Mortality in the British rubber industry 1946-85

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ABSTRACT The mortality experienced by a cohort of 36 691 rubber workers during 1946-85 has been investigated. These workers were all male operatives first employed in any one of the 13 participating factories in 1946-60; all had worked continuously in the industry for a minimum period of one year. Compared with the general population, statistically significant excesses relating to cancer mortality were found for cancer of the pharynx ($E = 20.2$, $O = 30$, $SMR = 149$), oesophagus ($E = 87.6$, $O = 107$, $SMR = 122$), stomach ($E = 316.5$, $O = 359$, $SMR = 113$), lung ($E = 1219.2$, $O = 1592$, $SMR = 131$), and all neoplasms ($E = 2965.6$, $O = 3344$, $SMR = 113$). Statistically significant deficits were found for cancer of the prostate ($E = 128.2$, $O = 91$, $SMR = 71$), testis ($E = 11.0$, $O = 4$, $SMR = 36$), and Hodgkin's disease ($E = 26.9$, $O = 16$, $SMR = 59$). Involvement of occupational exposures was assessed by the method of regression models and life tables (RMLT). This method was used to compare the duration of employment in the industry, the duration in "dust exposed" jobs, and the duration in "fume and/or solvent exposed" jobs of those dying from causes of interest with those of all matching survivors. Positive associations (approaching formal levels of statistical significance) were found only for cancers of the stomach and the lung. The results of the RMLT analysis are independent of those from the SMR analysis, and the study continues to provide limited evidence of a causal association between the risks of stomach cancer and dust exposures, and the risks of lung cancer and fume or solvent exposures in the rubber industry during the period under study.

In 1982 an IARC working group published an evaluation of carcinogenic risks in the rubber industry.¹ For lung cancer and stomach cancer, this report concluded that there was sufficient evidence for an excess occurrence in rubber workers and limited evidence for a causal association with occupational exposures.

An analysis of cancer mortality among the British Rubber Manufacturers' Association (BRMA) study cohort for the period 1946-75² was included in the IARC evaluation. Following the publication of the IARC evaluation, an analysis of cancer mortality among the BRMA study cohort for the period 1946-80 has been published,³ as have reports from Sweden,^{4,5} Norway,⁶ Italy,⁷ and China.⁸ These latter studies provided little support for the hypothesis of a "causal association between the risks of lung and stomach cancer and certain occupational exposures in the rubber industry."³

The present report incorporates the data from earlier work and includes a further five year period of follow up to the end of December 1985.

Study population

The study population has been described elsewhere^{2,3} but may be summarised as all male operatives first employed in any one of the 13 participating factories in the period 1946-60 inclusive who worked continuously in the industry for a minimum period of one year. Detailed job histories—defined in terms of 10 broad occupational groups (see table 1)—were recorded for each employee. Job histories for the period 1976-85 had recently been provided by the participating factories.

Follow up procedures have also been described elsewhere.^{2,3} Follow up particulars are now provided either by the National Health Service Central Register (NHSCR) at Southport, the General Register Office at Edinburgh, or the Health and Safety Executive. (The latter provided follow up information on those men who also featured in their own study of rubber workers.⁹)

Table 2 shows the vital status of the study population on the closing date of the survey. For those who had died a death certificate was obtained with the

Table 1 *Description of occupations*

Job code	No (%) of men ever employed in this job*	Description
1	768 (2.1)	Crude material storeman
2	3851 (10.5)	Compounding, weighing, mixing, reforming, washing, etc
3	1793 (4.9)	Latex mixing, frothing, dipping
4	4908 (13.4)	Extruding, calendering spreading, etc
5	17154 (46.8)	Component building, preparation, assembly, etc
6	7005 (19.1)	Vulcanising, curing, moulding press, autoclave, pan
7	2508 (6.8)	Inspection, painting
8	2845 (7.8)	Finished goods, stores, packaging, despatch
9	2901 (7.9)	Site workers, internal transport, general truck drivers, etc
10	6974 (19.0)	Engineering and building maintenance

*Percentages do not total 100 as individuals may have had more than one job: 8628 workers had some period of employment in jobs 1, 2, or 4; 24 605 workers in jobs 4, 5, 6, or 7; and 6124 workers in both of the preceding job groupings.

underlying cause of death coded to the 8th revision of the International Classification of Diseases (ICD).

Methods

Expected numbers of deaths were calculated by applying quinary-quinquennial rates of mortality for either England and Wales or for Scotland to similarly defined arrays of person-years at risk (pyr). Individuals entered the pyr at the end of the first year of their employment and left the pyr on the date of death, date of embarkation, date last known alive, or the closing date of the study (31 December 1985), whichever was the earlier. Individuals were censored on reaching their 85th birthday—that is, they make no further contributions to expected or observed numbers past this age. There were two reasons for this: firstly, national mortality rates are only available for the open ended age-group ≥ 85 , the composition of which in the general population by individual years of

Table 2 *Vital status at closing date of study, 31 December 1985*

	No	%
Traced alive	22 292	60.8
Emigrated*	1 408	3.8
No trace†	1 226	3.3
Dead	11 765	32.1
Total	36 691‡	100.0

*Percentage emigrated was 2.6% for Scottish factories and 4.1% for English factories.

†Percentage no trace was 9.3% for Scottish factories and 2.3% for English factories.

‡Note: 246 workers removed from our last report² because they were believed to be canteen workers were, in fact, production workers—job not known. They are now included in the study cohort and appear in tables 10–14 in the not known group.

Sorahan, Parkes, Veys, Waterhouse, Straughan, Nutt age may differ from that of the study population and, secondly, any individual incorrectly traced, for whatever reason, as still living would make a particularly large contribution to expectations for this age group.

The standardised mortality ratio (SMR) is defined as the ratio of the observed number of deaths compared with the expected number of deaths, expressed as a percentage.

The differences found between the mortality of an industrial cohort and an expected experience based on rates of mortality for the general population are also dependent on factors other than the specific occupational exposure. Such factors will include selection effects within the workforce as well as the regional, urban/rural, and social class composition of the study cohort. The method of regression models in life tables (RMLT) was used, therefore, to test the null hypothesis of no effect on mortality from duration of exposed employment in the rubber industry,^{2 10–12} contrasting groups from within the factory population. This approach was used because, by relying on internal comparisons, we believe we may control for selection effects, and regional, urban/rural, and social class effects.

The method (see refs 3, 10, 11, 12) was used to compare the duration of exposed employment of those who died in a given year of follow up with those of matching survivors in the same year of follow up while controlling for year of starting employment (cohort 1, 1946–50; cohort 2, 1951–5; cohort 3, 1956–60), age at starting employment (15–, 20–, 30–, 35–, 45–, ≥ 55), and factory (13 participating factories). In some instances it was also possible to include duration of employment in the rubber industry as a controlling factor, to try and control for any survivor population effect¹³ in the data.

Table 3 shows the jobs considered by the study team to have higher levels of exposure to various categories of dust, fume, and solvent. Thus we are considering job 2 to entail (on average) higher levels of exposure both to rubber chemicals dust and to any dust than does job 5 (say). For many categories of exposure it is

Table 3 *Jobs* considered to have higher levels of exposure to various categories of dust, fume, and solvent*

Form of occupational exposure	Job codes
Rubber chemicals dust	1, 2
Antitack dust	4
Any dust	1, 2, 4
Low temperature fume	4
High temperature (curing) fume	6, 7
Any fume	4, 6, 7
Solvent	5
Any fume or solvent	4, 5, 6, 7

*See table 1 for description of job codes.

Table 4 BRMA study: mortality 1946-85. Mortality from all causes, all neoplasms, and all non-neoplasms by successive periods from first employment (irrespective of how long any individual remains in the industry), 1946-85

Years since first employed	All causes			All neoplasms*			All non-neoplasms		
	O	E	SMR	O	E	SMR	O	E	SMR
1-4	508	579.8	88	139	127.8	109	369	452.0	82
5-9	924	940.0	98	244	226.1	108	680	713.9	95
10-14	1340	1269.0	106	374	317.2	118	966	951.8	101
15-19	1820	1679.9	108	510	429.7	119	1310	1250.2	105
20-24	2278	2087.8	109	625	553.0	113	1653	1534.8	108
25-29	2246	2186.5	103	653	594.2	110	1593	1592.3	100
≥30	2498	2590.7	96	799	717.8	111	1699	1872.9	91
Total	11614	11333.6	102	3344	2965.6	113	8270	8368.0	99

*ICD 8: 140-239

See footnotes to table 5.

difficult to make a definitive classification. Individual factories will differ in terms of chemicals found in the workplace, factory operating procedures, and lay out of the factory. There will also be changes over time. Table 3, then, is a broad classification.

The data were first divided into a large number of subgroups by levels of the controlling variables mentioned above. For each subgroup (or subcohort) a life table was constructed, giving for each year of follow up the number entering that year of follow up, the number dying from the cause under investigation, and the mean duration of exposed employment of these two categories.

The null hypothesis of no effect on mortality from duration of exposed employment is that the deaths in each year are a random sample from the entrants to that year and that the difference in the mean cumulative duration of exposed employment of these two categories should be zero.

A test statistic was calculated to determine the probability of observing by chance alone the difference found between the duration of exposed employment of those who have died and the duration of exposed employment of the matching survivors—that is, if the null hypothesis of no effect on mortality from duration of exposed employment is true. Thus with a test statistic greater than ± 1.96 , the null hypothesis is rejected at the 5% level.

A positive test statistic indicates that deaths from the cause under investigation are tending to occur among those with longer periods of exposed employment, which could be due to the existence of an occupational risk factor, or bias, or confounding, or chance. A negative test statistic indicates that deaths from the cause under investigation are tending to occur among those with shorter periods of exposed employment, which could be due to the existence of protective occupational exposures, or bias, or confounding, or chance. (Protective occupational exposures provide, in reality, an unlikely explanation for a negative test statistic.)

The method (see refs 3, 11) was also used to estimate parameters of a simple dose effect model involving latent period (L) and doubling dose (exposure required to double the risk). Latent period is not defined here as the interval between first exposure and

Table 5 Cancer mortality for the total study population, 1946-85

Site	ICD 8th	O	E	SMR
Lip†	140	1	1.4	71
Tongue†	141	9	9.6	97
Mouth†	143-5	12	8.9	135
Pharynx†	146-9	30*	20.2	149
Oesophagus	150	107*	87.6	122
Stomach	151	359*	316.5	113
Small intestine†	152	3	6.1	49
Large intestine†	153	169	177.6	95
Rectum	154	143	133.9	107
Liver†	155	28	19.4	144
Gallbladder†	156	20	16.9	118
Pancreas	157	114	124.9	91
Nose, sinuses†	160	7	6.4	109
Larynx†	161	33	27.8	119
Lung	162, 3	1592***	1219.2	131
Bone†	170	13	10.2	127
Skin†	172, 3	17	24.8	69
Breast†	174	3	3.8	79
Prostate	185	91(**)	128.2	71
Testis†	186	4(*)	11.0	36
Bladder	188	106	105.5	100
Other genital†	187	3	4.4	68
Other urinary†	189	47	52.5	90
Brain	191, 2	67	76.3	88
Thyroid	193	9	5.4	167
Lympho†	200, 202	50	54.9	91
Hodgkins†	201	16(*)	26.9	59
Myeloma†	203	21	28.8	73
Leukaemia	204-207	65	68.1	95
All neoplasms	140-239	3344***	2965.6	113

Two-tailed tests: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; () indicates significant deficit.

Expectations were calculated on the basis of rates for England and Wales (English factories) or for Scotland (Scottish factories) for 1946-84, except for those sites marked with a †, for which rates for England and Wales were used. No contributions are made to observed numbers or to expectations past age 85. SMRs are calculated using expectations given to three places of decimals.

The results of significance tests are not displayed in tables 4 and 6, as these tables are for the purpose of identifying patterns in the distribution of SMRs.

Table 6 *Mortality from cancer of the stomach and cancer of the lung 1946–85: SMRs (with observed numbers) by industry sector and by years from first employment*

Years from first employment	General rubber goods		Tyre		Total	
	SMR	(O)	SMR	(O)	SMR	(O)
Cancer of the stomach:						
1–4	156	(5)	123	(19)	128	(24)
5–9	113	(6)	86	(22)	90	(28)
10–14	152	(10)	145	(48)	146	(58)
15–19	127	(10)	151	(62)	147	(72)
20–24	135	(12)	94	(45)	100	(57)
≥25	125	(21)	95	(99)	99	(120)
Total	134	(64)	110	(295)	113	(359)
Cancer of the lung:						
1–4	141	(11)	151	(56)	150	(67)
5–9	146	(22)	110	(152)	151	(132)
10–14	152	(33)	119	(129)	125	(162)
15–19	149	(43)	122	(180)	127	(227)
20–24	164	(59)	129	(252)	135	(311)
≥25	139	(103)	125	(590)	127	(693)
Total	147	(271)	128	(1321)	131	(1592)

See footnotes to table 5.

death. Instead, exposure received in each year of employment is assumed to have a maximum effect L years later.

The RMLT procedures described above were repeated except that the cumulative duration of exposed employment for each individual in each year of follow up was transformed into a relative risk predicted by the model under consideration (by trying out different values of doubling dose (D) and latent period (L)). The risk of mortality predicted by the model for those who had died was compared with the risk of mortality predicted by the model for the matching survivors. A log likelihood was calculated to measure the goodness of fit of the specific dose effect model under consideration. The values of the parameters resulting in the largest likelihood were taken to be the best estimates of these parameters—that is, maximum likelihood estimates.

The approach used to estimate percentage attributable risk has been described before.³

Results

SMR APPROACH

The existence of any healthy worker effect in the data is best investigated by calculating SMRs for all causes for successive five year periods from first employment (irrespective of how long any individual remains in the industry).¹³ These are shown in table 4. There is a general trend of increasing SMRs over the follow up period, although the SMRs for the last two periods are not consistent with this trend. Results are also given

Sorahan, Parkes, Veys, Waterhouse, Straughan, Nutt for all neoplasms and for all other causes. There is little evidence of a healthy worker effect affecting cancer mortality.

Overall results for cancer mortality by site were calculated for the new period of follow up (1981–5). Compared with the general population, there was a statistically significant excess for lung cancer ($O = 384$, $E = 316.2$, $SMR = 121$) and a statistically significant deficit for cancer of the prostate ($O = 31$, $E = 47.0$, $SMR = 60$).

Table 5 shows the overall results for cancer mortality by site for the whole period 1946–85. Compared with the general population, there are statistically significant excesses for cancer of the pharynx, oesophagus, stomach, lung, and for all neoplasms, and statistically significant deficits for cancers of the prostate and testis and Hodgkin's disease.

Observed and expected numbers of deaths for cancer of the stomach and cancer of the lung were calculated by age at death. For cancer of the stomach a higher SMR was found for younger age groups than for older age groups (aged <50 , $SMR = 139$; aged ≥ 50 , $SMR = 110$), whereas for cancer of the lung a lower SMR was found for younger age groups than for older age groups (aged <50 , $SMR = 96$; aged ≥ 50 , $SMR = 134$).

Table 7 *Mortality from cancer of the stomach and cancer of the lung 1946–85: by industry sector and by entry cohort*

Entry cohort	Industry	O	E	SMR
Cancer of the stomach:				
Cohort 1	Tyre	173	154.7	112
	General rubber goods	38*	25.5	149
	Total	211**	180.2	117
Cohort 2	Tyre	72	74.5	97
	General rubber goods	15	15.9	94
	Total	87	90.4	96
Cohort 3	Tyre	50	38.7	129
	General rubber goods	11	7.3	151
	Total	61*	46.0	133
Cancer of the lung:				
Cohort 1	Tyre	773***	587.1	132
	General rubber goods	150***	92.0	163
	Total	923***	679.1	136
Cohort 2	Tyre	339**	291.6	116
	General rubber goods	91***	61.9	147
	Total	430***	353.5	122
Cohort 3	Tyre	209***	156.7	133
	General rubber goods	30	29.9	100
	Total	239***	186.6	128

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

See footnotes to table 5.

Cohort 1: first employed 1946–50;

Cohort 2: first employed 1951–55;

Cohort 3: first employed 1956–60.

Table 8 Testing the null hypothesis of no effect from duration of employment in the rubber industry on risk of mortality by the method of RMLT.† (Test factor = cumulative duration of employment in the rubber industry)

Cause of death	ICD 8th	No of deaths	Mean duration of exposed employment‡	Mean difference between deaths and matching survivors§	Test statistic
Ca pharynx	146-9	30	6.8	-2.6	-1.66
Ca buccal cavity	140-9	53	7.6	-1.9	-1.60
Ca oesophagus	150	107	8.7	-2.0	-2.26(*)
Ca stomach	151	359	10.5	+0.7	+1.69
Ca liver	155	28	9.6	-0.3	-0.19
Ca larynx	161	33	9.0	-1.5	-1.04
Ca lung	162, 3	1592	9.8	-0.4	-2.05(*)
Melanoma	172	5	5.3	-2.9	-0.93
Other skin cancer	173	12	14.2	+3.7	+1.43
Ca prostate	185	91	9.8	-0.9	-1.06
Ca bladder	188	106	11.2	+0.6	+0.75
Leukaemia	204-7	65	8.5	-1.5	-1.44
All RES neoplasms	200-209	152	9.7	-0.4	-0.56
All cancers	140-209	3320	10.0	-0.2	-1.56
Dis circulatory system	390-458	5255	10.0	-0.1	-1.13
Dis respiratory system	460-519	1638	9.5	-0.4	-2.06(*)
All causes		11614	9.7	-0.3	-3.85(***)

*p < 0.05; ***p < 0.001.

†Controlling for age at hire (15-, 20-, 25-, 30-, 35-, 45-, ≥55), entry cohort, and factory. The alternative to the null hypothesis is assumed to be a linear relative risk model ($RR = 1 + Bx$), where x is the cumulative duration of exposed employment and B is a constant.

‡In units of years of employment in the rubber industry.

§Mean difference between deaths and matching survivors in units of years of employment in the rubber industry.

||Asymptotically normally distributed.

RES = Reticuloendothelial system.

Table 6 shows the observed and expected numbers of deaths for cancers of the stomach and lung by industry sector and by successive periods from first employment (irrespective of how long any individual remains in the industry). No column of SMRs shows a monotonic trend of increase or decrease over time. For cancer of the stomach, the larger SMRs are shown for the period 10-19 years from first employment and unexceptional SMRs are shown for the later periods of

follow up (≥20 years).

Table 7 shows the observed and expected numbers of deaths for cancers of the stomach and lung by industry sector and by entry cohort. A similar table was also prepared for cancer of the bladder. The overall SMR for bladder cancer among cohorts 2 and 3 combined (those first employed after the withdrawal of the suspect bladder carcinogens) was 91 (O = 42, E = 46.2).

Table 9 Testing the null hypothesis of no effect from duration of employment in the rubber industry on risk of mortality from cancer of the stomach over levels of controlling variables by the method of RMLT.† (Test factor = cumulative duration of employment in the rubber industry)

Controlling variable	No of deaths	Mean duration of exposed employment‡	Mean difference between deaths and matching survivors§	Test statistic
By entry cohort:				
1946-50	211	11.3	+0.9	+1.61
1951-55	87	9.1	+0.1	+0.16
1956-60	61	9.5	+0.6	+0.82
By industry sector:				
Tyre	295	10.6	+0.8	+1.82
General rubber goods	64	9.6	0.0	+0.02
By years from first employment:				
0-9	52	4.4	-0.2	-0.73
10-19	130	9.3	+0.6	+1.26
≥20	177	13.1	+1.0	+1.36
Total	359	10.5	+0.7	+1.69

See footnotes to table 8.

Table 10 Testing the null hypothesis of no effect from duration of employment in dust exposure jobs on risk of mortality by the method of RMLT.[†] (Test factor = cumulative duration of employment in jobs 1, 2, or 4)

Cause of death	ICD 8th	No of deaths	Mean duration of exposed employment [‡]	Mean difference between deaths and matching survivors [§]	Test statistic
Ca pharynx	146-9	30	0.4	-0.8	-1.25
Ca buccal cavity	140-9	53	1.0	-0.6	-1.01
Ca oesophagus	150	107	1.4	+0.0	+0.03
Ca stomach	151	359	2.2	+0.3	+1.29
Ca liver	155	28	0.9	-0.8	-0.97
Ca larynx	161	33	2.2	+0.9	+1.33
Ca lung	162-3	1592	1.5	-0.2	-1.62
Melanoma	172	5	1.0	+0.3	+0.32
Other skin cancer	173	12	4.1	+1.7	+1.12
Ca prostate	185	91	1.2	-0.5	-1.12
Ca bladder	188	106	2.5	+0.5	+1.04
Leukaemia	204-7	65	0.9	-0.6	-1.22
All RES neoplasms	200-209	152	1.3	-0.4	-0.99
All cancers	140-209	3320	1.6	0.0	-1.07
Dis circulatory system	390-458	5255	1.7	0.0	+0.04
Dis respiratory system	460-519	1638	1.7	0.0	+0.38
All causes		11614	1.7	-0.0	-0.53

[†]Controlling for age at hire (15-, 20-, 25-, 30-, 35-, 45-, ≥55), entry cohort, and duration of employment in the rubber industry -1-2, 3-7, ≥8 years). The alternative to the null hypothesis is assumed to be a linear relative risk model ($RR = 1 + Bx$), where x is the cumulative duration of exposed employment and B is a constant.

[‡]In units of years of employment in jobs 1, 2, or 4.

[§]Mean difference between deaths and matching survivors in units of years of employment in jobs 1, 2, or 4.

^{||}Asymptotically normally distributed.

Regression models and life tables

Any association between the risk of cause specific mortality and duration of employment in the rubber industry, or duration of employment in particular job groupings, was investigated by means of the method of RMLT.

Table 8 shows the overall test statistics, derived from comparing the duration of employment in the rubber industry of those dying from causes of interest with those of all matching survivors. Statistically significant negative test statistics are shown for all causes, cancers of the oesophagus and lung, non-malignant diseases of the respiratory system, diseases of the digestive system, and accidents, poisonings, and violence. The presence of a survivor population effect in the data will tend to produce negative statistics for these particular tests. The positive test statistic shown for cancer of the stomach approaches statistical significance ($t = +1.69$, $p = 0.09$).

The method readily allows an inspection of the contribution from subcohorts to the overall test statistic and table 9 shows findings for cancer of the stomach by levels of controlling variables. The overall positive test statistic may be seen to be largely dependent on the findings for deaths occurring among the first entry cohort, among workers in the tyre factories, and occurring ten years or more from first employment. These groupings are not mutually exclusive.

For tables 8 and 9, exposed employment was considered to be any employment in the rubber industry. Nevertheless, if a hazard were only operating in certain departments such a test would dilute any effect. It was, therefore, important to test the null hypothesis of no effect on mortality from working in specific types of jobs.

Table 10 shows test statistics comparing an estimate of dust exposure (duration of employment in jobs 1, 2 or 4) among those who have died from causes of interest with those of all matching survivors. None of the statistics shown achieves significance, although a positive test statistic is shown for cancer of the stomach and a negative test statistic for cancer of the lung. Contributions from subcohorts to the overall test statistic for cancer of the stomach were calculated. A statistic approaching a formal level of significance was found for deaths occurring among the first entry cohort ($t = +1.90$, $p = 0.06$).

Table 11 shows test statistics comparing an estimate of fume and/or solvent exposure (duration of employment in jobs 4, 5, 6, or 7) among those who have died from causes of interest with those of all matching survivors. The positive test statistic shown for cancer of the lung approaches statistical significance ($p = 0.07$) and a negative test statistic (not statistically significant) is shown for cancer of the stomach. Contributions from subcohorts to the overall test statistic for cancer of the lung are shown in table 12. The positive statistic shown for deaths

Table 11 Testing the null hypothesis of no effect from duration of employment in fume and/or solvent exposure jobs on risk of mortality by the method of RMLT.† (Test factor = cumulative duration of employment in jobs 4, 5, 6, or 7)

Cause of death	ICD 8th	No of deaths	Mean duration of exposed employment‡	Mean difference between deaths and matching survivors§	Test statistic
Ca pharynx	146-9	30	3.1	-0.3	-0.36
Ca buccal cavity	140-9	53	3.5	-0.6	-0.78
Ca oesophagus	150	107	4.9	+0.4	+0.63
Ca stomach	151	359	5.2	-0.4	-1.31
Ca liver	155	28	4.7	-0.6	-0.47
Ca larynx	161	33	3.1	-1.3	-1.36
Ca lung	162, 3	1592	5.6	+0.3	+1.81
Melanoma	172	5	2.1	0.0	+0.01
Other skin cancer	173	12	8.7	+1.0	+0.46
Ca prostate	185	91	4.8	-0.1	-0.08
Ca bladder	188	106	6.1	-0.2	-0.22
Leukaemia	204-7	65	4.5	-0.5	-0.66
All RES neoplasms	200-209	152	5.2	0.0	+0.05
All cancers	140-209	3320	5.4	0.0	+0.34
Dis circulatory system	390-458	5255	5.2	-0.3	-2.98(**)
Dis respiratory system	460-519	1638	4.8	-0.3	-2.05(*)
All causes		11614	5.1	-0.2	-2.97(**)

*p < 0.05; **p < 0.001.

†See footnote to table 10.

‡In units of years of employment in jobs 4, 5, 6, or 7.

§Mean difference between deaths and matching survivors in units of years of employment in jobs 4, 5, 6, or 7.

||Asymptotically normally distributed.

occurring among the first entry cohort is statistically significant ($p < 0.05$). The positive statistic shown for deaths occurring among workers in the tyre sector is also significant at the 5% level. A negative test statistic is found for deaths among workers in the general rubber goods sector. A test statistic for cancer of the lung was also calculated with exposures lagged by ten years—that is, exposed employment occurring in the

preceding 10 years is ignored. The overall test statistic, so obtained, was statistically significant at the 5% level ($t = +1.98$).

Statistics as described in tables 8, 10, and 11 were also calculated for the following cause of death groupings: infective and parasitic disease; endocrine, nutritional, and metabolic diseases; diseases of the blood and blood forming organs; mental disorders;

Table 12 Testing the null hypothesis of no effect from duration of employment in fume and/or solvent exposure jobs on risk of mortality from cancer of the lung over levels of controlling variables by the method of RMLT.† (Test factor = cumulative duration of employment in jobs 4, 5, 6, or 7)

Controlling variable	No of deaths	Mean duration of exposed employment‡	Mean difference between deaths and matching survivors§	Test statistic
By entry cohort:				
1946-50	923	6.0	+0.5	+2.34*
1951-55	430	5.0	-0.1	-0.40
1956-60	239	4.7	+0.1	+0.28
By duration of employment in industry (y):				
1-2	461	1.0	0.0	-0.93
3-7	404	2.7	+0.1	+0.56
≥ 8	727	10.0	+0.6	+1.82
By industry sector:				
Tyre	1321	5.8	+0.4	+2.39*
General rubber goods	271	4.6	-0.4	-1.10
By years from first employment:				
0-9	199	2.3	-0.1	-0.34
10-19	389	4.5	+0.2	+0.87
≥ 20	1004	6.6	+0.4	+1.68
Total	1592	5.6	+0.3	+1.81

*p < 0.05.

See footnotes to table 11.

Table 13 Testing the null hypothesis of no effect from duration of employment in various job groupings on risk of stomach cancer mortality ($n = 359$) by the method of RMLT†

Form of occupational exposure‡	Job codes§	Mean duration of exposed employment	Mean difference between deaths and matching survivors¶	Test statistic††
Rubber chemicals dust	1, 2	1.2	+0.22	+1.16
Antitack dust	4	1.0	+0.09	+0.52
Any dust	1, 2, 4	2.2	+0.31	+1.29
Low temperature fume	4	See above		
High temperature fume (curing)	6, 7	1.3	-0.11	-0.54
Solvent	5	2.8	-0.41	-1.43
Any fume	4, 6, 7	2.3	-0.03	-0.10
Any fume or solvent	4, 5, 6, 7	5.2	-0.43	-1.31

† See footnote to table 10. ‡ See table 3. § See table 1. || In units of years of employment in stated jobs.

¶ Mean difference between deaths and matching survivors in units of years of employment in stated jobs. †† Asymptotically normally distributed.

diseases of the nervous system and sense organs; ischaemic heart disease; cerebrovascular disease; bronchitis, emphysema, and asthma; diseases of the digestive system; diseases of the genitourinary system; and accidents, poisonings, and violence. No significant positive test statistics were obtained.

Table 13 shows test statistics comparing durations of exposed employment (variously defined) for those dying from cancer of the stomach with those of matching survivors. None of the differences shown is statistically significant. The statistics shown for solvent, any fume, and any fume or solvent are negative, whereas that shown for any dust is positive.

Table 14 shows test statistics comparing durations of exposed employment (variously defined) for those dying from cancer of the lung with those of all matching survivors. A statistically significant negative test statistic is shown for rubber chemicals dust, whereas, as has been stated previously, the test statistic for any fume or solvent approaches statistical significance ($p = 0.07$). These statistics were also calculated for all causes. No significant positive test statistics were obtained.

Fitting of models

A model allowing for cancer latency and doubling dose (see refs 3, 10) was applied to mortality from cancer of the stomach in relation to duration of employment in the industry (irrespective of which departments were worked in). Results may be summarised as follows:

- (1) Doubling dose D: maximum likelihood estimate for D is exposure (or insult) equivalent to that received in 45 years of employment in the industry (95% confidence interval 20–500, given that $L = 10$ years).
- (2) Latent period L: maximum likelihood estimate of 10 years.

The percentage of deaths from stomach cancer attributable to occupational exposure (including any synergistic effects with other factors) assuming the above model ($D = 45$ years of employment in the industry, $L = 10$ years) was estimated as 14%, 95% confidence interval 2%–25%.

A model allowing for cancer latency and doubling dose was also applied to mortality from cancer of the lung in relation to duration of employment in jobs

Table 14 Testing the null hypothesis of no effect from duration of employment in various job groupings on risk of lung cancer mortality ($n = 1592$) by the method of RMLT†

Form of occupational exposure‡	Job codes§	Mean duration of exposed employment	Mean difference between deaths and matching survivors¶	Test statistic††
Rubber chemicals dust	1, 2	0.7	-0.20	-2.33(*)
Antitack dust	4	0.8	+0.02	+0.33
Any dust	1, 2, 4	1.5	-0.18	-1.62
Low temperature fume	4	See above		
High temperature fume (curing)	6, 7	1.5	+0.12	+1.28
Solvent	5	3.3	+0.13	+0.98
Any fume	4, 6, 7	2.3	+0.15	+1.29
Any fume or solvent	4, 5, 6, 7	5.6	+0.28	+1.81

† See footnote to table 10. ‡ See table 3. § See table 1. || In units of years of employment in stated jobs. ¶ Mean difference between deaths and matching survivors in units of years of employment in stated jobs. †† Asymptotically normally distributed.

Mortality in the British rubber industry 1946–85

principally associated with fume and/or solvent exposure (jobs 4, 5, 6, or 7). Results may be summarised as follows:

(1) Doubling dose D: maximum likelihood estimate for D is exposure (or insult) equivalent to that received in 65 years of employment in jobs 4, 5, 6, or 7 (95% confidence interval 40–500, given that L = 30 years).

(2) Latent period L: maximum likelihood estimate of 30 years.

The percentage of deaths from lung cancer attributable to occupational exposure (including any synergistic effects with other factors such as smoking) assuming the above model (D = 65 years of employment in jobs 4, 5, 6, or 7, L = 30 years) was estimated as 6%, 95% confidence interval 1%–9%.

Both models assumed a linear dose effect (exponent for non-linearity, E = 1.0).

Discussion

In the general population there is a steep positive social class gradient for mortality from all cancers, cancers of the stomach, oesophagus, and respiratory system, and for many other sites.¹⁴ There is a negative class gradient for certain other sites of cancer including melanoma, cancer of the testis, and Hodgkin's disease. It is, therefore, not surprising that, compared with the general population, this study cohort has an overall significant excess mortality from cancers of the stomach and lung; nor is it surprising that compared with the general population there was a deficit of deaths from cancer of the testis and Hodgkin's disease. (There was also, in fact, low overall mortality from melanoma.)

In the last published report from the HSE study of rubber workers⁹ over 70% of the cohort were judged to be members of social class III M (skilled manual). Social class standardisation led to increases in expectations for stomach and lung cancer of 29% and 24% respectively.⁹ A separate standardisation for region in the HSE study led to corresponding increases in expectations of 8% and 7%. Other standardisations, such as ever employed compared with never employed, may have led to lower values for expected numbers. Clearly, then, the use of different external standards may give different values for SMRs.

The key question to be answered, then, is this: given that the mortality experience of the cohort differs from that of the general population in several ways are occupational factors involved in the observed pattern of mortality? To answer this question, we have used a method involving an internal standard (RMLT). The reasonableness of any approach using an internal standard depends on one main assumption: that we are comparing like with like, that after controlling for certain variables such as year of hire, age at hire, or

year of follow up, exposed and non-exposed workers are similar with respect to factors other than exposure. In this study cohort all were manual workers in one industry and nearly all would have lived in the vicinity of their place of work.

The power of any mortality study must depend not only on the number of cause specific deaths available for analysis and on the method of analysis adopted but also on the extent of discrimination in exposure within subcohorts. In this analysis the exposure variables used (duration of employment in various job groupings) are relatively crude but they merited consideration.

For the first test factor (duration of employment in the rubber industry), it was not possible to control for any "survivor population effect" in the data. This limitation would tend to produce negative test statistics. Such a statistic was found for all causes of death and for 13 of the other 16 causes of death shown in table 8. This tendency increases the importance to be attached to the positive statistic found for cancer of the stomach. A positive statistic was also found for cancer of the skin (non-melanoma), although this was based on only 12 deaths.

For the remaining test factors, it was possible, at least to some extent, to control for any survivor population effect in the data by stratifying over duration of employment in the industry. Thus in table 10 there are eight positive statistics and nine negative statistics and in table 11 six positive statistics and eleven negative statistics. One limitation of, say, the dust exposure estimates, however, would be that some of the non-exposed jobs would also necessitate at least some exposure to dust. This could also, to some extent, work against the demonstration of any potential hazard. Also, if a carcinogen had only been present in certain departments for a few calendar years the test factors used in the preceding analyses would be unreliable estimates of exposure.

Despite these limitations, however, there was some evidence of involvement of occupational exposures in mortality from cancers of the stomach and lung. Exposures to dust seem to be a more likely hazard than exposures to fumes or solvents for cancer of the stomach, and exposures to fumes or solvents seem to be a more likely hazard than exposures to dust for cancer of the lung. The evidence presented here for an occupational involvement in cancer of the stomach is weaker than that present in our last report,³ whereas the evidence presented here for an occupational involvement in cancer of the lung is more suggestive. In absolute terms, however, the extent of evidence for such an effect remains limited.

Although the overall SMR for cancer of the oesophagus was 122 (table 5), no evidence has been found in the RMLT analysis to associate the observed excess

mortality with occupational exposure.

It was not being suggested that any occupational hazards would operate precisely in the way predicted by the models that were fitted to the data. Nevertheless, if we reject the null hypothesis of no occupational effect on lung cancer mortality and stomach cancer mortality (even though formal levels of statistical significance were not always obtained for the overall tests of the null hypothesis) then these models provide our current estimates of the size of risk factors which may have been present, as distinct from the earlier test statistics which merely indicate levels of statistical significance. There are problems in fitting models to occupational cohort studies, particularly when personal exposure data or occupational hygiene data are not available, leading to wide confidence intervals around each estimated parameter. Inevitably, many assumptions had to be made to make such estimates, and the estimates also include any synergistic effects with other factors such as smoking.

One hypothesis stated in our previous report³—namely, that there may have been a risk factor present in the rubber industry acting as a promoter on a late stage of the disease process resulting in a relatively short interval between exposure and onset of lung cancer—is not supported by the findings presented here.

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