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A cohort mortality and cancer incidence survey of recent entrants (1982–91) to the UK rubber industry: findings for 1983–2004

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Aim	To monitor the occurrence of cancer in a recently defined cohort of UK rubber workers.
Methods	A cohort of 8651 male and female workers from 41 UK rubber factories has been enumerated. All employees had a minimum of 12 months employment and were first employed at one of the participating factories in the period 1982–91. Mortality and cancer incidence data for the period 1983–2004 were compared with expected values based on appropriate national rates.
Results	Mortality from lung cancer was close to expectation for males [observed 22, standardized mortality ratio (SMR) 93] and females (observed 2, SMR 70). Mortality from stomach cancer was also unexceptional in males (observed 4, SMR 86) and females (observed 0, SMR 0). Although based on small numbers, significantly elevated mortality was shown for multiple myeloma in males (observed 5, SMR 385) and females (observed 2, SMR 952). All seven of these latter deaths occurred in workers from the general rubber goods (GRG) sector.
Conclusions	The findings should be treated with caution as they relate to a relatively early period of follow-up. Nevertheless, they hold out the prospect that the elevated SMRs for stomach and lung cancers reported for historical cohorts of UK rubber workers will not be present in more recent cohorts. The elevated occurrence of multiple myeloma may represent no more than a chance finding. Alternatively, these findings may reflect the presence of an unrecognized occupational cancer hazard in parts of the GRG sector of the UK rubber industry.
Key words	Cohort study; lung cancer; multiple myeloma; rubber workers; stomach cancer.

Introduction

The evidence of a carcinogenic risk in the rubber industry was last reviewed in detail by the International Agency for Research on Cancer in 1982 [1]. More recently published epidemiological studies concerning the rubber industry have been reviewed by Kogevinas *et al.* [2], and their likely relevance to the current UK industry has been commented upon [3,4]. Rubber industry work was highlighted as a possible cause of prostate cancer in a recent literature review of occupation and prostate cancer risks [5], although two large UK studies that found no excess of prostate cancer were ignored [6,7]. Following the Kogevinas review, studies of cancer risks in German [8–11], Polish [12] and UK rubber workers [13–15] have been published, although only one of these studies is concerned with rubber workers first employed in recent decades [15].

The present study [15] was initiated in the 1980s and for two main reasons; firstly, to determine whether or not the improvements in working conditions introduced in the UK rubber industry have been accompanied by an elimination of concerns relating to occupational lung and stomach cancers in this industry [6,7] and secondly, to provide an early warning of any new serious health problems.

Methods

A total of 41 rubber factories from England and Wales (n = 37) and from Scotland (n = 4), all members of the

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former British Rubber Manufacturers' Association (BRMA), supplied identifying particulars, work histories and smoking status information for all those 7561 male and 1090 female workers first employed in the factory environment of the participating facilities during the 10-year period 1982–91. Office workers are thus excluded whereas maintenance workers are included in the cohort. [There are now two trade associations representing the UK rubber industry: the British Tyre Manufacturers' Association represents the tyre industry and the British Rubber and Polyurethane Products Association (BRPPA) represents the general rubber goods (GRG) sector.] All study subjects were employed for a minimum period of 12 months. Each period of working has been classified by principal industry sector (tyre, GRG) and by one of 12 broad BRMA job types (e.g. 'curing or vulcanizing', 'component building and assembly'). Information on cigarette smoking at the time of hire was available for 4821 study subjects, but only in terms of current smoker ($n = 2108$), ex-smoker ($n = 372$) and lifelong non-smoker ($n = 2341$).

The Office for National Statistics (ONS) provided information on the vital status of each study subject up to the current closing date of the survey (31 December 2004): 8130 (94.0%) subjects were alive, 61 (0.7%) subjects had emigrated, 301 (3.5%) were deceased and 159 (1.8%) subjects were untraced. ('Flagging' is not available in Northern Ireland, and 380 workers from a further factory from Northern Ireland are not included in the present analysis. The experience of these workers will be included in the next update using the 'one-off tracing' that is available in Northern Ireland. The main study file also includes 330 workers from seven BRPPA member companies engaged in the manufacture of polymers from 4,4′-methylene-bis-ortho-chloroaniline; findings for this sub-cohort will be provided separately at a later date.) The underlying cause of death was coded according to the contemporaneous revision of the International Classification of Diseases. The ONS also supplied information on cancer registrations (incident cancers) for the period 1983–2004. Initially, there were 20 deaths from cancer with no corresponding cancer registration particulars. Requests for further assistance were made to the ONS to locate these 'missing' cancer registrations and all but four registrations were identified.

Expected numbers of deaths were calculated by applying sex-, age- and period-specific mortality rates for England and Wales and rates for Scotland to corresponding person-years-at-risk (PYR) for workers from factories in England and Wales and Scotland, respectively. Each study subject contributed PYR from the end of the first 12 months of employment to the closing date of the study, death, emigration or date last known alive, whichever was the earliest. Standardized mortality ratios (SMRs) were calculated as the ratio of observed deaths to expected deaths, expressed as a percentage. These procedures were carried out using the PERSONYEARS programme. Standardized registration ratios (SRRs) were calculated in the same way for the cancer morbidity data, except that incidence rates for England and Wales were applied to the total cohort. The mean age at commencing employment was 28.5 years (males 28.1 years, females 30.7 years) and follow-up ranged from 1 to 23 years (males: mean 17.6 years, median 17.6 years; females: mean 17.8 years, median 18.1 years).

Results

Observed and expected numbers of deaths and cancer registrations are shown in Table 1 for most sites of cancer, together with observed and expected numbers of deaths for the larger non-cancer groupings. Marked deficits in mortality are shown in male workers for diseases of the circulatory system, suicide and all causes. The only significant excesses shown for mortality are those for multiple myeloma in males (SMR 385, Obs 5) and females (SMR 952, Obs 2). There was also a significant excess incidence of multiple myeloma in females (SMR 811, Obs 3). There was no elevated mortality from stomach or lung cancer in males or females although a non-significant excess incidence of stomach cancer is shown in males (SRR 137, Obs 10).

Mortality (males and females combined) from stomach cancer, lung cancer, multiple myeloma and all causes are shown by period from commencing employment in Table 2. A significant positive trend is shown only for all causes mortality ($P < 0.001$), indicating the presence of a strong healthy worker effect in the data. Corresponding findings by industry sector are shown in Table 3. The excess mortality from multiple myeloma was found to be limited to the GRG sector (SMR 714, Obs 7). There is also a highly significant deficit from all causes mortality in tyre sector workers (SMR 55, Obs 99). Analyses were also carried out by first job. Numbers were too small for meaningful statistical interpretation although three of the seven deaths from multiple myeloma had been first employed in curing or vulcanizing.

Discussion

There was an excess occurrence of multiple myeloma in this study although it is not usually possible to interpret findings based on small numbers with any confidence. There were five deaths from multiple myeloma in males but only three corresponding cancer registrations. This was because one of the deaths was recorded in the national cancer registration system as a 'secondary malignant neoplasm of bone and bone marrow'. It is thus at least possible that one of the multiple myeloma deaths has been incorrectly assigned on the death certificate.

Table 1. Overall findings from BRMA Health Research Project II (7561 males and 1090 females) first employed in the UK rubber industry in the period 1982–91

Disease	ICD9	Mortality (1983–2004)				Cancer registrations (1983–2004)			
		Obs	Exp	SMR	95% CI	Obs	Exp	SRR	95% CI
Males									
Cancers									
Mouth and pharynx	140–149	1	2.5	40	1–223	8	6.9	116	50–228
Oesophagus	150	6	5.6	107	39–233	7	5.8	121	49–249
Stomach	151	4	4.7	86	23–219	10	7.3	137	66–252
Large intestine	153	4	6.0	67	18–171	8	12.6	64	27–125
Rectum	154	3	3.8	78	16–228	6	10.4	58	21–126
Pancreas	157	5	4.1	121	39–283	4	4.4	91	25–232
Nose and sinuses	160	0	0.2	0	–	1	0.5	200	5–1114
Larynx	161	1	1.0	103	3–574	1	3.2	32	1–176
Lung and bronchus	162	22	23.7	93	58–140	27	27.5	98	65–143
Pleura (mesothelioma)	163	1	1.1	89	2–497	2	2.0	102	12–367
Melanoma	172	2	2.2	91	11–330	8	8.6	93	40–183
Other skin	173	0	0.3	0	–	28	39.5	71	47–102
Prostate	185	3	4.3	70	14–205	16	19.1	84	48–136
Testis	186	3	0.7	441	91–1289	10	13.9	72	35–132
Bladder	188	3	2.3	128	26–375	12	9.6	125	65–219
Other urinary	189	2	2.9	69	8–250	6	6.3	95	35–208
Brain	191–192	4	5.4	74	20–190	5	7.4	68	22–159
Hodgkins disease	201	2	0.9	235	28–850	1	4.3	23	1–129
Lymphosarcoma	200, 202	2	4.3	47	6–170	7	11.1	63	25–130
Multiple myeloma	203	5	1.3	385*	125–898	3	2.4	124	26–364
Leukaemia	204–208	0	3.6	0	–	4	6.4	63	17–160
All neoplasms	140–239	88	95.8	92	74–113	167	189.7	88[a]	75–102
Non-cancers									
Diseases of circulatory system	390–459	78	111.4	70 (**)	55–87				
Diseases of respiratory system	460–519	28	22.6	124	82–179				
Accidents	800–949	20	29.8	67	41–104				
Suicide	950–959	11	21.8	50 (*)	58–90				
All causes		268	352.1	76 (***)	67–86				
Females									
Cancers									
Mouth and pharynx	140–149	0	0.2	0	–	1	0.6	156	4–871
Oesophagus	150	0	0.4	0	–	0	0.5	0	–
Stomach	151	0	0.4	0	–	0	0.6	0	–
Large intestine	153	0	1.0	0	–	3	2.3	130	27–381
Rectum	154	0	0.4	0	–	0	1.4	0	–
Pancreas	157	0	0.6	0	–	0	0.7	0	–
Nose and sinuses	160	0	0.02	0	–	0	0.06	0	–
Larynx	161	0	0.04	0	–	0	0.1	0	–
Lung and bronchus	162	2	2.9	70	8–253	2	3.5	58	7–208
Pleura (mesothelioma)	163	0	0.04	0	–	0	0.1	0	–
Melanoma	172	0	0.3	0	–	0	2.1	0	–
Skin	173	0	0.02	0	–	5	6.8	73	24–171
Breast	174	5	5.0	100	32–233	24	20.5	117	75–174
Cervix	180	2	0.8	260	31–938	3	2.7	112	23–328
Uterus	182	0	0.2	0	–	1	2.0	49	1–273
Ovary	183	1	1.5	65	2–364	2	2.9	68	8–247
Bladder	188	0	0.2	0	–	2	0.7	308	37–1111
Other urinary	189	1	0.3	333	8–1857	0	0.7	0	–
Brain	191–192	1	0.7	154	4–857	1	0.9	111	3–619
Hodgkins disease	201	0	0.1	0	–	0	0.4	0	–
Lymphosarcoma	200, 202	0	0.5	0	–	0	1.4	0	–
Multiple myeloma	203	2	0.2	952*	115–3440	3	0.4	811*	167–2370
Leukaemia	204–208	0	0.5	0	–	1	0.8	130	3–724
All cancers	140–239	103	114.5	90	73–109	45	49.1	92[a]	67–123

Table 1. *Continued*

Disease	ICD9	Mortality (1983–2004)				Cancer registrations (1983–2004)			
		Obs	Exp	SMR	95% CI	Obs	Exp	SRR	95% CI
Non-cancers									
Diseases of circulatory system	390–459	7	9.3	76	30–156				
Diseases of respiratory system	460–519	5	2.9	170	55–397				
Accidents	800–949	1	1.3	80	2–446				
Suicide	950–959	2	0.8	267	32–963				
All causes		32	39.9	80	55–113				

ICD, International Classification of Diseases; Obs, observed; Exp, expected.

[a]All malignant neoplasms (ICD9, 140–208) excluding non-melatanous skin cancer (ICD9, 173) for which cancer registration data are unreliable. Findings for benign tumours were not included in the incidence findings because of the variable quality of registrations for such tumours in the different cancer registries.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, () indicates deficit.

Table 2. Mortality[a] from selected causes by period from hire, 1983–2004

Period from hire (years)	Obs	Exp	SMR	95% CI
Stomach cancer				
1–4	0	0.7	0	–
5–9	2	1.2	165	20–597
10–19	2	3.0	67	8–241
≥20	0	0.2	0	–
Total	4	5.1	79	21–201
Lung cancer				
1–4	2	3.0	66	8–240
5–9	2	5.9	34	4–122
10–19	19	16.4	116	70–181
≥20	1	1.3	78	2–435
Total	24	26.6	90	58–134
Multiple myeloma				
1–4	0	0.2	0	–
5–9	2	0.3	667	81–2408
10–19	4	1.0	412*	112–1056
≥20	1	0.1	1250	32–6965
Total	7	1.5	464**	186–955
All causes				
1–4	23	56.4	41 (***)	26–61
5–9	67	93.0	72 (**)	56–92
10–19	193	227.0	85 (*)	73–98
≥20	17	15.7	109	63–174
Total	300	391.9	77 (***)	68–86

[a]Males and females combined.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, () indicates deficit.

Table 3. Mortality[a] from selected causes by industry sector, 1983–2004

Industry sector	Obs	Exp	SMR	95% CI
Stomach cancer				
Tyre	1	1.9	52	1–287
GRG	3	3.2	95	20–278
Lung cancer				
Tyre	9	9.5	95	43–180
GRG	15	17.1	88	49–145
Multiple myeloma				
Tyre	0	0.5	0	0–696
GRG	7	1.0	714***	287–1472
All causes				
Tyre	99	179.3	55 (***)	45–67
GRG	201	212.6	95	82–109

[a]Males and females combined, totals shown in Table 2.

***$P < 0.001$, () indicates deficit.

In addition, while one of the other multiple myeloma deaths occurred 8 years after commencing employment, the original cancer was diagnosed within 12 months of hire (i.e. before completing the minimum period of employment for entry to the study) and was thus not included in the incidence findings. It would seem very unlikely that this case could be occupational in origin. Nevertheless, taken together (males and females, mortality and incidence), the findings for multiple myeloma are a cause for possible concern. The earlier larger BRMA study of UK rubber workers found deficits for multiple myeloma for all three follow-up periods [6,16,17]. However, this latter study was dominated by the tyre sector and these reassuring results may not be so relevant to the current concern, an excess of multiple myeloma in the GRG sector. Further epidemiological investigations of multiple myeloma risks may benefit from occupational hygiene and toxicological insights into exposures present in the recent UK rubber industry, particularly the GRG sector.

This study of recent entrants to the UK industry, whist still at a relatively early stage of follow-up, indicates, however, that overall health, as judged by mortality from all causes and all cancers, is better than the national average. The findings for stomach and lung cancer will also continue to be welcome news for UK rubber workers and are consistent with the time trends of decreasing exposure to rubber dust and fume in the UK rubber industry [18]. At

this stage of follow-up, however, it is only possible to conclude that there is no discernible evidence of late-stage lung and stomach carcinogens in the industry.

An elevated mortality from cancer of the testes (based on three deaths) was highlighted in the earlier report from this study [15]. There were, however, no further deaths from this cancer in the new period of follow-up (1999–2004) and the incidence of testicular cancer is now below expectation. There is, therefore, no reason to believe that working in the UK rubber industry has an effect on risks for this cancer.

In the course of time, there will be a sufficient number of events in this new cohort study to make use of the detailed work history information and the smoking status information in a single analysis of the various cancers under investigation; the position relating to multiple myeloma will need to be monitored carefully.

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Conflicts of interest

None declared

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