wide variety of chemicals — natural and synthetic rubber, rubber additives, dust, organic solvents, and substances formed during the vulcanization process (19). An epidemiologic investigation published in 1954 showed an excess of bladder cancer (6) among rubber workers in the United Kingdom. Exposure to 2-aminonaphthalene, an aromatic amine present in rubber antioxidants as an impurity, was pointed out as the causative agent for bladder cancer (6). Such compounds were abandoned around 1950 in the United Kingdom. Further investigations of the rubber industry in this same country showed an increased frequency of lung cancer and cancer of the gastrointestinal organs (5, 14, 15, 30, 32, 34).

In contrast to the British rubber industry, reports of increased malignancies of the hematopoietic system are frequent from the rubber industry in the United States (3, 24, 25, 27). Increases of bladder cancer (8, 27), lung cancer (2, 27), esophageal cancer (9), and prostatic cancer (16, 24) have also been reported. A Swedish record-linkage study of vulcanization workers

has shown an increased incidence of esophageal cancer (29).

Some rubber additives used in the manufacturing process are mutagenic in bacterial test systems (18), and vulcanization gases also have mutagenic properties (10, 17). Biological monitoring of workers in the weighing and mixing departments showed an increased frequency of chromosome aberrations in peripheral lymphocytes (23), and an increased mutagenic activity in the urine (31). These observations indicate that rubber workers are exposed to mutagenic substances in the work environment, and they are consistent with the epidemiologic findings of increased cancer risks. The cancer hazard in the rubber industry was evaluated by the International Agency for Research on Cancer in 1982 (21).

A retrospective cohort study from two Swedish rubber manufacturing industries was initiated in the middle of the 1970s, and the results of a follow-up during the period 1961 to 1977 have been reported earlier (20). The cohort comprised 13 114 individuals. Of these 2 492 were unexposed office workers, included as an internal reference group. The preliminary results showed an excess of malignancies in the lungs, gastrointestinal organs, urinary bladder, and skin among the exposed workers, as well as an increased mortality from coronary heart disease. However, several risk excesses were also detected among the unexposed office workers, a finding that made the interpretation of the results somewhat complicated.

The follow-up of this cohort of rubber workers has now been extended prospectively and retrospectively to cover the time period 1952 to 1981. Furthermore,

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the results have been analyzed with regard to employment time, latency period, calendar time, and the nationality of the cohort members.

Subjects

Company records were used as a source from which to gather information about the workers' personal identification number, name, exposure, employment period, and nationality at the time of first employment. All manufacturing workers, ie, workers in the weighing and mixing departments, calender workers, vulcanizers, pressing workers, tire builders, inspection and maintenance workers, cleaners, and storage handling workers, were included in the exposed group. All white-collar workers, ie, office workers and department heads, were included in the unexposed group. Persons changing their employment status from manufacturing worker to office worker were included in the exposed group, the change being accounted for in the calculation of exposure time.

The original cohort consisted of 14 611 persons, also including those who were lost to follow-up. The following restrictions or corrections were applied to the cohort:

- Individuals with an employment time of less than one year were excluded.
- Individuals leaving work before 1952 were excluded since follow-up was not possible via the national computerized registers before this year. However, many individuals started work several decades earlier.
- Personal identification numbers were checked, and duplicates in the registrations were corrected.

After these procedures the cohort consisted of 12 212 persons (7 932 men and 4 280 women). The total number of person-years at risk in the exposed group was 179 894. At the start of employment 9 105 individuals were Swedish citizens, and the rest were immigrants, mainly from the Nordic countries, Yugoslavia, and Greece.

Methods

The follow-up procedure included the matching of the personal identification numbers with computerized registers at the Swedish National Central Bureau of Statistics. Registers of the total living population, emigrations and immigrations since 1968, and deaths since 1952 were used. Mortality was investigated for the period 1952 to 1981. Cancer cases in the cohort were identified for the period 1959–1980 by matching with the National Cancer Register. Individuals not traced in these registers were considered lost to follow-up and were excluded. Individuals who had emigrated were also excluded from the statistical analysis.

The number of deaths, cancer cases, emigrations, and individuals lost to follow-up are presented in ta-

Table 1. Vital status at the end of follow-up (31 December 1981).

Group	Workers (N)	Deaths (N)	Cancers (N)	Emigrations (N)	Lost to follow-up (N)
Exposed					
Men	6 552	875	336	506	238
Women	3 267	173	143	261	80
Unexposed					
Men	1 380	101	53	17	19
Women	1 013	31	38	9	25
Total	12 212	1 180	570	793	362

ble 1. The proportion of individuals lost to follow-up was 3 % (362 of 12 212 persons). Among individuals with Swedish nationality the proportion was 1.2 % (110 of 9 105 persons).

The computation of expected values was based on national statistics for mortality and cancer incidence. The computations were performed according to the person-year method, counting man-years at risk specific for gender, calendar year, and five-year age class. The number of person-years in each stratum was multiplied with the disease rates in the corresponding stratum of the national statistics, and the number of expected cases was added over strata. The summary risk measure obtained was the standardized mortality (or morbidity) ratio (SMR) computed as (observed/expected) $\times 100$. Confidence limits for the SMR were computed with an exact method (28). Significance testing was based on the addition of probabilities derived from the Poisson distribution, and two-sided tests were used. Latency time was calculated as the time period from first employment until the start of risk calculation. The computations were performed with a computer program developed at the University of Linköping (1) for epidemiologic calculations.

Non-Swedish citizens at the time of first employment comprised 25 % of the total; this level is higher than the national average. Since cause-specific mortality and incidence of cancer vary between ethnic groups, the majority of the statistical analyses were performed on the Swedish citizens in the cohort (tables 2–10). Mortality and incidence of cancer among the immigrants was analyzed separately (table 11).

Table 2. Observed (O) and expected (E) numbers of deaths, 1952–1981. (SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval for the SMR)

Group	O	E	SMR	95 % CI
Exposed				
Men	798	904	88	82–94
Women	158	220	71	61–83
Unexposed				
Men	97	132	73	59–89
Women	31	37	83	56–117

Table 3. Mortality by cause among exposed male Swedish rubber workers. Risk calculation up to and including 79 years of age, latency requirement 10 years. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval for the SMR)

Cause of death ^a	O	E	SMR	95 % CI
Malignant tumors, all (140–209)	163	166.65	98	83–114
Esophagus (150)	1	3.55	28	0–156
Stomach (151)	18	20.41	88	52–139
Small and large intestine (152–153)	10	12.35	81	38–148
Rectum (154)	6	7.49	80	29–174
Liver (155)	4	3.56	112	30–287
Pancreas (157)	14	11.37	123	67–206
Lung (162)	32	29.91	107	73–151
Prostate (185)	13	16.95	77	40–131
Bladder (188)	4	5.33	75	20–192
Kidney (189)	8	7.91	101	43–199
Lymphoma and myeloma (200–203)	8	8.92	90	38–176
Leukemia (204–207)	6	6.58	91	33–198
Circulatory diseases (390–458)	331	332.69	99	89–110
Ischemic heart disease (410–414)	232	238.66	97	85–110
Cerebrovascular disease (430–438)	57	54.65	104	78–135
Respiratory diseases (460–519)	34	29.61	115	79–160
Asthma, bronchitis and emphysema (490–493)	16	12.70	126	72–204
Digestive diseases (520–577)	20	33.35	60	36–92
Liver cirrhosis (571)	5	13.24	38	12–88
Genitourinary diseases (580–607)	5	12.25	41	13–95
Nephritis and nephrosis (581–584)	3	4.72	64	13–185
External causes (800–999)	62	75.36	82	63–105
Other causes of death	35	59.10	59	41–82
Total deaths (0–999)	650	709.01	92	84–99

^a Code of the International Classification of Diseases, eighth revision, in parentheses.

Table 4. Observed (O) and expected (E) incidence of cancer, 1959–1980. (SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval for the SMR)

Group	O	E	SMR	95 % CI
Exposed				
Men	299	291.8	102	91–114
Women	126	139.2	91	75–107
Unexposed				
Men	52	44.6	117	87–152
Women	38	29.8	128	90–174

Results

The observed total mortality was lower than the expected (table 2) due to the so-called “healthy worker effect.” Cause-specific mortality was calculated for the exposed men (table 3). There was a slightly increased mortality from asthma, bronchitis, emphysema, and pancreatic cancer. None of these risk elevations was statistically significant.

The total cancer incidence corresponded well with the expected (table 4). Site-specific cancer incidence was calculated for the exposed men (table 5). No significant risk excesses were observed.

In the analysis of the mortality and incidence of cancer during different time periods after first employment (table 6), the SMR values for total numbers of deaths, coronary heart disease, and total cancer incidence increased with increasing follow-up time. There was a significantly increased incidence of lung cancer

Table 5. Cancer incidence by site among exposed male Swedish rubber workers, 1959–1980. Risk calculation up to and including age 79 years, latency requirement 10 years. (O = observed number of cases, E = expected number of cases, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval for the SMR)

Site of tumor ^a	O	E	SMR	95 % CI
Nasopharynx (146)	—	0.67	0	0–553
Esophagus (150)	1	3.33	30	0–167
Stomach (151)	20	20.57	97	59–150
Colon (153)	15	17.41	86	48–142
Liver (155)	7	5.96	117	47–242
Pancreas (157)	11	9.64	114	56–204
Nose and sinuses (160)	1	0.80	125	3–697
Larynx (161)	5	3.49	143	46–334
Lung, pleura (162)	32	28.89	111	75–156
Prostate (177)	34	41.29	82	57–115
Kidney (180)	12	12.12	99	51–173
Bladder (181)	17	16.25	105	60–167
Skin, malignant melanoma (190)	6	5.94	101	37–219
Skin, nonmelanoma (191)	7	6.48	108	43–222
Soft tissue sarcoma (197)	1	1.96	51	1–284
Multiple myeloma (203)	5	3.90	128	41–299
Leukemia (204–207)	7	7.46	94	37–193
Other sites	76	60.90	124	98–156
All sites (140–209)	257	247.06	104	91–117

^a Code of the International Classification of Disease, seventh revision, in parentheses.

after 40 years or more since first employment. The SMR for asthma, bronchitis, and emphysema fluctuated, the risk during follow-up between 20 and 40 years after first employment being nearly statistically significant [95 % confidence interval (CI) for the SMR

Table 6. Mortality and cancer incidence by time since first employment. Risk calculation up to and including 79 years of age. (SMR = standardized mortality ratio)

	Time since first employment (years)									
	≤ 9		10–19		20–29		30–39		≥ 40	
	Number	SMR	Number	SMR	Number	SMR	Number	SMR	Number	SMR
Total deaths	66	59	168	81	214	94	125	83	143	114
Ischemic heart disease	16	66	40	67	79	101	52	96	61	126
Asthma, bronchitis and emphysema	2	133	3	94	8	194	5	173	–	0
Cancer incidence	27	93	64	90	77	94	59	113	57	133*
Lung cancer	–	0	5	64	8	83	5	79	14	274*
Pancreatic cancer	3	283	3	113	4	126	2	96	2	116
Bladder cancer	2	121	2	69	6	110	7	196	1	35

* $p < 0.05$.

Table 7. Mortality and cancer incidence by employment time. Risk calculation up to and including 79 years of age, latency requirement 40 years. (SMR = standardized mortality ratio).

	Employment time (years)					
	< 20		20–29		≥ 30	
	Number	SMR	Number	SMR	Number	SMR
Total deaths	21	105	12	112	110	116
Circulatory diseases	8	74	6	103	71	141*
Ischemic heart disease	5	63	5	114	51	142*
Cancer incidence	10	149	7	186	40	124
Lung cancer	3	366	2	417	9	236*

* $p < 0.05$.

Table 8. Mortality among workers in the weighing and mixing departments, 1952–1981, as divided into two subgroups. Risk calculation up to and including 79 years of age. (SMR = standardized mortality ratio).

Cause of death ^a	Subgroup 1 ^b		Subgroup 2 ^c	
	Number	SMR	Number	SMR
Malignant tumors, all (140–209)	25	100	14	126
Esophagus (150)	–	0	–	0
Stomach (151)	3	96	2	141
Small and large intestine (152–153)	2	107	2	240
Rectum (154)	1	87	–	0
Liver (155)	–	0	–	0
Pancreas (157)	2	116	–	0
Lung (162)	5	109	4	197
Prostate (185)	2	71	–	0
Bladder (188)	2	235	2	524
Kidney (189)	2	173	1	192
Lymphoma and myeloma (200–203)	2	156	1	57
Leukemia (204–207)	–	0	–	0
Circulatory diseases (390–458)	55	106	30	130
Ischemic heart disease (410–414)	44	118	22	132
Cerebrovascular disease (430–438)	7	83	5	133
Respiratory diseases (460–519)	5	111	3	150
Asthma, bronchitis and emphysema (490–493)	1	51	1	115
Digestive diseases (520–577)	3	66	2	99
Liver cirrhosis (571)	–	0	–	0
Genitourinary diseases (580–607)	1	54	1	120
Nephritis and nephrosis (581–584)	1	154	1	341
External causes (800–999)	8	101	2	58
Other causes of death	5	72	4	112
Total deaths (0–999)	102	98	56	122

^a Code of the International Classification of Diseases, eighth revision, in parentheses.

^b Subgroup 1 had an exposure time of one year or more, a latency of at least 10 years, and no restriction on time of first employment.

^c Subgroup 2 had an exposure time of five years or more, a latency of at least 20 years, and first employment before 1951.

being 98–388]. The number of cases of pancreatic cancer and bladder cancer was small, the SMR fluctuated, and there was no time trend.

For a further evaluation of the observed risk excesses the relation between exposure time and SMR was investigated, with a latency requirement of 40 years

(table 7). The mortality from diseases of the circulatory system was positively correlated to duration of exposure. An increased incidence of lung cancer was observed in all three exposure-time categories, but the SMR was significantly raised only among those exposed for at least 30 years. The time trend could not be evaluated because of the small number of observed cases.

A group of exposed individuals had worked in the weighing and mixing departments, “mixers.” The SMR was computed for mixers with a latency requirement of 10 years (subgroup 1) and for a subgroup first employed before 1951, exposed more than five years, and with a latency requirement of 20 years (subgroup 2) (table 8). The latter subgroup was more heavily exposed since the exposure time was longer and the exposure occurred in a time period when dust control was less developed. The SMR was higher among the more heavily exposed for a majority of the causes of death, but it was not significantly raised for any of the studied diagnoses. The cancer incidence for the mixers is presented in table 9. Again the SMR was higher in the more highly exposed group when compared to that of all mixers. Four cases of bladder cancer were observed versus 1.08 expected, corresponding to an SMR of 368 ($p < 0.05$).

The mortality and cancer incidence by time of first employment was analyzed (table 10). There was an excess of lung cancer only among those employed before 1951. However, it should be pointed out that this is another reflection of the findings in the latency time analysis (table 6), since only those first employed before 1941 had a latency of 40 years within the study period, and therefore they were all included among those first employed before 1951.

Among the office workers, an increased incidence of tumors of the lung and larynx was found (11 observed versus 4.46 expected lung tumors and 3 observed versus 0.59 expected cases of laryngeal cancer). However, no relation to latency from first employment was found in this group, in contrast to the exposed group.

The mortality and incidence of cancer among the exposed male immigrants was analyzed (table 11). The Swedish national statistics were used as a reference, and the results must be interpreted with caution since ethnic factors, as well as occupational exposures, may

Table 9. Incidence of cancer among workers in the weighing and mixing departments, 1959–1980, as divided into two subgroups. Risk calculation up to and including 79 years of age. (SMR = standardized mortality ratio)

Site of tumor ^a	Subgroup 1 ^b		Subgroup 2 ^b	
	Number	SMR	Number	SMR
Nasopharynx (146)	—	0	—	0
Esophagus (150)	—	0	—	0
Stomach (151)	3	94	2	142
Colon (153)	2	77	2	174
Liver (155)	1	107	—	0
Pancreas (157)	1	67	—	0
Nose and sinuses (160)	—	0	—	0
Larynx (161)	1	197	—	0
Lung, pleura (162)	5	113	4	204
Prostate (177)	5	72	2	66
Kidney (180)	3	174	2	259
Bladder (181)	4	164	4	368*
Multiple myeloma (203)	1	168	1	379
Leukemia (204–207)	1	94	—	0
Other sites	10	124	6	168
All sites (140–209)	37	101	23	141

^a Code of the International Classification of Diseases, seventh revision, in parentheses.

^b Subgroups as in table 8.

* $p < 0.05$.

Table 10. Mortality and incidence of cancer by time of first employment. Risk calculation up to and including 79 years of age, latency requirement 10 years. (SMR = standardized mortality ratio).

	First employment			
	Before 1951		1951 or later	
	Number	SMR	Number	SMR
Total deaths	434	88	216	101
Ischemic heart disease	167	100	65	91
Asthma, bronchitis and emphysema	11	125	5	128
Cancer incidence	177	104	80	104
Lung cancer	25	124	7	80
Pancreatic cancer	7	102	4	142
Bladder cancer	12	103	5	98

Table 11. Mortality and incidence of cancer among immigrants by citizenship at time of employment. Swedish national statistics used as reference. Risk calculation up to and including 79 years of age.

	Finnish		Danish		Yugoslavian		Other	
	Number	SMR	Number	SMR	Number	SMR	Number	SMR
Total deaths	31	193*	16	86	6	83	26	98
Circulatory diseases	8	179	4	54	1	61	12	117
Violent death and intoxication	13	228*	1	28	4	140	4	77
Cancer incidence	8	151	13	194*	3	130	10	109
Lung cancer	3	633*	4	526*	—	0	2	199

* $p < 0.05$.

have influenced the results. Immigrants from Finland had an increased total mortality, an increased risk for violent death, and an increased lung cancer incidence. Immigrants from Denmark had a raised cancer incidence and lung cancer incidence. Immigrants from Yugoslavia and other immigrant groups did not exhibit significant excess risks.

Discussion

There was no significantly increased mortality or cancer incidence among the rubber workers when the cohort was analyzed without regard to latency or exposure time. However, the mortality from coronary heart disease and the incidence of lung cancer was increased when 40 years had elapsed since first employment. The SMR for coronary heart disease correlated positively with employment time. The finding of a dose-response relationship indicates that the risk excess was due to occupational factors. An increased risk for coronary heart disease was reported in two earlier studies (2, 26), but has not been found in the majority of studies on rubber workers.

The finding of a risk excess only after more than 40 years since first employment may be interpreted in the following two ways: first, the causative agent might not have been present after 1940, and, second, the toxic agent might take four decades or more to manifest its effect as increased mortality. A median latency time of 38.5 years was described for lung cancer caused by exposure to asbestos (4), and a similar relationship between lung cancer and rubber work is possible. No definite conclusions can be drawn on this point, and it remains unknown if the causative factor has been present in more recent time periods or not.

The mortality from asthma, bronchitis, and emphysema (ICD 490–493) was increased in the time period 20–40 years after first employment. The increase was of borderline statistical significance. An increased frequency of chronic bronchitis and reduced pulmonary function was earlier reported among rubber workers (11, 12, 13), but increased mortality from lung diseases has not been reported earlier.

Bladder cancer is well documented as an occupational cancer hazard among rubber workers. In this study, a risk excess was found only among individuals who had worked in the weighing and mixing departments before 1951. Similar results were obtained in a case-referent study from the rubber industry in the United States, where an excess risk of bladder cancer was noted especially among workers in a mixing department and among calender workers (7). It seems probable that the special exposure conditions in these departments are related to the bladder cancer excess, especially since an increased mutagenic activity in urine has been found among workers in mixing departments (31). However, excess risks for bladder cancer may exist also in other departments, even if not detected in this study.

The present results, obtained after an extension of the follow-up period to 1952–1981, differ on some points from the earlier report covering the time period 1961–1977 (20). The proportion of individuals lost to follow-up has been reduced by the restrictions made with regard to nationality, employment time, and employment period. Increased frequencies of liver and pancreas tumors and of malignant melanomas were observed among the exposed workers in the earlier report. After the extension of the follow-up period no excess risks were noted for these tumor sites. The excess risk for respiratory malignancies observed among unexposed men was unaffected by the extension. The exposure classification was rechecked and found to be correct. The excess remains unexplained, but could partially be due to smoking habits.

The number of observed cases of leukemia corresponded well with the number expected; this finding contrasts with the results of several American studies of rubber workers. Benzene was earlier used as a solvent in the rubber industry but was abandoned in the Swedish industry before 1950. It seems as if benzene has been used in more recent years in the American rubber industry (22), and its use could explain the epidemiologic finding.

The analysis of mortality and cancer incidence among the immigrants revealed some high excess risks. Immigrants from Finland had an increased total mortality and an increased incidence of lung cancer and violent deaths. It should be pointed out that the Swedish national statistics were used as reference. Therefore, the results reflect a combination of occupational and ethnic factors. Regarding the first, it is possible that the immigrants got the “worst” jobs and therefore had a higher exposure. However, no corresponding risk excesses were observed for immigrants from non-Scandinavian countries. Regarding the latter, the Finnish population has a higher incidence of lung cancer (33) and coronary heart disease (35) than the Swedish population, and the increased risks can, to a large extent, be explained by ethnic factors. Since no individual exposure data are available, this question remains unanswered, but the results are important from a methodological point and show that the ethnic composition of a cohort must be accounted for in the analysis.

The cohort comprised individuals of different job categories and, with the exception of mixers, a job-specific analysis was not possible. Additional excess risks, related to uncommon exposure factors, cannot be ruled out. The conclusions that can be drawn concerning the risks associated with the present exposure situation in the rubber industry are limited. Exposure levels have been reduced in comparison to the situation in the 1930s and 1940s. The long latency time for the diseases under study makes it impossible to evaluate epidemiologically the effects of exposures during more recent decades. However, the results from gen-

otoxicologic investigations made during recent years corroborate the epidemiologic findings and indicate that a further reduction of exposure is warranted.

Acknowledgments

We thank Dr A Englund, Dr K Gumaelius, Mr L Holmlund, Dr L Kestrup, Mr R Maasing, Dr G Molina, and Dr P Westerholm who have contributed to the study at different stages. Ms A Gustavsson skillfully assisted with the data analysis.

The study was supported by a grant from the Swedish National Board of Occupational Safety and Health.

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Received for publication: 4 July 1986.