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British rubber and cable industry cohort: 49-year mortality follow-up

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Abstract

Background: The International Agency for Research on Cancer (IARC) has determined there is sufficient evidence that working in the rubber manufacturing industry increases the risk of cancers of the stomach, lung, bladder, and leukaemia and lymphoma.

Objectives: To examine mortality patterns of a prospective cohort of men from the rubber and cable manufacturing industries in Great Britain.

Methods: Standardised Mortality Ratios (SMRs) were calculated for males aged 35+ at start of follow-up in 1967 to 2015 using the population of England and Wales as the external comparator. Tests for homogeneity and trends in SMRs were also completed.

Results: For all causes, all malignant neoplasms (MNs), non-malignant respiratory diseases (NMRDs), and circulatory diseases (CDs), SMRs were significantly elevated, and also particularly for cancers of the stomach (SMR = 1.26 [95% Confidence Interval [CI] 1.18 to 1.36]), lung (1.25 [95% CI 1.21 to 1.29]), and bladder (1.16 [95% CI 1.05 to 1.28]). However, the observed deaths for leukaemia, non-Hodgkin's lymphoma (NHL), and multiple myeloma were as expected. Bladder cancer risks were elevated only in workers exposed to antioxidants containing 1- and 2-naphthylamine.

Conclusions: This study provides evidence of excess risks in the rubber industry for some non-cancer diseases and supports IARC's conclusions in relation to risks for cancers of the bladder, lung, and stomach, but not for leukaemia, NHL, or multiple myeloma.

Key Words: rubber and cable industry; industrial cohort study; mortality; cancer; circulatory and respiratory diseases

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Key Messages:

1. According to the International Agency for Research on Cancer (IARC), working in the rubber industry increases the risk of cancer of the urinary bladder, lung, stomach and of leukaemia, non-Hodgkin's lymphoma (NHL) and multiple myeloma.
2. This paper confirms earlier findings from this study that removal of antioxidants containing 1-naphthylamine and 2-naphthylamine has reduced the bladder cancer risk in the cohort. It confirms IARC's views of an increased risk for cancers of the urinary bladder, lung and stomach, but does not provide support for increased risks of leukaemia, NHL or multiple myeloma and provides evidence that work in the rubber industry is associated with an increased risk in circulatory diseases (ischaemic heart diseases and cerebrovascular disease) and non-malignant respiratory diseases (bronchitis).
3. Occupational physicians and health and safety managers within the industry should remain aware of the associated hazardous exposures and ensure they are kept to a level that is as low as reasonably practical.

Introduction

The International Agency for Research on Cancer (IARC) working group assessment of the rubber manufacturing industry in 1982 concluded that workers with documented exposure to 2-naphthylamine were at an increased risk of cancer of the urinary bladder [1]. In its most recent evaluation, in 2012, the IARC working group identified an increased risk for leukaemia, possibly due to exposure to solvents, such as benzene, as well as sufficient evidence of increased risks of non-Hodgkin's lymphoma (NHL), multiple myeloma, and lung and stomach cancers. The evidence for laryngeal cancer and prostate cancer was deemed inconsistent, and that for oesophageal cancer was considered weak. For other cancer sites, the evidence was regarded as insufficient [2]. In addition to these increased cancer risks, several other studies of rubber industry workers suggest potentially higher levels of certain respiratory [3,4] and circulatory [4,5] diseases.

The previous analysis of the current study cohort examined the mortality of 40,867 men in the British industry over a 10-year follow-up period. The main finding was that an excess risk of bladder cancer was shown in men with exposure to antioxidants (containing trace amounts of 1- and 2-naphthylamine) that may have occurred before the compounds were withdrawn in 1949, with no such risk in men who had joined after 1949 or who had worked in factories where those antioxidants had never been used. Other significant findings included an overall excess of lung cancer in the industry, associated with rubber fume, and an excess of stomach cancer, probably associated with exposure to rubber dust in the tyre manufacturing sector [6].

The current study extends the previous 10-year follow-up to 49 years and compares the mortality experience of this cohort of rubber industry workers with the general population of England and Wales, examining Standardised Mortality Ratios (SMR) by decade of employment start, industrial sector, and department. *A priori* important disease groups were those cancer sites examined previously by IARC, namely leukaemia, NHL, multiple myeloma, and cancers of the urinary bladder, lung, stomach, prostate, oesophagus, and larynx, as well as non-malignant respiratory diseases (NMRDs) and circulatory diseases (CDs).

Methods

Assembly of Study Cohort

The original census to recruit workers into the cohort was initiated in 1967 by a predecessor to the UK Health and Safety Executive (HSE). In the previous analysis[6], 40,867 workers were included once women, men younger than 35 years of age, or those employed in the rubber industry for less than one year, together with those who could not be traced, were excluded. As well as the start year for working in the industry, the occupational data ascertained during the original survey included job position, factory of employment, industry sector (e.g., tyres, cables, hoses), and department, all at the time of study recruitment only, with the information for each participant recorded on individual study cards. In addition, exposure to antioxidants was recorded based on the findings from a 1965 survey by the HM Factory Inspectorate. The categories were as follows: group A - started work before 1 January 1950 in a factory which used the suspect antioxidants; group B started work on or after 1 January 1950 in a factory which had used the suspect antioxidants; and group C – worked in factories which had never used the suspect antioxidants [6-9]. For this analysis, the cohort had to be retraced from original study cards, which could only be located for 37,626 (92%) workers. Individuals were censored at the time of cancellation of registration with a GP or emigration (n = 136). Although the tracing exercise extended beyond 2015, the number of deaths reported in 2016 was incomplete compared to 2014 and 2015 (125 deaths vs 306 and 297, respectively). Thus, follow-up was extended until 31 December, 2015, a total of 49 years. After exclusion of unmatched or non-uniquely matched records, those not adhering to the initial study inclusion criteria (e.g., <35 years of age at study start), and checks for internal consistency (e.g., year of first employment ≥ birth year+14), the final cohort for available analysis consisted of 36,442 workers (89.2% of the original cohort). A total of 1939 deceased workers included a death date, but no cause of death; these deaths were included only in the all-cause mortality analysis. Fifteen job groups, based on the British Rubber Manufacturing Association classification, were originally included in the survey, and were allocated into four departments for analysis purposes (see Table 1).

The study obtained clearances from an NHS ethics committee (Ref: 13/NW/0543), the Health Research Authority's Confidentiality Advisory Group (Ref: CAG 5-08(d)/2013), the Office for National Statistics, and NHS Digital's Data Access Advisory Group (now Independent Group Advising on the Release of Data, Ref: NIC-323309-L2G9T).

Data Analysis

Population estimates and number of deaths by cause for males in England and Wales from 1967-2015 were obtained from the Office for National Statistics (ONS). Annual 5-year male reference rates were calculated for causes of death for each year in the follow-up period (1967-2015) (see Supplementary Table 1 for a list of ICD disease codes). Person-years, SMRs, 95% Confidence Intervals (CIs), and Breslow & Day tests for trends and homogeneity [8,9] were carried out using Stata's 'strate' and 'smrby' commands [10]. SMRs were reported where there are at least five observed deaths.

For *a priori* important causes of death (based on the IARC monograph conclusions and some early studies for non-malignant diseases) SMRs were also compared by decade of start in the industry, tyre and non-tyre (e.g., moulding, footwear) industries, and department. Sensitivity analyses were undertaken to examine any differences in SMR results for rubber industry-related health outcomes if individuals aged 90 years or older were censored, as well as for all individual job groups (Supplementary Table 3).

Results

Table 1 presents descriptive characteristics of the study cohort. The workforce was distributed fairly evenly across the age groups 35-44, 45-54, and 55-64 at start of follow-up, with 2.1% of the cohort aged 65 or over. Almost 5% of the cohort began work in the industry before 1930, nearly 10% during the 1930s, and just over 20% during the 1940s. Slightly over 40% of workers were employed in tyre manufacturing. Around 10% worked with crude materials, and around 20% were involved in pre-processing operations, with over 10% in curing/vulcanising and the remainder in finishing. Over 90%

of the cohort were deceased at the end of follow-up with just under 95% of the deaths including a coded cause of death.

For the *a priori* selected causes of death, statistically significantly elevated SMRs were obtained for all causes, all MNs, and for cancers of the stomach, lung, bladder, and NMRDs and CDs (Table 2). SMRs were not different to those expected for multiple myeloma, leukaemia, NHL, and cancers of the larynx, oesophagus, and prostate. Undertaking the SMR analysis with the exclusion of those aged 90 years or older had a negligible impact on study findings (data not shown).

Assessing SMRs across decade of employment start (Table 3) showed statistically significant increasing trends for all causes ($p < 0.001$), all neoplasms ($p = 0.017$), all causes excluding neoplasms ($p < 0.001$), lung cancer ($p < 0.001$), CDs ($p = 0.041$), and NMRDs ($p < 0.001$). The exception to the direction of these trends was bladder cancer, which exhibited a strong decreasing SMR trend across decade ($p = 0.015$) and only demonstrated a significantly increased SMR for those starting employment before 1930 (n = 36) (1.89 [95% CI 1.37 to 2.63]). Bladder cancer was the only *a priori* selected endpoint that was increased in workers starting before 1949 (n = 170) (1.33 [95% CI 1.15 to 1.55]), but not during or after 1949 (n=247) (1.06 [95% CI 0.94 to 1.20]) (See Supplementary Table 2). SMRs were significantly increased for bladder cancer only amongst those who worked in factories that used 1- and 2-naphthylamine prior to 1949 (n = 156) (1.32 [95% CI 1.13 to 1.54]). No increase was evident for those who started work in such factories after 1949 (n = 165) (1.07 [95% CI 0.92 to 1.25]), nor in facilities in which those substances had never been used (n = 96) (1.10 [95% CI 0.90 to 1.34]).

Examination of SMRs in the tyre and non-tyre sectors of the rubber industry (Table 4) indicated significant differences for stomach cancer, which was higher in the tyre (n = 343) (1.38 [95% CI 1.23 to 1.53]) than non-tyre industries (n = 425) (1.19 [95% CI 1.08 to 1.31]) ($p = 0.042$), but still significantly elevated in both sectors. The risk of NMRDs, whilst also significantly raised in both sectors, was higher in the non-tyre (n = 2,856) (1.17 [95% CI 1.13 to 1.21]) compared to the tyre sector (n = 1,874) (1.09 [95% CI 1.04 to 1.14]) (p = 0.019). The NHL SMR was found to be significantly lower in the tyre sector of the rubber industry (n = 47) (0.69 [95% CI 0.52 to 0.92]), but was not different

from unity in the non-tyre sectors (n = 96) (0.99 [95% CI 0.81 to 1.21]) (p = 0.037). No differential excess risks were observed in the tyre or non-tyre sectors for cancers of the oesophagus, larynx, or prostate, or for leukaemia, multiple myeloma, or CDs.

Conducting analyses by departments (Table 5) showed that SMRs tended to be highest in "Crude materials" and lowest in "Finishing" across many of the *a priori* important disease groups. Formally assessing SMRs gave statistically significant heterogeneity for all causes ($p < 0.001$), all malignant neoplasms ($p < 0.001$), all causes excluding neoplasms ($p < 0.001$), lung cancer ($p < 0.001$), CDs (p = 0.003), and NMRDs ($p < 0.001$). The pattern was noticeably different for bladder cancer, with the highest SMR in "Pre-processing" (n = 107) (1.41 [95% CI 1.16 to 1.70]; p = 0.131). For the other *a priori* important disease groups, risks were homogeneous between departments.

The results by individual job groups mainly presented the same patterns as the analysis by department. However, there were additional instances of significantly increased SMRs that had not been evident in the analysis by department: leukaemia in commercial staff and oesophageal cancer in both extruding and inspection workers (see Supplementary Table 3).

Discussion

This study sought evidence in relation to the risks of working in the British rubber and cable manufacturing industry using a large cohort that has not been studied since 1980 [6], by extending the follow-up to 49 years, and which resulted in 93% mortality. The overall SMR for bladder cancer of 1.16 is lower than that for lung cancer, and is also potentially influenced by tobacco smoking. In contrast to lung cancer, the SMR by decade first employed has decreased substantially, from just under 2.0 for those first employed before 1930 to not significantly raised above one for those first employed in any subsequent decade. Bladder cancer SMRs were significantly elevated for the tyre and non-tyre sectors, but only elevated for pre-processing operations, and, in particular, those working in extruding and component buildings. The data support the notion that working in the industry conferred an increased risk of bladder cancer, but only for those exposed to antioxidants containing 1-

and 2-naphthylamine (and maybe others), which were withdrawn from use in 1949. Research from other countries has also identified increased bladder cancer risks only for pre-1950s employment in the industry [4].

This study provided some evidence of raised risks of ischaemic heart disease and bronchitis, risks of which are both strongly influenced by tobacco smoking. The finding for ischaemic heart disease seems to be uniformly elevated across all decades workers first started employment in the industry, whereas for bronchitis the risk increased with decade starting employment. The excesses of both of these endpoints were found in the non-tyre industries and in the four main job groups for ischaemic heart disease, but, for bronchitis, only in the crude materials and pre-processing groups. An excess of mortality from chronic, but not acute, ischaemic heart disease was identified in an earlier study [11], whilst a meta-analysis (excluding the earlier study) identified lowered risks in rubber industry workers [12]; meta-SMRs for bronchitis were as expected in that study. Our findings of increased mortality in these non-cancer endpoints warrant further investigation to see if they are related to working in the industry.

Our study found statistically significantly increased SMRs for cancers of the stomach, lung, and bladder, but not for multiple myeloma, leukaemia, NHL, or for cancers of the oesophagus, larynx, or prostate. Thus, our findings are largely consistent with those of IARC, except that we found no increase in risk for leukaemia, NHL, or multiple myeloma.

The overall SMR for lung cancer of 1.25 is at a level where the excess risk could be due to confounding by tobacco smoking; however, we did not have data on the smoking history of cohort members. A study examining the role of tobacco smoking and lung cancer in the rubber industry found excess rate ratios in the curing department after adjusting for smoking, and suggested that the excess could be partially due to exposure to n-Nitrosamines in the process [13]. In the present study there was a highly statistically significant trend for increasing lung cancer SMRs from those first employed in the industry before 1930 through to those first employed in the 1960s, which mirrors the

general rise of per capita tobacco product use in the UK [14,15]. This SMR is significantly raised in the tyre and non-tyre sectors and, although raised in all job groups, is lower in finishing than the others. Such analyses need to be treated cautiously since surrogate indicators of exposure in occupational cohort studies can lead to an over-estimation of risks, especially for low-risk jobs and work areas [16]. Studies published since the latest IARC review [2] have also found increased lung cancer risks [17,18].

The overall SMR for stomach cancer was similar to that for lung cancer; tobacco smoking also influences the risk of this tumour. No trend in SMRs by decade of first employment was seen for stomach cancer and, as in the earlier follow-up[6], the excess was higher in the tyre sector, but also significantly raised in the non-tyre sectors. Stomach cancer risk was elevated for workers in the crude materials and pre-processing departments and particularly for compounding, latex mixing, extruding, inspection, site working, and engineering jobs. Recent studies have not found an increased stomach cancer risk in the rubber industry.[17-22]

None of the overall SMRs for multiple myeloma, leukaemia, or NHL was in excess. Another study based on the UK rubber industry identified a significantly increased risk of mortality from multiple myeloma, but this was based on only seven cases [23]. In the current study, there was a significant excess of leukaemia among commercial staff, but this could be due to chance rather than employment in the rubber industry given the low number of cases involved. Since the IARC review, only one study has found a relationship between time since first exposure and leukaemia risk, but there was no overall excess [22]. Although a meta-analysis found consistent evidence of raised risks for laryngeal cancer, with some positive findings for oesophageal cancer and prostate cancer from working in the rubber manufacturing industry [24], such risks were not identified in the present study. The absence of laryngeal and oesophageal cancers may suggest that smoking levels may not have been higher in the rubber industry compared to the general population, since these cancers are also linked to tobacco smoking [25].

To the best of our knowledge, this study constitutes the longest and most complete follow-up of the mortality of men employed in the rubber manufacturing industry in the UK. We carried out sensitivity

analyses relating to deaths in older ages and this had no impact on any of our analyses and, therefore, our conclusions. These strengths notwithstanding, the study had a number of limitations that warrant discussion. Firstly, this was a prospective cohort based on a census of the industry carried out in 1967. As such, there is evidence, including increasing trends with later decade of employment start, that suggests there is a healthy worker survivor effect [26-29] operating in this study; workers in the industry would have had to have survived and still be working in the industry by 1967 to have been included in the cohort. At the same time, it should also be noted that there is a distinct absence of a healthy worker effect due to the long follow-up of the cohort [29,30] as exemplified by significantly elevated SMRs from NMRDs and CDs, and so it is unlikely that the SMRs in this study will be biased towards the null by this. Secondly, we did not have complete work histories for the cohort, only job held at the time of recruitment into the study. This limited our ability to take account of different jobs over time and to explore carcinogenic and other mortality risks by job title in more detail. Thirdly, we had no information on smoking or any other important risk factors, such as work in other industries, exposure to asbestos, or diet. This omission could have resulted in a bias in those SMRs potentially affected by these risk factors. Our findings will also be subject to multiple significance testing [31]. In addition, this analysis only contained mortality data, and a future analysis of cancer incidence data is warranted for less fatal cancers, such as leukaemia.

An internet search of a sample of factories suggested that most incorporated in the original study have since closed, and remaining factories in the UK will have experienced improved hygiene standards and/or employed enhanced automation, both contributing to observed reductions in overall exposures [32]. Nevertheless, with global production of natural and synthetic rubber in 2016 in excess of 25 million tonnes, many workers around the world remain exposed to process generated emissions in rubber manufacturing [33]. Our results indicate potentially higher risks in the earlier stages of manufacturing, so continued research is needed to identify causative agents, especially in this stage of the process. Efforts should continue be made to reduce employee exposures to dust and fumes throughout the production process.

This study provides evidence that bladder cancer risk has declined in the industry, that there are increased risks for mortality from ischaemic heart disease and bronchitis and supports IARC's conclusions in relation to risks in the rubber industry for cancers of the bladder, lung, and stomach. IARC's conclusions for leukaemia, NHL, or multiple myeloma were not supported. Extension of this study to include cancer incidence and its inclusion in an international pooled study would further help clarify carcinogenicity from working in the industry.

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Table 1. Characteristics of study population of rubber workers (n = 36,442).

Characteristic	n (%)	Person-years
Age in 1967 (at study start) (years)		
35-44	11,595 (31.8)	387,592
45-54	13,220 (36.3)	315,067
55-64	10,852 (29.8)	170,706
65+	775 (2.1)	8,822
Decade of employment start		
<1930	1801 (4.9)	29,533
1930-1939	3570 (9.8)	76,074
1940-1949	7798 (21.4)	180,841
1950-1959	12,439 (31.1)	314,239
1960-1966	10,834 (29.7)	281,500
Industry sector		
Tyre	14,906 (40.9)	362,093
Non-tyre	21,536 (59.1)	520,094
Departments		
Job groups		
Crude Materials		
Storeman	178 (0.5)	3,767
Compounding	3574 (9.8)	83,431
Pre-processing		
Latex Mixing	424 (1.2)	9,586
Extruding & calendaring	3461 (9.5)	82,664
Component building	4037 (11.1)	101,068
Curing/Vulcanising		
Moulding	4710 (12.9)	118,909
Finishing		
Inspection	1954 (5.4)	46,239
Finished goods	2375 (6.5)	52,914
Site workers	2056 (5.6)	42,105
Engineering	6137 (16.8)	144,483
Canteens	30 (0.1)	606
Factory operations	5728 (15.7)	146,273
Commercial staff	485 (1.3)	13,381
Engineering staff	378 (1.0)	10,490
Technical staff	915 (2.5)	26,272
Vital Status		
Alive[1]	2125 (5.8%)	99,110
Dead	34,181 (93.8%)	781,001
Dead, no cause of death	1939 (5.3%)	38,976
Embarked/ Registration cancelled	136 (0.4%)	2,075

Total[2]	**36,442 (100)**	**882,187**

[1] Includes 125 deaths where date of death > 31 December, 2015

[2] Excludes 4425 untraced individuals from the original study (n=40,867).

Table 2 – Overall Standardised Mortality Ratios (SMRs) using England & Wales reference rates during 1967-2015.

Cause of death	n	SMR	95% CI
Including missing cause of death	**34,181**	**1.11**	**1.10 to 1.12**
Excluding missing cause of death	**32,242**	**1.08**	**1.07 to 1.10**
All neoplasms	**9,227**	**1.13**	**1.11 to 1.16**
All causes excluding neoplasms	**23,025**	**1.06**	**1.05 to 1.08**
All malignant neoplasms (MNs)	**9,101**	**1.14**	**1.12 to 1.16**
MN Buccal cavity and pharynx	89	0.93	0.75 to 1.14
MN Nasopharynx	6	0.80	0.36 to 1.78
MN Larynx	**62**	**0.94**	**0.74 to 1.21**
MN Oesophagus	**333**	**1.05**	**0.95 to 1.17**
MN Stomach	**768**	**1.26**	**1.18 to 1.36**
MN Colon	569	1.08	1.00 to 1.17
MN Rectum and rectosigmoid junction	407	1.22	1.10 to 1.34
MN Liver	122	0.95	0.80 to 1.14
MN Pancreas	328	1.01	0.91 to 1.12
MN Nose	7	0.72	0.34 to 1.51
MN Trachea, bronchus and lung	**3,380**	**1.25**	**1.21 to 1.29**
MN Prostate	**885**	**1.01**	**0.94 to 1.07**
MN Bladder	**417**	**1.16**	**1.05 to 1.28**
MN Kidney and other urinary organs	167	1.09	0.94 to 1.27
MN Brain	106	0.88	0.73 to 1.07
MN Lymphatic and haematopoietic tissue:	462	0.94	0.86 to 1.03
Hodgkin's disease	19	0.84	0.54 to 1.32
Multiple Myeloma	**105**	**1.00**	**0.82 to 1.21**
Leukaemia	**195**	**1.04**	**0.90 to 1.19**
Non-Hodgkin's lymphoma (NHL)	**143**	**0.87**	**0.74 to 1.02**
Endocrine nutritional and metabolic diseases	308	0.90	0.80 to 1.01
Diabetes mellitus	263	0.90	0.80 to 1.01
Diseases of circulatory system (CDs)	**14,627**	**1.07**	**1.05 to 1.09**
Ischaemic heart disease	9,349	1.08	1.06 to 1.10
Cerebrovascular disease	2,795	1.04	1.00 to 1.08
Diseases of respiratory system (NMRDs)	**4,730**	**1.14**	**1.10 to 1.17**
Bronchitis	842	1.09	1.02 to 1.17
Emphysema	163	1.19	1.02 to 1.38
Asthma	63	1.15	0.90 to 1.47
Diseases of the digestive system	828	1.00	0.93 to 1.07
Diseases of oral cavity, salivary grands and jaws	3	-	-
Diseases of oesophagus, stomach and duodenum	258	1.01	0.89 to 1.14
Peptic ulcer	220	1.02	0.89 to 1.16
Disease of the liver	106	0.79	0.65 to 0.95
Cirrhosis of liver	83	0.76	0.61 to 0.94
Diseases of genitourinary system	435	1.03	0.93 to 1.13
Nephritis and nephrosis	207	1.01	0.88 to 1.16

Accidents	440	1.00	0.92 to 1.10
Suicides	82	0.63	0.50 to 0.78

Notes:
A priori important diseases in **bold**.
See Supplementary Table 1 for ICD codes used.

Table 3. Standardised Mortality Ratios (SMRs) by decade of employment start in the rubber industry for selected causes of death during 1967-2015 (using England & Wales reference rates).

	Decade of Employment Start															
	<1930			1930-39			1940-49			1950-59			1960-66			
Cause of Death	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**p-value for Trend**
All causes																
Incl missing cause of death	1,787	1.04	0.99 to 1.09	3,505	1.06	1.02 to 1.09	7,410	1.08	1.05 to 1.10	11,515	1.11	1.09 to 1.13	9,964	1.17	1.14 to 1.19	<0.001
Excl missing cause of death	1,671	1.04	0.99 to 1.09	3,288	1.04	1.00 to 1.07	6,985	1.06	1.03 to 1.08	10,876	1.08	1.06 to 1.10	9,422	1.13	1.11 to 1.16	<0.001
All neoplasms	420	1.08	0.98 to 1.18	920	1.11	1.04 to 1.18	1,983	1.12	1.07 to 1.16	3,096	1.11	1.07 to 1.15	2,808	1.20	1.15 to 1.24	0.017
All cause excl neoplasms	1,251	1.03	0.97 to 1.09	2,368	1.01	0.97 to 1.05	5,002	1.03	1.00 to 1.06	7,785	1.07	1.04 to 1.09	6,619	1.11	1.08 to 1.13	<0.001
All malignant neoplasms	415	1.08	0.97 to 1.18	909	1.12	1.04 to 1.19	1,956	1.12	1.07 to 1.17	3,048	1.11	1.07 to 1.15	2,773	1.21	1.16 to 1.25	0.012
MN Larynx	4	-	-	6	0.90	0.33 to 1.96	9	0.63	0.29 to 1.19	25	1.11	0.72 to 1.64	18	0.95	0.56 to 1.50	0.822
MN Oesophagus	14	1.18	0.65 to 1.99	27	0.91	0.60 to 1.33	57	0.85	0.64 to 1.10	118	1.06	0.87 to 1.27	117	1.22	1.01 to 1.46	0.130
MN Stomach cancer	41	1.11	0.80 to 1.51	76	1.14	0.90 to 1.43	176	1.29	1.11 to 1.50	262	1.30	1.14 to 1.46	213	1.29	1.12 to 1.47	0.365
MN Trachea, bronchus and lung	143	0.98	0.83 to 1.16	331	1.16	1.03 to 1.29	739	1.24	1.15 to 1.33	1,080	1.18	1.11 to 1.25	1,087	1.43	1.34 to 1.51	<0.001
MN Prostate	33	0.80	0.57 to 1.13	114	1.24	1.03 to 1.48	208	1.07	0.93 to 1.22	278	0.92	0.82 to 1.03	252	1.01	0.89 to 1.14	0.446
MN Bladder	36	1.89	1.37 to 2.63	47	1.24	0.93 to 1.65	93	1.16	0.95 to 1.43	139	1.14	0.96 to 1.34	102	1.01	0.83 to 1.23	0.015
Multiple Myeloma	5	1.11	0.46 to 2.66	12	1.13	0.64 to 2.00	25	1.10	0.74 to 1.62	29	0.79	0.55 to 1.14	34	1.10	0.78 to 1.54	0.779
Leukaemia	12	1.44	0.82 to 2.54	24	1.31	0.88 to 1.95	34	0.84	0.60 to 1.17	66	1.01	0.79 to 1.28	59	1.06	0.82 to 1.37	0.542
Non-Hodgkin's Lymphoma	3	-	-	9	0.59	0.31 to 1.14	35	1.00	0.72 to 1.40	46	0.79	0.59 to 1.05	50	0.99	0.75 to 1.30	0.272
Circulatory Diseases	842	1.08	1.01 to 1.15	1,552	1.04	0.99 to 1.09	3,170	1.03	1.00 to 1.07	4,949	1.08	1.05 to 1.09	4,114	1.09	1.06 to 1.13	0.091

Ischaemic Heart Disease	514	1.08	0.99 to 1.18	992	1.06	0.99 to 1.13	2054	1.07	1.02 to 1.11	3159	1.09	1.05 to 1.13	2630	1.09	1.05 to 1.14	0.423
Respiratory Diseases	226	0.88	0.78 to 1.01	443	0.95	0.87 to 1.05	1,051	1.11	1.05 to 1.18	1,595	1.15	1.10 to 1.21	1,415	1.27	1.21 to 1.34	<0.001
Bronchitis	63	0.85	0.66 to 1.08	86	0.92	0.74 to 1.13	189	1.03	0.90 to 1.19	264	1.11	0.99 to 1.26	240	1.32	1.17 to 1.50	<0.001
Emphysema	10	1.28	0.69 to 2.38	12	0.79	0.45 to 1.39	34	1.10	0.79 to 1.54	53	1.15	0.88 to 1.51	54	1.44	1.10 to 1.87	0.186

Table 4. Standardised Mortality Ratios (SMRs) for workers in tyre and non-tyre sectors in the rubber industry for selected causes of death during 1967-2015 (using England & Wales reference rates).

	Industry Group							
	Tyre			Non-Tyre				
Cause of death	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**Test for homogeneity (X^2)**	**p-value**
All causes								
Incl missing cause of death	13,929	1.10	1.08 to 1.12	20,252	1.11	1.10 to 1.13	1.64	0.201
Excl missing cause of death	13,223	1.08	1.06 to 1.09	19,019	1.09	1.07 to 1.10	0.87	0.352
All neoplasms	3,837	1.14	1.11 to 1.18	5,390	1.13	1.10 to 1.16	0.36	0.549
All cause excl neoplasms	9,390	1.05	1.03 to 1.07	13,635	1.07	1.05 to 1.09	2.23	0.136
All malignant neoplasms	3,789	1.15	1.11 to 1.19	5,312	1.13	1.10 to 1.16	0.25	0.614
MN Larynx	26	0.96	0.63 to 1.41	36	0.93	0.65 to 1.29	0.02	0.899
MN Oesophagus	150	1.15	0.97 to 1.35	183	0.99	0.85 to 1.14	1.86	0.172
MN Stomach cancer	343	1.38	1.23 to 1.53	425	1.19	1.08 to 1.31	4.13	0.042
MN Trachea, bronchus and lung	1,393	1.25	1.19 to 1.32	1,987	1.25	1.19 to 1.30	0.01	0.94
MN Prostate	383	1.05	0.95 to 1.16	502	0.98	0.89 to 1.07	1.09	0.297
MN Bladder	173	1.16	1.00 to 1.35	244	1.16	1.02 to 1.31	0.01	0.94
Multiple Myeloma	49	1.13	0.85 to 1.49	56	0.90	0.70 to 1.18	1.25	0.264
Leukaemia	78	1.00	0.80 to 1.25	117	1.06	0.88 to 1.27	0.15	0.699
Non-Hodgkin's Lymphoma	47	0.69	0.52 to 0.92	96	0.99	0.81 to 1.22	4.33	0.037
Circulatory Diseases	5,968	1.06	1.03 to 1.09	8,659	1.08	1.05 to 1.10	0.82	0.365
Ischaemic Heart Disease	3,811	1.07	1.04 to 1.11	5,538	1.09	1.06 to 1.12	0.57	0.449
Respiratory Diseases	1,874	1.09	1.04 to 1.14	2,856	1.17	1.13 to 1.21	5.49	0.019
Bronchitis	322	1.03	0.93 to 1.15	520	1.13	1.04 to 1.24	1.71	0.192
Emphysema	54	0.96	0.73 to 1.25	109	1.35	1.12 to 1.63	4.34	0.037

Table 5. Standardised Mortality Ratios (SMRs) for workers in different departments in the rubber industry for selected causes of death during 1967-2015 (using England & Wales reference rates).

	Job Groups													
	Crude Materials			Pre-processing			Curing/vulcanising			Finishing				
Cause of death	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**n**	**SMR**	**95% CI**	**Test for homogeneity (X^2)**	**p-value**
All causes														
Incl missing cause of death	3,578	1.19	1.15 to 1.23	7,441	1.14	1.12 to 1.17	4,434	1.14	1.10 to 1.17	18,728	1.07	1.06 to 1.09	49.8	<0.001
Excl missing cause of death	3,359	1.17	1.13 to 1.21	7,037	1.12	1.09 to 1.15	4,193	1.11	1.08 to 1.15	17,653	1.05	1.03 to 1.06	49.72	<0.001
All neoplasms	972	1.24	1.16 to 1.32	2,064	1.19	1.14 to 1.24	1,244	1.19	1.12 to 1.25	4,947	1.08	1.05 to 1.11	25.11	<0.001
All cause excl neoplasms	2,388	1.14	1.10 to 1.19	4,976	1.09	1.06 to 1.12	2,949	1.08	1.06 to 1.12	12,712	1.03	1.02 to 1.05	27.07	<0.001
All malignant neoplasms	956	1.24	1.16 to 1.32	2,037	1.20	1.14 to 1.25	1,228	1.20	1.13 to 1.26	4,880	1.09	1.06 to 1.12	24.02	<0.001
MN Larynx	9	1.40	0.64 to 2.66	14	1.00	0.54 to 1.67	4	-	-	35	0.95	0.66 to 1.32	3.48	0.323
MN Oesophagus	28	0.94	0.62 to 1.35	83	1.22	0.97 to 1.51	48	1.15	0.85 to 1.53	174	0.99	0.84 to 1.14	3.36	0.339
MN Stomach cancer	86	1.42	1.14 to 1.75	180	1.40	1.20 to 1.62	89	1.16	0.93 to 1.43	413	1.21	1.10 to 1.33	4.38	0.223
MN Trachea, bronchus and lung	393	1.47	1.32 to 1.62	775	1.34	1.25 to 1.44	467	1.35	1.23 to 1.47	1,745	1.15	1.10 to 1.21	27.52	<0.001
MN Prostate	76	0.93	0.75 to 1.17	165	0.89	0.76 to 1.04	123	1.10	0.92 to 1.32	521	1.04	0.95 to 1.13	4.39	0.222
MN Bladder	39	1.13	0.83 to 1.55	107	1.41	1.16 to 1.70	54	1.18	0.91 to 1.55	217	1.06	0.93 to 1.22	5.64	0.131
Multiple Myeloma	9	0.89	0.46 to 1.71	22	0.97	0.64 to 1.48	15	1.09	0.66 to 1.81	59	1.00	0.77 to 1.29	0.25	0.969
Leukaemia	23	1.29	0.86 to 1.94	41	1.02	0.75 to 1.38	28	1.15	0.79 to 1.67	103	0.97	0.80 to 1.18	1.8	0.614
Non-Hodgkin's Lymphoma	12	0.77	0.44 to 1.36	35	0.98	0.71 to 1.37	17	0.78	0.49 to 1.26	79	0.86	0.69 to 1.07	0.91	0.824
Circulatory Diseases	1,512	1.13	1.08 to 1.19	3,206	1.11	1.07 to 1.15	1,838	1.06	1.02 to 1.11	8,071	1.04	1.02 to 1.07	14.04	0.003
Ischaemic Heart Disease	961	1.13	1.06 to 1.20	1999	1.09	1.04 to 1.14	1166	1.06	1.00 to 1.12	5223	1.07	1.05 to 1.10	2.65	0.448
Respiratory Diseases	512	1.29	1.18 to 1.41	1,024	1.18	1.11 to 1.26	647	1.26	1.16 to 1.36	2,547	1.07	1.03 to 1.11	26.55	<0.001
Bronchitis	101	1.25	1.03 to 1.52	185	1.17	1.01 to 1.35	102	1.12	0.93 to 1.36	454	1.03	0.94 to 1.13	4.22	0.239
Emphysema	12	0.89	0.51 to 1.57	27	0.93	0.64 to 1.35	20	1.15	0.74 to 1.78	104	1.34	1.11 to 1.63	4.20	0.241