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Retrospective cohort study of two plants in the Swedish rubber industry

by Bo Holmberg, PhD,[1] Peter Westerholm, MD,[2] Rein Maasing, BSc,[3] Lars Kestrup, MD,[4] Karl Gumaelius, MD,[5] Lars Holmlund,[3,6] Anders Englund, MD[7]

HOLMBERG B, WESTERHOLM P, MAASING R, KESTRUP L, GUMAELIUS K, HOLMLUND L, ENGLUND A. Retrospective cohort study of two plants in the Swedish rubber industry. *Scand j work environ health* 9 (1983): suppl 2, 59–68. A cohort of 13,114 workers employed during 1930–1975 in two Swedish plants producing tires and industrial rubber goods was investigated with regard to cancer mortality and cancer incidence. Separate analyses were performed on the following subgroups of the cohort: mixers/weighers, other production workers, and white-collar employees. For all causes of death no increase of risk was observed in the population as a whole. Mixers/weighers showed however an increased overall standardized mortality ratio. The pattern of causes of death was not changed in the total cohort. An increased risk to die from liver cancer (risk ratio 4.12) and pancreatic cancer (risk ratio 2.70) was, however, observed for the category other production workers. An increased risk of death from tumors of the respiratory organs was also observed for the categories other production workers (risk ratio 1.89) and white-collar employees (risk ratio 2.63). For tumors in the urinary bladder (risk ratio 2.50) and for ischemic heart diseases (risk ratio 1.27) the death risk was elevated for the category other production workers. The cancer morbidity pattern showed an increase in malignant melanomas (risk ratio 2.50) for the category other production workers and for lung cancer (risk ratio 2.09), as well as for tumors in the nervous system (risk ratio 3.18) for white-collar employees.

Key terms: gastrointestinal tumors, ischemic heart disease, liver cancer, malignant melanomas, pancreas cancer, retrospective cohort study, tumors of respiratory organs, tumors of the nervous system, tumors of the urinary bladder.

The rubber industry is characterized by a broad exposure panorama in terms of added chemicals (19) and emitted gases and vapors (22). This industry belongs to the most extensively studied at the international level (22). A diversified cancer mortality and cancer morbidity pattern has been described. Cancer of the urinary bladder is strongly associated with rubber work; it is probably induced by bicyclic aromatic amines (9, 15, 27, 41). American studies (22) also show an elevated risk to leukemia. Other cancer sites associated with an elevated risk in the rubber industry or found in case studies are brain tumors, lung cancer, and gastrointestinal cancer (22).

No Swedish cohort study from the rubber industry has earlier been published. A noteworthy number of cases of brain cancer has, however, been reported in a study using the central Cancer Register (13).

Materials and methods

Data collection and treatment

The following data were collected from two plants in the rubber industry: personal identification number, name, start and end

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(year and month) of (each) employment period, and class of exposure.

For a worker to be included in the original cohort, employment should have started on 1 January 1931 or later and should have lasted at least 12 months. No lower time limit was set for exposure class 1. The last date for entry into the cohort was set at 31 December 1975. For persons employed more than once, the beginning of the first period was counted as the beginning of exposure.

The exposure was classified as (i) work in the weighing and mixing department, (ii) other production work (eg, calendering, vulcanization, pressing, tire building, inspection, service work, floor cleaning, storage work), (iii) white-collar work (office personnel, department heads).

The collected data were transferred to magnetic tape for the statistical analyses. By means of computerized record linkage operations the magnetic tape was completed with data on persons still alive and those who had died between 1 January 1961 and 31 December 1978. The data sources for this follow-up procedure were the Total Population Register and the Causes of Death Register of the Central Bureau of Statistics. The latter register is based on centrally performed coding and classification of certificates of death. Persons who emigrated during the 1970s were identified in the Emigration Registry. The magnetic tape was also compared with data in the central Cancer Register for cancer incidence from 1959 to 1977, inclusive.

The statistical calculations were made according to two models (A and B). In model A the observed and expected number of deaths and cancer cases were calculated per calendar year. In model B the observed and expected yearly risks were calculated per risk year.

For information on whether the length of exposure affected the pattern of causes of deaths, the following latency times were defined:

Short latency time: total exposure time of less than five years; time under risk was defined as from the start of exposure until five years after the end of exposure.

Long latency time: total exposure time of five years or more; the duration of time under risk was defined as from five years after the start of exposure until 25 years after the end of exposure.

Number of persons employed in 1961 or later, calculated with length of time under risk defined as from the start of exposure.

Latency time and length of time under risk, calculated from the start of exposure regardless of when the start of exposure occurred.

For all the preceding definitions the causes of deaths before 1961 were not possible to determine. All the calculations were thus made from 1961 onwards. Therefore, for short latency times only those persons who had started their exposure in 1951 or later were included. For long latency time only those persons were included who started their exposure in 1931 or later.

For model B the death risk in a particular risk year x, x + 1, was calculated according to the formula $q_x = 1\text{-}p_x$, where p_x is the probability for surviving that particular year (10).

$$P_x = \{-0.5\, d_x' + [d_x'^2/4 + 4(N_x - n_x/2)\,(s_x + w_x/2)]^{1/2} / [2(N_x - n_x/2)]\}^2,$$

where N_x is the number of persons entering the time interval x, $x + 1$, and n_x is the number of persons in their last interval, s_x the number of persons surviving the entire interval, w_x the number of persons who lived during the time interval but who were excluded from the model cohort under the time interval, and, finally, d_x' the number of persons who died between the start of the interval and before the time for exclusion from the model cohort.

The expected risk was calculated as the mean value of the risks of each individual, calendar year and age being taken into consideration. The cumulated probability P_{0x} for observed and expected survival was calculated according to

$$p_{0x} = p_0 \times p_1 \times \cdots \times p_{x\text{-}1.}$$

Results

The original total cohort consisted of 16,611 persons. Two thousand persons had either terminated their employment before the end of 1931 or began their employment after 1974; 739 persons had emigrated; 758 persons (5.5 %) were lost from the cohort; and 13,114 remained in the cohort for the analyses.

In the final cohort 739 persons belonged to exposure class 1 (weighers/mixers), 9,883 to class 2 (other production workers), and 2,492 to class 3 (white-collar employees). The age distribution is shown in table 1.

There was no elevation of the total death risk in the cohort as a whole, 1,059 deaths being observed and 1,056.3 expected (table 2). However, for exposure class 1, 144 deaths were observed against 121.4 expected. The tendency towards an elevation of the death risk was still found when a subdivision was made for short exposure time/short risk time (table 3) and long exposure time/long risk time (table 4). For persons employed in 1961 or later (table 5) there was also an elevation.

A similar picture is obtained when the cumulated deaths for all causes were structured according to year. For weighers/mixers the observed cases were elevated in comparison to the expected number. For other exposure classes the observed data were lower than expected. For the short-time perspective, however, there was a tendency towards an elevated risk for all exposure classes.

When the cumulated survival probabilities were studied with reference to year under risk (tables 5–8), no increase of overall death rate was observed. For the short-time perspective (table 7) there was, however, a tendency towards an overrisk for weighers and mixers. When other periods of observations were considered, ie, the observations made during the full length of the observation time, the observed and expected data coincided also for this exposure class (tables 6–9). This discrepancy depends on the fact that the numbers of observed deaths were lower than expected for the time

Table 1. Age distribution in percentages at the start of exposure.

Age class (years)	Mixers/ weighers (N = 739)	Other production workers (N = 9,883)	White-collar employees (N = 2,492)
≤19	29	35	27
20–24	17	21	27
25–29	14	13	20
30–34	11	10	11
35–39	7	8	7
40–44	8	4	5
45–49	7	4	2
50–54	4	2	1
55–59	2	1	1
≥ 60	1	1	0

Table 2. Observed (obs) and expected (exp) number of deaths during various time periods for persons employed in 1931 or later. Risk is calculated from the start of exposure (not earlier than year 1961).

Period	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
1961–1965	13	17.5	0.74	97	120.4	0.81	7	15.5	0.45	117	153.3	0.76
1966–1970	41*	29.0	1.41	194	194.2	1.00	24	26.4	0.91	259	249.7	1.04
1971–1975	42	42.5	0.99	297	286.1	1.04	41	40.4	1.01	380	369.0	1.03
1976–1978	48**	32.4	1.48	226	220.1	1.03	29	31.8	0.91	303	284.3	1.07
1961–1978	144*	121.4	1.19	814	820.8	0.99	101	114.1	0.89	1,059	1,056.3	1.00

* $p < 0.05$, ** $p < 0.01$.

Table 3. Observed (obs) and expected (exp) number of deaths during different time periods among persons with less than five years of exposure. Risk calculated from the start of exposure (not earlier than 1961) and until five years after the end of exposure.

Period	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
1961 - 1965	0	1.3	0.0	9	7.9	1.14	1	0.9	–	10	10.1	0.99
1971–1975	1	1.3	0.77	17	11.3	1.50	3	2.2	1.36	21	14.8	1.42
1976–1978	1	0.8	–	6	7.3	0.82	0	1.3	0.00	7	9.5	0.74
1961–1978	7	4.8	1.46	39	35.1	1.11	7	5.9	1.19	53	45.8	1.16

Table 4. Observed (obs) and expected (exp) number of deaths during different time periods among persons with at least five years of exposure. Risk calculated from five years after the start of exposure (not earlier than 1961) and until 25 years after the end of exposure.

Period	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
1961–1965	11	11.8	0.93	65	82.3	0.79	6	11.3	0.53	82	105.4	0.78
1966–1970	31*	20	1.55	135	132.4	1.02	15	19.4	0.77	181	171.9	1.05
1971–1975	28	29.1	0.96	192	181.7	1.06	28	28.8	0.97	248	239.6	1.04
1976–1978	34**	21.6	1.57	125	135.4	0.92	22	23.1	0.95	181	179.7	1.01
1961–1978	104**	82.5	1.26	517	531.8	0.97	71	82.6	0.86	692	696.9	0.99

* $p \leq 0.05$, ** $p \leq 0.01$.

Table 5. Observed (obs) and expected (exp) number of deaths during different time periods among persons with their first employment year during 1961 or later. Risk calculated from the start of exposure.

Period	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
1961–1965	0	1.4	0.00	1	5.3	0.19	0	1	0.00	1	7.7	0.13
1966–1970	6	3.7	1.62	12	16.0	0.75	3	3.9	0.77	21	23.6	0.89
1971–1975	10	6.6	1.52	37	35.2	1.05	7	8.0	0.88	54	49.9	1.08
1976–1978	5	5.6	0.89	25	19.2	1.30	5	6.6	0.76	35	41.3	0.85
1961–1978	21	17.3	1.21	75	75.7	0.99	15	19.5	0.77	111	122.5	0.91

Table 6. Observed (obs) and expected (exp) cumulated probability for survival when risk is calculated from the start of exposure (not earlier than 1961).

Risk period (years)	Mixers/weighers		Other production workers		White-collar employees	
	Obs	Exp	Obs	Exp	Obs	Exp
0– 2	99.6	98.9	99.6	99.4	100.0	99.7
0– 4	98.1	97.5	99.2	98.7	99.7	99.3
0– 6	97.0	95.9	98.5	97.9	99.4	98.8
0– 8	94.9	93.9	97.7	96.9	99.0	98.2
0–10	91.9	91.5	96.6	95.6	98.4	97.5
0–12	89.3	88.5	95.4	94.1	97.8	96.6
0–14	87.1	84.8	94.0	92.2	96.9	95.6
0–16	82.2	80.2	92.0	89.8	95.9	94.2
0–18	75.6	75.1	90.0	87.1	94.7	92.6

Table 7. Observed (obs) and expected (exp) cumulated probability for survival among persons with less than five years of exposure. Risk calculated from the start of exposure (not earlier than 1961) and until five years after the end of exposure.

Risk period (years)	Mixers/weighers		Other production workers		White-collar employees	
	Obs	Exp	Obs	Exp	Obs	Exp
0– 2	100.0	99.4	99.7	99.7	100.0	99.8
0– 4	98.9	98.7	99.5	99.3	99.4	99.5
0– 6	97.6	97.9	98.7	98.8	99.0	99.3
0– 8	93.8	96.7	98.2	98.3	99.0	98.9
0–10	87.9	95.1	98.0	97.7	97.0	98.2

Table 8. Observed (obs) and expected (exp) cumulated probability for survival among persons with at least five years of exposure. Risk calculated from the start of exposure (not earlier than 1961) and until 25 years after the end of exposure.

Risk period (years)	Mixers/weighers		Other production workers		White-collar employees	
	Obs	Exp	Obs	Exp	Obs	Exp
0– 2	99.0	98.6	99.3	99.3	99.8	99.5
0– 4	97.2	96.9	98.8	98.4	99.4	99.0
0– 6	95.8	94.9	97.9	97.3	99.1	98.3
0– 8	91.7	92.5	96.9	96.0	98.6	97.4
0–10	88.0	89.6	95.5	94.4	97.9	96.5
0–12	85.2	86.1	94.0	92.4	97.3	95.3
0–14	83.7	81.9	92.1	90.0	95.8	93.8
0–16	76.9	77.1	89.9	87.0	94.2	92.0
0–18	70.0	71.1	87.7	83.3	92.2	89.3

Table 9. Observed (obs) and expected (exp) cumulated probability for survival among persons who started their exposure in 1961 or later. Risk calculated from the start of exposure.

Risk period (years)	Mixers/weighers		Other production workers		White-collar employees	
	Obs	Exp	Obs	Exp	Obs	Exp
0– 2	100.0	99.4	99.9	99.7	100.0	99.8
0– 4	99.2	98.6	99.8	99.3	99.7	99.5
0– 6	98.4	97.7	99.3	98.9	99.5	99.2
0– 8	97.0	96.6	98.9	98.3	99.3	98.8
0–10	96.4	95.2	98.3	97.7	98.9	98.4
0–12	93.6	93.3	97.8	97.0	98.7	97.9
0–14	91.1	90.9	97.1	96.2	98.2	97.3
0–16	84.2	87.5	96.3	95.2	97.9	96.8
0–18	84.2	83.7	95.3	93.7	96.4	96.4

Table 10. Causes of death (International Classification of Diseases, eighth revision) – Observed (obs) and expected (exp) numbers and the observed : expected ratio. Risk calculated from the start of exposure (not earlier than 1961).

Cause of death	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
All tumors (II)	40	38.6	1.04	236	231.8	1.02	35	31.6	1.11	311	302.0	1.03
Gastrointestinal organs, peritoneum (150–159)	15	11.8	1.27	84*	68.4	1.23	6	8.2	0.73	105	88.4	1.19
Liver (155)	1	0.3	–	7**	1.7	4.12	1*	0.2	–	9**	2.2	4.09
Pancreas (157)	3	1.4	2.14	20**	7.4	2.70	2	1.0	2.00	25**	9.8	2.55
Respiratory organs (160–163)	7	5.2	1.35	47**	24.9	1.89	10**	3.8	2.63	64**	33.9	1.89
Lung (162)	7	4.9	1.43	39**	22.9	1.70	9**	3.4	2.65	55**	31.2	1.76
Skin (172–173)	1	0.5	–	5	3.5	1.43	0	0.5	–	6	4.5	1.33
Urinary bladder (188)	1	0.4	–	5*	2.0	2.50	0	0.2	–	6*	2.6	2.31
Brain (191)	0	0.6	–	6	4.3	1.40	2	0.8	–	8	5.7	1.40
Lymphatic tissue, leukemia (200–209)	2	3.3	0.61	21	20.1	1.04	4	2.9	1.38	27	26.3	1.03
Diseases of the circulatory organs (VII)	78*	62.4	1.25	353*	311.2	1.13	37	32.2	1.15	468**	405.8	1.15
Ischemic heart disease (410–414)	55	45.5	1.21	234**	184.7	1.27	24	18.8	1.28	313**	249.0	1.26
Violence (XVII)	15*	8.2	1.83	91*	68.0	1.34	13	12.0	1.08	119**	88.2	1.35
Other	11**	34.8	0.32	134**	203.1	0.66	16	25.2	0.63	161**	263.1	0.61

* $p \leq 0.05$, ** $p \leq 0.01$.

period 1961 to 1965. This occurrence balanced the increases of risks observed after 1965.

There was a shift in the causes of deaths (table 10) in the cohort as a whole. An elevated but statistically nonsignificant risk for deaths from gastrointestinal tumors was observed among weighers/mixers. Other production workers (exposure class 2) had a statistically significant elevation for the same tumor category with a relative risk of 1.23. For both exposure class 2 and 3 a statistically significant elevation was found for the risk for deaths from tumors of the respiratory organs. For exposure class 1 there was an elevated but not statistically significant risk for deaths from tumors of the respiratory organs. For exposure class 2 an elevated death risk for tumors in the urinary bladder was observed. For the same exposure class the death risk was significantly elevated [rate ratio (RR) 1.27] for ischemic heart diseases (ICD 410–414). Death risks from accidents, suicide, etc (ICD XVII), were also elevated for exposure classes 1 and 2. The use of different observation times (tables 11 & 12) does not change the pattern.

For deaths from tumor diagnoses [International Classification of Diseases (ICD), eighth revision] 150–159 and 160–163 elevated risk ratios (table 10) were observed in the cohort as a whole, for instance, for liver tumors (RR 4.09), pancreatic tumors (RR 2.55), and lung cancer (RR 1.76). Exposure class 2, other production workers, was responsible for the majority of the increase in risk for deaths from liver tumors (RR 4.12) and pancreatic tumors (RR 2.70). The increase in death risks from lung tumors in the cohort as a whole depended mainly on increases for exposure classes 2 (RR 1.70) and 3 (RR 2.65).

In the Cancer Register 533 cancer cases were reported for the cohort. The distribution of these cases for exposure classes and time periods is found in table 13. For the time period 1971–1975 the observed numbers were higher than expected for exposure class 2.

The distribution according to selected diagnoses is found in table 14. The number of malignant melanomas (ICD 190) was significantly increased for exposure class 2. Exposure class 3, white-collar employees, had increased incidences for lung cancer (ICD 160–163) and tumors of the nervous system (ICD 193, particularly the brain). For exposure class 2 a rate ratio of 1.54 was observed for stomach cancer (ICD 151). This rate ratio was not statistically significant but could possibly be compared with the figures for exposure classes 2 (RR 0.40) and 3 (no cases).

Table 11. Causes of death (International Classification of Diseases, eighth revision) – Observed (obs) and expected (exp) numbers and the observed : expected ratio, for persons with at least five years of exposure. Risk calculated from five years after the start exposure (not earlier than 1961) and until 25 years after the end of exposure.

Cause of death	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
All tumors (II)	26	26.4	0.98	140	135.8	1.03	22	20.4	1.08	188	182.6	1.03
Gastrointestinal organs, peritoneum (150–159)	10	7.9	1.27	48	41.7	1.15	3	6.0	0.50	61	55.6	1.10
Liver (155)	1*	0.2	–	5**	1.0	5.00	0	0.2	–	6**	1.4	4.29
Pancreas (157)	2	1.0	2.0	17**	4.4	3.86	0	0.7	–	19**	6.1	3.11
Respiratory organs (160–163)	6	3.6	1.67	27**	15.7	1.72	8**	1.9	4.21	41**	21.2	1.93
Lung (162)	6	3.4	1.76	21*	14.4	1.46	7**	1.8	3.89	34**	19.6	1.73
Skin (172–173)	0	0.3	–	5*	1.9	2.63	0	0.3	–	5	2.5	2.00
Urinary bladder (188)	1	0.3	–	2	1.2	1.67	0	0.2	–	3	1.7	1.76
Brain (191)	0	0.4	–	5*	2.0	2.5	1	0.5	–	6*	2.9	2.07
Lymphatic tissue, leukemia (200–209)	0	2.2	–	10	11.4	0.88	3	1.7	1.76	13	15.3	0.85
Diseases in circulatory organs (VII)	56	43.2	1.30	246**	207.1	1.19	27	23.9	1.13	329**	274.2	1.20
Ischemic heart disease (410–414)	38	33.9	1.12	166**	127.0	1.31	17	14.3	1.19	221**	175.2	1.26
Violence (XVII)	10	5.5	1.82	36	33.1	1.09	4	5.4	0.74	50	44	1.14
Other	7**	23.9	0.29	83**	127.0	0.65	11	16.3	0.67	101**	167.2	0.60

*$p \leq 0.05$, ** $p \leq 0.01$.

Table 12. Causes of death (International Classification of Diseases, eighth revision) – Observed (obs) and expected (exp) numbers and the observed : expected ratio for persons starting their exposure in 1961 or later. Risk calculated from the start of exposure.

Cause of death	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs.	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
All tumors (II)	8	6.7	1.19	20	24.2	0.83	3	5.3	0.57	31	36.2	0.86
Gastrointestinal organs, peritoneum (150–159)	6*	1.9	3.16	6	6.0	1.00	0	1.1	0.00	12	9.0	1.33
Liver (155)	0	0.1	–	0	0.2	–	0	0.1	–	0	0.4	–
Pancreas (157)	3**	0.3	–	3*	0.7	–	0	0.1	–	6**	1.1	5.45
Respiratory organs (160–163)	1	0.5	–	5*	1.2	4.17	1*	0.2	–	7**	1.9	3.68
Lung (162)	1	0.4	–	5**	0.7	–	1**	0.1	–	7**	1.2	5.83
Skin (172–173)	1**	0.1	–	0	0.5	–	0	0.1	–	1	0.7	–
Urinary bladder (188)	0	0.1	–	2*	0.2	–	0	0.1	–	2*	0.4	–
Brain (191)	0	0.2	–	1	0.7	–	1**	0.1	–	2	1.0	2.00
Lymphatic tissue, leukemia (200–209)	0	0.6	–	2	2.6	0.77	1	0.6	–	3	3.8	0.79
Diseases in circulatory organs (VII)	8	7.7	1.04	24	19.7	1.22	5	3.0	1.67	37	30.4	1.22
Ischemic heart disease (410–414)	5	5.2	0.96	19**	9.5	2.00	5**	1.5	3.33	29**	16.2	1.79
Violence (XVII)	3	1.6	1.88	21**	11.7	1.79	5	2.8	1.79	29**	16.1	1.80
Other	2	5.0	0.40	10*	19.4	0.52	2	3.9	0.51	14**	28.3	0.49

* $p \leq 0.05$, ** $p \leq 0.01$

Table 13. Observed (obs) and expected (exp) cancer cases appearing during different time periods.

	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
1959–1965	6	7.8	0.77	86	96.2	0.89	14	13.2	1.06	106	117.2	0.90
1966–1970	11	10.4	1.06	108	109.7	0.98	24	16.8	1.43	143	136.9	1.04
1971–1975	16	15.0	1.07	181*	155.2	1.17	27	25.3	1.07	224	195.5	1.15
1976–1977	4	7.0	0.57	47	72.6	0.65	9	12.8	0.70	60	92.7	0.65
1959–1977	37	41.6	0.89	422	433.8	0.97	74	68.2	1.09	533	543.5	0.98

* $p \leq 0.05$

Table 14. Observed (obs) and expected (exp) number of diagnosed cancer cases of selected diagnoses (International Classification of Diseases, eighth revision).

Cancer diagnosis	Mixers/weighers			Other production workers			White-collar employees			Entire cohort		
	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp	Obs	Exp	Obs:exp
Gastrointestinal organs, peritoneum (150–159)	13	11.6	1.12	114	116.4	0.98	8	18.2	0.44	135	146.2	0.92
Stomach (151)	6	3.9	1.54	15	37.2	0.40	0	5.7	0.00	21	46.8	0.45
Liver, etc (155)	1	1.1	0.91	2	12.1	0.17	1	1.9	0.53	4	15.1	0.26
Pancreas (157)	3	1.6	1.88	20	15.8	1.27	2	2.5	0.80	25	19.9	1.26
Respiratory organs (160–163)	4	4.2	0.95	42	36.1	1.16	13**	5.3	2.45	59*	45.6	1.29
Lung (162)	3	3.4	0.88	36	28.8	1.25	9*	4.3	2.09	48	36.5	1.32
Urinary bladder (kidney excluded) (181)	2	2.2	0.91	20	18.0	1.11	3	2.7	1.11	25	29.7	0.84
Malignant melanoma (190)	1	0.7	–	18**	7.2	2.50	2	1.2	1.67	21**	9.1	2.31
Nervous system (193)	1	1.2	0.83	12	13.5	0.89	7*	2.2	3.18	20	16.9	1.18
Lymphatic tissue and blood forming organs (200–205)	2	3.2	0.63	33	31.4	1.05	3	4.9	0.61	38	39.5	0.96
Others	14	17.3	0.81	183	198.8	0.92	38	31.7	1.20	235	247.8	0.95

* $p \leq 0.05$, ** $p \leq 0.01$

Discussion

The total mortality of the cohort was close to the expected when compared to that of the general population. The subpopulation belonging to exposure class 1, weighers and mixers, showed a slightly elevated death risk in comparison to the age-standardized male general population. When discussing these data, one should remember that causes of deaths before 1961 could not be found in the central registers. This situation may imply that the risk ratios may be underestimated in those risk calculations which started in 1961. The reason is obviously that deaths, particularly at older ages, had occurred before that year.

An overrisk for cancer of different sites has been observed in many studies. [For a recent review, see the report published by the International Agency for Research on Cancer (22).] The most important sites have been the urinary bladder (1, 7, 8, 15), the lung (32), the blood (2), the lymph tissue (28), the brain (24, 31) and the skin (31).

For lung cancer many studies show contradictory results. In some an increased risk has been found (31, 35); in others a decrease of risk was obtained (12, 29, 33). Weighers and mixers belong to the risk groups (35), but also other production workers may be under risk.

In a recent Swedish investigation (34) using data from the Cancer-Environment Registry an increase in lung cancer was found for rubber workers. The number of observed cases in this study was 68 against 47.7 expected (RR 1.42).

The differences in the lung cancer observations of various studies depends on several factors. The criteria for inclusion in the examined cohort may differ, and there may be considerable differences in work conditions and in the organization of work at the plants studied. It is also important to consider possible differences in the diagnostic standards and in the quality of the information sources used, ie, the cancer registers and the causes of death registers.

There is a well-known relationship between smoking and lung cancer (38). Smoking pattern and behavior may influence both the observed and the expected numbers of lung cancer. In the present study there was no information available on smoking.

The relative risks for deaths from lung cancer were 1.7 and 1.43 for exposure class 2 and 1, respectively. The latter number was not significantly increased. For exposure class 3 the rate ratio for lung cancer deaths was 2.65. It should be observed that for lung cancer diagnoses exposure class 3, white-collar employees, was the only one significantly differing from the expected (RR 2.09). It is not possible to identify the cause(s) for the observed differences. If one assumes that the smoking habits of the exposure class 2 subpopulation do not differ from those of the general population, it is reasonable to assume that the observed tendency towards an increase in lung cancer deaths is associated with a work environment exposure. On the other hand, if one invokes smoking habits as a causal factor for the high risk of dying from lung cancer, one also has to assume that smoking is much more prevalent among exposure class 2 individuals than among the general population, which in itself consists of both smokers and nonsmokers. In fact almost all individuals in the study group have to be assumed to be smokers or exsmokers. For a discussion on the influence of smoking as a contributing risk factor see Axelson (3).

A disturbing observation in this study was the elevated risk for lung cancer morbidity and mortality among white-collar workers. A recheck of the lung cancer cases in this group has ensured that these individuals have not been misclassified in terms of exposure.

In conclusion, the observed risks of lung cancer deaths among workers in the rubber industry cannot, with scientific certainty, be attributed to the work environment. In our opinion, however, they do constitute a note of warning.

The risk ratio for deaths from gastrointestinal tumors among exposure class 2 was 1.23, that for liver tumors 4.12, and that for pancreatic tumors 2.7. An elevated risk for stomach cancer has been observed in other studies (16, 35), but liver cancer as a specific cancer site among rubber workers has not been described elsewhere. The increased mortality from liver tumors should be viewed with caution. In practice it often happens that liver metastases originating from a primary tumor in other organs are falsely designated as liver tumors in the production of official mortality statistics. This factor inflates the number of both observed and expected liver tumors. For this reason the figures obtained in this study for liver tumor mortality should not be accepted at face value. It is also sobering to note that the figures for liver cancer incidence, derived from the use of the national cancer register as the source of information, do not suggest an increased risk for liver tumors. Pancreatic tumors are, however, observed among the employees in the rubber industry (2, 11, 31). For this tumor it should be remembered that smoking (42), alcohol (25), and coffee consumption (25, 26) may also play a role. In summary, an association between gastrointestinal tumors, including pancreatic tumors, and work environment exposure among rubber workers may exist.

Five cases of death from cancer of the urinary bladder were observed for exposure class 2 against two expected cases. Although the figures are small, they serve as a reminder of this risk, described in earlier studies (22).

An important observation in this study was the increased mortality due to atherosclerotic diseases (ICD 410–414). For exposure class 2 the rate ratio was 1.27; for class 1 and 3 it was 1.21 and 1.28, respectively. The elevation in the rate ratio was moderate, but nevertheless the absolute number of additional cases is high when the high prevalence of this disease group in the general population is born in mind. Social class as a determinant in coronary heart disease should be taken into account. A high mortality in the lowest social class has been found in a Norwegian study (21), and the conclusion was drawn that social class is a potent risk factor for death from coronary heart disease. Work in the rubber industry is an indication both of social class and of specific work environment risks. Both contribute to the risk and are inseparable from each other in a study of this design. Nor is it possible to analyze for other coronary heart disease factors such as high blood pressure, smoking, blood lipids, body weight, and emotional stress. These risk factors are also to a certain extent unevenly distributed between social classes. In the interpretation of the present data we have assumed that the diagnostic standard for coronary heart disease does not differ between the rubber industry population and the general population. The observation of an increased mortality from coronary heart disease in this study is worthy of observation even if one takes into account all the uncertainties and unknown risk factors and their distribution. We do not accept social class stratification or differences in diagnostic standard as the only explanation for the increase in mortality from coronary heart disease. Of course we cannot claim, on the grounds of our own data only, that it is caused by the work environment. It is still less possible to identify or even suggest a specific chemical or group of chemicals associated with an increased mortality from coronary heart disease. It is, in this connection, interesting that somatic cell mutations have been considered (5, 23) to be associated not only with cancer, but also with coronary heart disease. An association between exposure to mutagens and carcinogens, such as tobacco smoke (38), arsenic (4), and vinyl chloride (6, 30), and increased risks for coronary heart disease mortality also fit into the same hypothesis. It should also be born in mind that a risk factor need not necessarily increase coronary heart disease morbidity to result in an increase in mortality due to coronary heart disease. It may also increase the mortality of already existing coronary heart diseases.

On the basis of such considerations we feel that it is important to report our observations on mortality from coronary heart disease. Whether or not the increased mortality from coronary heart disease found in the present study is related to work conditions is however an open question.

The exposure panorama in the rubber industry is complex and undergoing constant changes (19, 22). It has also changed with time due to exclusions of specific risk chemicals, such as the aminonaphthalenes. Studies on individual chemicals (18), on urine samples from rubber workers (14, 36, 37, 39, 40), and on newly formed gases and vapors (17) show that additives and other air pollutants may still be potential risk factors. It is not possible to identify single chemicals as etiological agents for the disease pattern observed in this and other studies. The interaction between individual rubber chemicals (20) and between emissions from the rubber processing steps and other environmental factors all contribute to the risk observed.

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