

# Exhibit 304

# Mortality of United Kingdom oil refinery and petroleum distribution workers, 1951–1998

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The mortality experienced by cohorts of 28 630 oil refinery workers and 16 480 petroleum distribution workers has been investigated. Study subjects were all those male employees first employed in the period 1946–1974 at one of eight UK oil refineries or at one of 476 UK petroleum distribution centres; all subjects had a minimum of 12 months employment with some employment after 1 January 1951. The observed numbers of cause-specific deaths were compared with expectations based on national mortality rates. The resultant standardized mortality ratios (SMRs) were significantly below 100 for all causes, in both oil refinery workers (observed, 9341; expected, 10 649.7; SMR = 88) and petroleum distribution workers (observed, 6083; expected, 6460.3; SMR = 94). Significantly elevated SMRs were shown in oil refinery workers for cancer of the gall bladder (observed, 24; expected, 14.0; SMR = 172), cancer of the pleura (observed, 38; expected, 15.0; SMR = 254) and melanoma (observed, 36; expected, 22.2; SMR = 162). Significantly elevated SMRs were not found in petroleum distribution workers for any site of cancer. SMRs for selected causes of death were calculated by period from commencing employment, by year of hire and by job type. The only findings that suggested the presence of an occupational cancer hazard were an excess of mesothelioma in oil refinery workers and an excess of leukaemia in petroleum distribution workers, both excesses occurring in long-term follow-up for workers first employed >30 years ago.

**Key words:** Cancer mortality; oil refinery workers; petroleum distribution workers.

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## Introduction

In the 1970s, the Institute of Petroleum developed epidemiological cohort studies into the mortality and cancer morbidity experience of male employees from eight oil refineries and 476 petroleum distribution centres in the UK [1,2]; follow-up in the most recent reports was to the end of 1989 [3,4]. A large number of cohort studies of petroleum industry workers in different parts of the world have been carried out; a meta-analysis of findings by site of cancer is available [5].

The original cohorts comprised 34 569 oil refinery workers [1] and 23 358 petroleum distribution workers [2]. All these male employees had a minimum period of

employment of 12 months in the period 1950–1975; some study subjects were first employed around the turn of the century. The cohorts reported here have been redefined so that the findings will be relevant to more recent work conditions that can be described with some confidence. The updated analyses are limited to those workers first employed after 1 January 1946. The new findings refer in the main to an entry cohort (workers first employed in the period 1950–1974). The extent of any ‘survivor population effect’ present in the subcohort of workers first employed in the period 1946–1949 is judged likely to be modest; workers who commenced employment in this period would only appear in the study if they remained (‘survived’) in the industry until 1 January 1951.

The mortality data for a further 9 years (1990–1998) were available for analysis in the overall period of follow-up (1951–1998), together with cancer registration data

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for the period 1971–1994. Unfortunately, it was clear from initial analyses that the cancer registration data were very incomplete, and this part of the proposed study has been postponed until more reliable information becomes available.

The objectives of the study were to summarize available mortality data and to determine whether any part of the mortality experience of the cohort might be related to occupational exposures (in which event, further analyses capable of investigating the potential role of occupational exposures might be needed).

## Materials and methods

The computer file for the revised cohorts contained identifying particulars (name and date of birth), work history information (oil refinery or petroleum distribution centre, dates of commencing and leaving employment, job title in 1975 or last job if left employment before 1975) and follow-up information (date of death, underlying cause of death and contributory causes of death) for 28 630 oil refinery workers and 16 480 petroleum distribution workers first employed in the period 1946–1974. All subjects had a minimum of 12 months employment, with some employment after 1 January 1951. Six of the oil refineries were in England and Wales, while the remaining two were located in Scotland. A total of 403 of the petroleum distribution centres were in England and Wales, while the remaining 73 centres were located in Scotland.

The National Health Service Central Register of the Office for National Statistics and the General Register Office for Scotland provided vital status information on the closing date of the survey, 31 December 1998. For those refinery workers who had died ( $n = 9627$ ), a copy of the death certificate was supplied with the underlying cause of death and other causes of death coded to the contemporaneous revision of the *International Classification of Diseases* (ICD); the recorded cause of death was untraced for only 84 deaths (0.9%). A total of 1659 refinery workers (5.8%) had emigrated and 254 refinery workers were untraceable (0.9%). A total of 6269 decedents were identified in the petroleum distribution workers; the recorded cause of death was untraced for only 60 deaths (1.0%). A total of 306 distribution workers (1.9%) had emigrated and 367 distribution workers were untraceable (2.2%).

Expected numbers of deaths were calculated from male mortality rates [specified by 5 year age groups, 5 year calendar periods and country (England and Wales or Scotland)] applied to similarly defined arrays of person years at risk (pyr) generated by the data. Workers entered the pyr at the end of the 12 months minimum period of employment or 1 January 1951, whichever was the later date. They left the pyr on the closing date of the study

(31 December 1998), the date of death, the date of emigration or the date last known alive, whichever was the earlier. These procedures were accomplished by means of the PERSONYEARS software. No contributions were made to observed or expected numbers past the age of 85 years. This censoring at age 85 years was applied for three reasons. First, published mortality rates are only available for the 'open-ended' age group  $\geq 85$  years and the distribution of the cohort pyr by single years of age might be very different from that of the general population; secondly, the reliability of cause of death particulars is probably poorer at later ages; thirdly, any study subjects incorrectly classified as traced alive at the end of the study would have a disproportionate effect on the expected numbers for the open-ended age group.

Observed and expected numbers for workers in England and Wales were then combined with those for Scottish workers. Overall standardized mortality ratios (SMRs) were calculated as the ratio of observed deaths to expected deaths, expressed as a percentage. The significance of the differences between observed numbers and their corresponding expectations was assessed by means of the Poisson distribution. In addition, evidence was sought for any trend (linear component) in the pattern of SMRs (e.g. any tendency for SMRs to increase or decrease with time since first employment) [6]. Tests of heterogeneity were also carried out (e.g. could the differences in SMRs by job title represent no more than random variation in subgroups) [6]. Both tests assume a similar null hypothesis: no trend and homogeneous SMRs. Small  $P$  values indicate statistical significance, either that the trend is unlikely to have occurred by chance alone or that the amount of heterogeneity is unlikely to have occurred by chance alone. All significance tests were two-tailed.

## Results

Overall observed and expected numbers of deaths for the main disease groupings are shown in Table 1. Mortality from all causes was significantly below that expected on the basis of national mortality rates for both oil refinery workers [observed, 9341; expected, 10 649.7; SMR = 88, 95% confidence interval (CI) = 86–90,  $P < 0.001$ ] and petroleum distribution workers (observed, 6083; expected, 6460.3; SMR = 94, 95% CI = 92–97,  $P < 0.001$ ). Significant deficits are shown for most of the important non-cancer disease groupings for both oil refinery and petroleum distribution workers.

Overall observed and expected numbers of deaths for individual cancer sites (three-digit ICD codes) are also shown in Table 1. In oil refinery workers, mortality from all neoplasms was significantly below expectations (observed, 2862; expected, 3072.0; SMR = 93, 95% CI = 90–97,  $P < 0.001$ ). Significant deficits are also

**Table 1.** Cause-specific mortality of UK oil refinery ( $n = 28\,630$ ) and petroleum distribution ( $n = 16\,480$ ) workers, 1951–1998

Cause of death	ICD9	Refinery workers				Distribution workers			
		Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)
Cancers									
Lip	140	0	1.0	0		0	0.6	0	
Tongue	141	4	10.2	39	(11–100)	9	6.4	140	(64–266)
Salivary gland	142	3	4.1	72	(15–212)	0	2.6	0	
Mouth	143–145	6	10.4	58	(21–126)	6	6.6	91	(33–198)
Pharynx	146–149	16	21.1	76	(43–123)	8	13.3	60	(26–118)
Oesophagus	150	106	118.5	89	(73–108)	64	74.0	86	(67–110)
Stomach	151	238	253.9	94	(82–106)	174	154.3	113	(97–131)
Small intestine	152	7	5.7	122	(49–252)	6	3.5	170	(63–371)
Large intestine	153	184	198.2	93	(80–107)	118	121.7	97	(80–116)
Rectum	154	116	130.4	89	(74–107)	71	80.3	88	(69–112)
Liver	155.0, 155.1	18	26.9	67	(40–106)	17	16.8	101	(59–162)
Gall bladder	156	24	14.0	172 <sup>a</sup>	(110–256)	6	8.5	71	(26–154)
Pancreas	157	92	126.6	73 <sup>(b)</sup>	(59–89)	88	77.5	114	(91–140)
Peritoneum	158	8	5.8	137	(59–270)	7	3.6	194	(78–400)
Other digestive	159	15	13.7	110	(61–181)	12	8.4	143	(74–250)
Nose and sinuses	160	5	5.2	97	(31–225)	2	3.1	64	(8–230)
Larynx	161	28	29.0	97	(64–140)	25	18.0	139	(90–205)
Lung and bronchus	162	959	1120.0	86 <sup>(c)</sup>	(80–91)	686	685.0	100	(93–108)
Pleura	163	38	15.0	254 <sup>c</sup>	(180–348)	7	9.5	73	(30–151)
Bone	170	4	7.7	52	(14–133)	1	4.5	22	(1–124)
Connective tissue	171	12	10.4	115	(59–201)	4	6.3	64	(17–163)
Melanoma	172	36	22.2	162 <sup>b</sup>	(113–224)	8	13.5	59	(26–117)
Skin, other	173	11	8.4	132	(66–236)	2	5.0	40	(5–144)
Breast	175	2	3.6	55	(7–200)	3	2.2	137	(28–400)
Prostate	185	200	201.9	99	(86–114)	137	118.8	115	(97–136)
Testis	186	4	9.8	41	(11–105)	5	5.3	94	(31–219)
Other genital	187	0	4.4	0		3	2.7	113	(23–331)
Bladder	188	113	112.8	100	(83–120)	68	68.1	100	(78–127)
Kidney	189.0	66	60.2	110	(85–139)	45	37.5	120	(88–161)
Other urinary	189.1–189.9	3	3.1	96	(20–280)	2	1.9	104	(13–376)
Eye	190	1	3.2	31	(1–172)	1	2.0	51	(1–281)
Brain	191–192	74	78.7	94	(74–118)	37	48.3	77	(54–106)
Thyroid	193	3	4.9	61	(13–178)	5	3.0	165	(54–385)
Other endocrine glands	194	0	2.5	0		1	1.5	66	(2–369)
Secondary and other cancers	195–199	211	182.0	116 <sup>a</sup>	(101–133)	117	110.8	106	(87–127)
Hodgkins disease	201	13	20.1	65	(34–110)	14	11.6	121	(66–203)
Lymphosarcoma	200, 202	84	68.8	122	(97–151)	37	41.8	89	(62–122)
Multiple myeloma	203	34	38.5	88	(61–123)	19	23.5	81	(49–126)
Leukaemia	204–208	80	73.8	108	(86–135)	57	43.8	130	(98–168)
Lymphoid leukaemia	204	21	21.5	98	(61–150)	20	12.9	156	(95–240)
Myeloid leukaemia	205	44	40.7	108	(79–145)	29	24.4	119	(80–171)
Monocytic leukaemia	206	5	2.3	216	(70–505)	1	1.3	75	(2–419)
Other leukaemia	207, 208	10	9.4	106	(51–196)	7	5.3	132	(53–272)
All neoplasms	140–239	2862	3072.0	93 <sup>(c)</sup>	(90–97)	1913	1873.0	102	(98–107)
Non-cancers									
Infectious and parasitic diseases	1–139	30	80.4	37 <sup>(c)</sup>	(25–53)	20	47.4	42 <sup>(c)</sup>	(26–65)
Endocrine/nutritional/metabolic diseases	240–279	81	123.5	66 <sup>(c)</sup>	(52–82)	64	74.2	86	(66–110)
Diseases of blood	280–289	19	26.0	73	(44–114)	8	15.4	52	(22–103)
Mental disorders	290–319	60	61.7	97	(74–125)	34	35.6	96	(66–134)
Diseases of nervous system	320–389	125	151.0	83 <sup>(a)</sup>	(69–99)	66	88.4	75 <sup>(a)</sup>	(58–95)
Diseases of circulatory system	390–459	4428	5035.0	88 <sup>(c)</sup>	(85–91)	2909	3073.9	95 <sup>(b)</sup>	(91–98)
Diseases of respiratory system	460–519	848	1112.0	76 <sup>(c)</sup>	(71–82)	552	665.8	83 <sup>(c)</sup>	(76–90)
Diseases of digestive system	520–579	250	295.6	85 <sup>(b)</sup>	(74–96)	149	180.4	83 <sup>(a)</sup>	(70–97)
Diseases of genitourinary system	580–629	97	112.3	86	(70–105)	55	66.9	82	(62–107)
Diseases of skin	680–709	4	5.8	69	(19–176)	8	3.5	232	(100–457)
Diseases of musculo-skeletal system	710–739	17	29.9	57 <sup>(a)</sup>	(33–91)	15	17.7	85	(47–140)
Accidents	800–949	286	302.5	95	(84–106)	152	168.9	90	(76–105)
Suicide	950–959	101	136.7	74 <sup>(b)</sup>	(60–90)	48	78.3	61 <sup>(c)</sup>	(45–81)
All causes		9341	10 649.7	88 <sup>(c)</sup>	(86–90)	6083	6460.3	94 <sup>(c)</sup>	(92–97)

Obs, observed; Exp, expected.

<sup>a</sup> $P < 0.05$ ; <sup>b</sup> $P < 0.01$ ; <sup>c</sup> $P < 0.001$ ; () indicates deficit.



shown for cancer of the pancreas (observed, 92; expected, 126.6; SMR = 73, 95% CI = 59–89,  $P < 0.05$ ) and for lung cancer (observed, 959; expected, 1120.0; SMR = 86, 95% CI = 80–91,  $P < 0.001$ ). Significant excesses are shown for cancer of the gall bladder (observed, 24; expected, 14.0; SMR = 172, 95% CI = 110–256,  $P < 0.05$ ), cancer of the pleura (observed, 38; expected, 15.0; SMR = 254, 95% CI = 180–348,  $P < 0.001$ ), melanoma (observed, 36; expected, 22.2; SMR = 162, 95% CI = 113–224,  $P < 0.01$ ) and a residual category (secondary and other cancers) (observed, 211; expected, 182.0; SMR = 116, 95% CI = 101–133,  $P < 0.05$ ). Leukaemia mortality was unexceptional (observed, 80; expected, 73.8; SMR = 108, 95% CI = 86–135). In petroleum distribution workers, mortality from all neoplasms was close to expectation (observed, 1913; expected, 1873.0; SMR = 102, 95% CI = 98–107). There were no statistically significant differences between observed and expected numbers for any individual site of cancer. The SMR for leukaemia was  $>100$ , but not sig-

nificantly so (observed, 57; expected, 43.8; SMR = 130, 95% CI = 98–168).

Expectations for leukaemia subtypes were not available for the full period of study, but these could be calculated for the period 1968–1998 (national statistics coded to the eighth and ninth revisions of the ICD). In refinery workers, SMRs for leukaemia subtypes were unexceptional. In distribution workers, non-significant excesses were shown for acute lymphatic leukaemia (ALL) (observed, 5; expected, 2.10; SMR = 238, 95% CI = 77–556), chronic lymphatic leukaemia (CLL) (observed, 15; expected, 9.23; SMR = 163, 95% CI = 91–268) and acute myeloid leukaemia (AML) (observed, 24; expected, 15.91; SMR = 151, 95% CI = 97–224). A non-significant deficit was shown for chronic myeloid leukaemia (CML) in distribution workers (observed, 4; expected, 6.35; SMR = 63, 95% CI = 17–161).

The overall findings were reviewed in order to select causes of death that warranted further investigation. Cancer of the gall bladder, cancer of the pleura (meso-

**Table 2.** Mortality from cancer of the gall bladder, cancer of the pleura, melanoma, leukaemia and all causes in UK oil refinery ( $n = 28\,630$ ) and petroleum distribution ( $n = 16\,480$ ) workers by successive periods from commencing employment, 1951–1998

Period from commencing employment (years)	Refinery workers					Distribution workers				
	Obs	Exp	SMR	(95% CI)	Statistical evaluation <sup>a</sup>	Obs	Exp	SMR	(95% CI)	Statistical evaluation <sup>a</sup>
Cancer of the gall bladder										
1–9	1	0.6	175	(4–977)	$P = 0.94, P = 0.92$	1	0.5	204	(5–1137)	$P = 0.52, P = 0.11$
10–19	5	2.4	208	(68–486)		2	1.7	120	(15–433)	
20–29	6	4.2	142	(52–308)		2	2.7	73	(9–265)	
≥30	12	6.8	178	(92–311)		1	3.6	28	(1–156)	
Total	24	14.0	172 <sup>b</sup>	(110–256)		6	8.5	71	(26–154)	
Cancer of the pleura										
1–9	1	0.1	1000	(25–5572)	$P = 0.23, P = 0.46$	0	0.1	0		$P = 0.34, P = 0.11$
10–19	2	1.1	190	(23–688)		2	1.0	202	(24–730)	
20–29	6	3.8	159	(58–345)		3	3.1	98	(20–286)	
≥30	29	10.0	289 <sup>d</sup>	(193–415)		2	5.3	38	(5–136)	
Total	38	15.0	254 <sup>d</sup>	(180–348)		7	9.5	73	(30–151)	
Melanoma										
1–9	9	1.7	533 <sup>d</sup>	(244–1011)	$P < 0.001, P < 0.001$	0	1.2	0		$P = 0.27, P = 0.76$
10–19	8	3.8	210	(91–414)		1	2.7	38	(1–210)	
20–29	9	6.3	144	(66–273)		5	4.2	118	(38–277)	
≥30	10	10.5	96	(46–176)		2	5.4	37	(4–133)	
Total	36	22.2	162 <sup>c</sup>	(113–224)		8	13.5	59	(26–117)	
Leukaemia										
1–9	9	7.4	121	(55–230)	$P = 0.93, P = 0.89$	3	4.6	65	(13–191)	$P = 0.43, P = 0.11$
10–19	11	11.9	92	(46–165)		8	7.9	101	(44–199)	
20–29	19	18.0	106	(64–165)		17	12.2	139	(81–223)	
≥30	41	36.5	112	(81–152)		29	19.1	152 <sup>b</sup>	(102–218)	
Total	80	73.8	108	(86–135)		57	43.8	130	(98–168)	
All causes										
1–9	525	697.7	75 <sup>(d)</sup>	(69–82)	$P < 0.001, P < 0.001$	396	487.3	81 <sup>(d)</sup>	(73–90)	$P = 0.002, P < 0.001$
10–19	1296	1588.0	82 <sup>(d)</sup>	(77–86)		1005	1118.0	90 <sup>(d)</sup>	(84–96)	
20–29	2514	2808.3	90 <sup>(d)</sup>	(86–93)		1789	1902.2	94 <sup>(d)</sup>	(90–99)	
≥30	5006	5555.7	90 <sup>(d)</sup>	(88–93)		2893	2952.7	98	(94–102)	
Total	9341	10 649.7	88 <sup>(d)</sup>	(86–90)		6083	6460.3	94 <sup>(d)</sup>	(92–97)	

<sup>a</sup>The  $P$  value for heterogeneity is followed by the  $P$  value for trend for each set of four SMRs.

<sup>b</sup> $P < 0.05$ ; <sup>c</sup> $P < 0.01$ ; <sup>d</sup> $P < 0.001$ ; ( ) indicates deficit.

thelioma) and melanoma were selected on the basis of the excess SMRs in refinery workers. Leukaemia was selected on the basis of previous interest in the occurrence of this disease in petroleum industry workers [7–9]. All causes mortality was selected to gauge the likely influence of selection and socio-economic effects.

Mortality from selected causes of death is shown by period from commencing employment in Table 2. Highly significant positive trends are shown for all causes mortality in both refinery and distribution workers. A highly significant negative trend is shown for melanoma in oil refinery workers. Significantly elevated SMRs are shown for cancer of the pleura in refinery workers and leukaemia in distribution workers, both excesses occurring  $\geq 30$  years from date of hire. In distribution workers, there were no significant trends of SMRs increasing with period from hire for ALL, CLL or AML (not shown in Table 2).

Mortality from selected causes of death is shown by year of hire in Table 3. Highly significant trends are shown for all causes mortality in both refinery and distribution

workers, such that earlier decades of hire tend to be associated with elevated mortality. A similar tendency is shown for cancer of the pleura in refinery workers, although the trend is not statistically significant.

Mortality in refinery workers from selected causes of death is shown by job type in Table 4. There is a highly significant heterogeneity shown in the set of SMRs for all causes mortality. Cancer of the pleura is significantly elevated in operators, labourers and engineers. Melanoma is significantly elevated in administrative and clerical staff.

Mortality in petroleum distribution workers from selected causes of death is shown by job type in Table 5. There is a highly significant heterogeneity shown in the set of SMRs for all causes mortality; significant heterogeneity is also shown for cancer of the pleura. Further analyses in relation to year of death are available in two technical reports [10,11].

## Discussion

Occupational exposures are unlikely to have discernible

**Table 3.** Mortality from cancer of the gall bladder, cancer of the pleura, melanoma, leukaemia and all causes in UK oil refinery ( $n = 28\ 630$ ) and petroleum distribution ( $n = 16\ 480$ ) workers by year of hire, 1951–1998

Year of hire	Refinery workers					Distribution workers				
	Obs	Exp	SMR	(95% CI)	Statistical evaluation <sup>a</sup>	Obs	Exp	SMR	(95% CI)	Statistical evaluation <sup>a</sup>
Cancer of the gall bladder										
1946–1949	8	3.1	261 <sup>b</sup>	(113–515)	$P = 0.30, P = 0.25$	1	2.5	40	(1–225)	$P = 0.30, P = 0.14$
1950–1959	15	9.6	157	(88–258)		2	3.7	54	(7–197)	
1960–1969	0	1.0	0			2	2.0	99	(12–356)	
1970–1974	1	0.3	333	(8–1857)		1	0.3	345	(9–1921)	
Total	24	14.0	172 <sup>b</sup>	(110–256)		6	8.5	71	(26–154)	
Cancer of the pleura										
1946–1949	5	2.6	194	(63–452)	$P = 0.15, P = 0.38$	0	1.9	0		$P = 0.39, P = 0.34$
1950–1959	31	9.8	316 <sup>d</sup>	(215–449)		3	3.8	80	(16–234)	
1960–1969	1	1.9	53	(1–295)		4	3.2	123	(34–316)	
1970–1974	1	0.7	147	(4–819)		0	0.6	0		
Total	38	15.0	254 <sup>d</sup>	(180–348)		7	9.5	73	(30–151)	
Melanoma										
1946–1949	6	3.5	171	(63–372)	$P = 0.16, P = 0.15$	0	2.7	0		$P = 0.50, P = 0.14$
1950–1959	18	13.5	133	(79–210)		3	5.1	59	(12–172)	
1960–1969	6	3.6	167	(61–364)		4	4.8	84	(23–216)	
1970–1974	6	1.6	377 <sup>b</sup>	(138–821)		1	1.0	97	(2–541)	
Total	36	22.2	162 <sup>c</sup>	(113–224)		8	13.5	59	(26–117)	
Leukaemia										
1946–1949	19	14.7	129	(78–202)	$P = 0.49, P = 0.14$	12	11.5	105	(54–183)	$P = 0.08, P = 0.22$
1950–1959	53	48.4	110	(82–143)		20	18.3	109	(67–169)	
1960–1969	7	7.8	90	(36–186)		24	12.0	200 <sup>b</sup>	(120–297)	
1970–1974	1	3.0	34	(1–187)		1	2.1	49	(1–270)	
Total	80	73.8	108	(86–135)		57	43.8	130	(98–168)	
All causes										
1946–1949	2159	2312.4	93 <sup>(o)</sup>	(89–97)	$P < 0.001, P < 0.001$	1815	1894.1	96	(96–100)	$P < 0.001, P = 0.001$
1950–1959	6370	7183.6	89 <sup>(d)</sup>	(87–91)		2684	2753.4	97	(94–101)	
1960–1969	600	861.4	70 <sup>(d)</sup>	(64–75)		1415	1570.5	90 <sup>(d)</sup>	(85–95)	
1970–1974	212	292.3	73 <sup>(d)</sup>	(63–83)		169	242.2	70 <sup>(d)</sup>	(60–81)	
Total	9341	10 649.7	88 <sup>(d)</sup>	(86–90)		6083	6460.3	94 <sup>(d)</sup>	(92–97)	

<sup>a</sup>The  $P$  value for heterogeneity is followed by the  $P$  value for trend for each set of four SMRs.

<sup>b</sup> $P < 0.05$ ; <sup>c</sup> $P < 0.01$ ; <sup>d</sup> $P < 0.001$ ; ( ) indicates deficit.



**Table 4.** Mortality from cancer of the gall bladder, cancer of the pleura, melanoma, leukaemia and all causes in 28 630 UK oil refinery workers by job title, 1951–1998

Job	Gall bladder cancer				Pleural cancer				Melanoma				Leukaemia				All causes			
	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)
Operator	7	3.9	182	(73–375)	10	4.3	231 <sup>a</sup>	(111–425)	14	6.4	219 <sup>a</sup>	(120–368)	28	20.6	136	(90–196)	2567	2924.4	88 <sup>(c)</sup>	(84–91)
Fitter	3	0.7	405	(84–1185)	3	0.8	361	(75–1056)	1	1.3	78	(2–435)	4	4.1	98	(27–251)	497	577.6	86 <sup>(c)</sup>	(79–94)
Pipefitter	0	0.6	0		2	0.6	328	(40–1184)	0	0.9	0		7	3.1	228	(92–470)	402	443.0	91	(82–100)
Rigger	1	0.4	263	(7–1466)	1	0.4	250	(6–1393)	0	0.6	0		3	1.9	157	(32–459)	255	283.6	90	(79–102)
Other	2	1.3	150	(18–543)	4	1.5	268	(73–687)	4	2.4	167	(45–427)	5	7.6	66	(22–155)	878	1035.3	85 <sup>(c)</sup>	(79–91)
Labourer	3	2.1	141	(29–412)	6	1.8	331 <sup>a</sup>	(122–722)	3	2.7	112	(23–327)	9	10.3	88	(40–167)	1768	1617.8	109 <sup>c</sup>	(104–115)
Storeman	0	0.3	0		1	0.2	476	(12–2653)	0	0.3	0		1	1.2	83	(2–460)	204	190.7	107	(93–123)
Driver	1	0.5	208	(5–1161)	2	0.5	400	(48–1445)	1	0.7	143	(4–796)	3	2.4	123	(25–359)	354	363.4	97	(88–108)
F & S	0	0.6	0		2	0.4	465	(56–1680)	0	0.6	0		5	2.6	196	(64–458)	405	415.7	97	(88–107)
S/T	0	0.6	0		0	0.8	0		1	1.4	73	(2–407)	4	3.6	111	(30–284)	298	441.0	68 <sup>(c)</sup>	(60–76)
A/C	2	1.4	143	(17–516)	1	1.6	64	(2–357)	7	2.3	308 <sup>a</sup>	(124–635)	3	7.5	40	(8–117)	831	1072.0	78 <sup>(c)</sup>	(72–83)
Foreman	3	1.0	288	(59–843)	2	1.1	175	(21–634)	3	1.6	192	(40–562)	5	5.4	93	(30–216)	598	785.5	76 <sup>(c)</sup>	(70–82)
Engineer	2	0.7	312	(38–1129)	4	0.8	488 <sup>a</sup>	(133–1249)	2	1.2	167	(20–602)	3	3.6	83	(17–242)	284	499.7	57 <sup>(c)</sup>	(50–64)
Total	24	14.0	172 <sup>a</sup>	(110–256)	38	15.0	254 <sup>c</sup>	(180–348)	36	22.2	162 <sup>b</sup>	(113–224)	80	73.8	108	(86–135)	9341	10 649.7	88 <sup>(c)</sup>	(86–90)
Statistical evaluation <sup>d</sup>	$P = 0.77$				$P = 0.67$				$P = 0.62$				$P = 0.37$				$P < 0.001$			

Other, other craftsmen; F & S, fire and safety; S/T, scientific/technical; A/C, administrative/clerical.

<sup>a</sup> $P < 0.05$ ; <sup>b</sup> $P < 0.01$ ; <sup>c</sup> $P < 0.001$ .

<sup>d</sup>The  $P$  value for heterogeneity for each set of 13 SMRs.

**Table 5.** Mortality from cancer of the gall bladder, cancer of the pleura, melanoma, leukaemia and all causes in 16 480 UK petroleum distribution workers by job title, 1951–1998

Job	Gall bladder cancer				Pleural cancer				Melanoma				Leukaemia				All causes			
	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)	Obs	Exp	SMR	(95% CI)
Operator	2	2.2	92	(11–331)	0	2.2	0		2	3.0	66	(8–239)	17	10.7	159	(93–254)	1557	1646.0	95 <sup>(a)</sup>	(90–99)
Driver	4	3.4	117	(32–300)	3	4.5	67	(14–197)	4	6.2	64	(18–165)	23	18.5	124	(79–186)	2440	2601.7	94 <sup>(b)</sup>	(90–98)
Craftsmen	0	0.2	0		1	0.3	385	(10–2143)	0	0.4	0		1	1.2	83	(2–460)	158	177.2	89	(76–104)
Motor mech.	0	0.2	0		0	0.3	0		0	0.4	0		0	1.1	0		96	142.6	67 <sup>(c)</sup>	(55–82)
Gen. man.	0	0.7	0		3	0.7	462	(95–1349)	0	1.0	0		5	3.5	143	(46–333)	650	542.8	120 <sup>c</sup>	(111–129)
Security	0	0.3	0		0	0.1	0		0	0.2	0		1	1.2	85	(2–472)	270	251.5	107	(95–121)
S/T	0	0.0	0		0	0.1	0		0	0.1	0		0	0.3	0		33	33.9	97	(67–137)
A/C	0	0.7	0		0	0.8	0		1	1.2	83	(2–464)	6	3.8	156	(57–340)	513	556.5	92	(84–101)
Supervisors	0	0.5	0		0	0.5	0		1	0.7	154	(4–857)	4	2.3	176	(48–451)	258	339.6	76 <sup>(c)</sup>	(67–86)
Managerial	0	0.2	0		0	0.3	0		0	0.5	0		0	1.3	0		108	168.6	64 <sup>(c)</sup>	(53–77)
Total	6	8.5	71	(26–154)	7	9.5	73	(30–151)	8	13.5	59	(26–117)	57	43.8	130	(98–168)	6083	6460.3	94 <sup>(c)</sup>	(92–97)
Statistical evaluation <sup>d</sup>	$P = 0.96$				$P = 0.03$				$P = 0.98$				$P = 0.81$				$P < 0.001$			

Motor mech., motor mechanic; gen. man., general manual worker; S/T, scientific/technical; A/C, administrative/clerical.

<sup>a</sup> $P < 0.05$ ; <sup>b</sup> $P < 0.01$ ; <sup>c</sup> $P < 0.001$ .

<sup>d</sup>The  $P$  value for heterogeneity for each set of 13 SMRs.

effects on the risks of mortality from all causes combined. Consequently, patterns of mortality from all causes are more likely to be due to selection effects, socio-economic gradients, regional effects or lifestyle effects than they are to occupational exposures. In this study, there is evidence of a healthy worker effect, with mortality rates being well below the national average in the early periods of follow-up (population selected for health at entry to the industry) and with the magnitude of this deficit reducing with time (regression towards the mean). It is important to gauge the size of this effect, because this sort of pattern

(SMRs increasing with period from hire) is the same as we might expect to see with occupational cancers. The all causes analyses also suggested strongly (and not unexpectedly) that workers employed in different jobs did not have the same socio-economic profile; mortality tended to be higher in blue collar workers than it was in white collar/coat workers. It is also important to gauge the size of this effect, because this pattern is the same pattern we might expect to see with most occupational cancers.

More detailed findings for cancer of the gall bladder did not indicate the influence of an occupational cancer

hazard in either oil refinery or petroleum distribution workers and the overall excess SMR in oil refinery workers may well be no more than a chance finding. Given the large number of comparisons that were made, it was to be expected that a few would achieve statistical significance even if all null hypotheses were true.

The more detailed analyses did not suggest the presence of an occupational cancer hazard for melanoma in either of the two subcohorts. An overall excess mortality for melanoma in UK oil refinery workers has been noted previously [1,2], and it seems likely that lifestyle factors, such as sunbathing practices and number of foreign holidays taken in hot climates, may be involved in this excess. Unfortunately, the present study does not include any information on such variables and these hypotheses cannot be tested.

The overall SMR for cancer of the pleura was much higher in oil refinery workers than it was in petroleum distribution workers. There was no significant trend of SMRs in oil refinery workers increasing with period from commencing employment. Nevertheless, the highly significant SMR for the final period ( $\geq 30$  years) cannot be ignored. It is known that asbestos was used in refineries in earlier decades, and at least some of the excess mortality from mesothelioma is likely to have been caused by exposure to this asbestos. At face value, the findings by job type suggest that asbestos exposure in oil refineries may have been a plant-wide problem rather than concentrated in one or two jobs. Alternatively, the use of a single job category per study subject may be misleading.

For leukaemia, there was no overall excess SMR in oil refinery workers that needed any explanation, and the more detailed analyses did not suggest the presence of an occupational cancer hazard. For distribution workers, the findings were a little more complex. Whilst there was a general lack of statistical significance in the various tests that were carried out, it must remain a possibility that occupational exposures received  $>30$  years ago have had some effect on leukaemia mortality in recent years. The obvious candidate for such an effect would be the higher levels of benzene exposure found in various parts of the distribution industry many years ago.

In conclusion, the findings of this analysis should be welcome news for UK oil refinery and petroleum distribution workers. Their overall mortality is well below the national average. The only findings that suggested the presence of an occupational cancer hazard were the excess of mesothelioma in oil refinery employees and the excess of leukaemia mortality in petroleum distribution workers, both excesses occurring in long-term follow-up for workers first exposed  $>30$  years ago. More sophisticated analyses, involving retrospective quantitative exposure assessments, would probably make a negligible contribution to what is known about mesothelioma risks

in relation to asbestos exposure, and such analyses are not planned. Similar analyses concerning leukaemia risks and benzene exposure in petroleum distribution workers have already been carried out on this cohort [7].

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## References

1. Rushton L, Alderson MR. An epidemiological survey of eight oil refineries in Britain. *Br J Ind Med* 1981; **38**: 225–234.
2. Rushton L, Alderson MR. Epidemiological survey of oil distribution centres in Britain. *Br J Ind Med* 1983; **40**: 330–339.
3. Rushton L. Further follow up of mortality in a United Kingdom oil refinery cohort. *Br J Ind Med* 1993; **50**: 549–560.
4. Rushton L. Further follow up of mortality in a United Kingdom oil distribution centre cohort. *Br J Ind Med* 1993; **50**: 561–569.
5. Wong O, Raabe GK. Critical review of cancer epidemiology in petroleum industry employees, with a quantitative meta-analysis by cancer site. *Am J Ind Med* 1989; **15**: 283–310.
6. Breslow NE, Day NE. *The Design and Analysis of Cohort Studies*, Vol. II, *Statistical Methods in Cancer Research*, IARC Scientific Publication no. 82. Lyon: IARC, 1987.
7. Rushton L, Romaniuk H. A case-control study to investigate the risk of leukaemia associated with exposure to benzene in petroleum marketing and distribution workers in the United Kingdom. *Occup Environ Med* 1997; **54**: 152–166.
8. Schnatter RA, Armstrong TW, Thompson LS, Nicolich MJ, Katz AM, Huebner WW. The relationship between low-level benzene exposure and leukaemia in Canadian petroleum distribution workers. *Environ Health Perspect* 1996; **104**: 1375–1379.
9. Wong O, Harris F, Smith TJ. Health effects of gasoline exposure II. Mortality patterns of distribution workers in the United States. *Environ Health Perspect* 1993; **101**(Suppl. 6): 63–76.
10. Sorahan T, Hamilton L, Harrington M. *Mortality of United Kingdom Oil Refinery Workers 1951–98*. London: Institute of Petroleum, 2001.
11. Sorahan T, Hamilton L, Harrington M. *Mortality of United Kingdom Petroleum Distribution Workers 1951–98*. London: Institute of Petroleum, 2001.