ORIGINAL ARTICLE

# Cancer risks in a historical UK cohort of benzene exposed workers

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*Occup Environ Med* 2005;**62**:231–236. doi: 10.1136/oem.2004.015628

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Accepted 15 December 2004

**Aims:** To examine mortality from different causes and cancer incidence among a cohort of benzene workers in England and Wales.

**Methods:** A cohort of 5514 workers who had been occupationally exposed to benzene in 1966/67 or earlier was assembled by the former Factory Inspectorate and the Medical Research Council from details provided by 233 employers in England and Wales. The cohort was followed up for mortality (1968–2002) and cancer registrations (1971–2001). National mortality rates and cancer registration (incidence) rates were used to calculate standardised mortality ratios and standardised registration ratios.

**Results:** Mortality was close to expectation for all causes and significantly increased for cancer of the lip, cancer of the lung and bronchus, secondary and unspecified cancers, acute non-lymphocytic leukaemia (ANLL), and all neoplasms. Significant deficits were shown for three non-malignant categories (mental disorders, diseases of the digestive system, accidents). SMRs for other leukaemia, lymphomas, and multiple myeloma were close to or below expectation. There was some evidence of under-ascertainment of cancer registrations, although significantly increased SRRs were shown for lung cancer and cancer of the pleura (mesothelioma).

**Conclusions:** Many study subjects would have been exposed to carcinogens other than benzene (for example, asbestos, rubber industry fumes, foundry fumes, polycyclic aromatic hydrocarbons), and the excesses of lung cancer and mesothelioma are likely to reflect exposures to these other carcinogens. The carcinogenic effects of benzene exposure on the lymphohaematopoietic system were limited to ANLL.

Benzene exposure is known to increase the risk of acute non-lymphocytic leukaemia (ANLL),[1–4] though certain studies have suggested that other haematopoietic malignancies may also be increased.[5–11] We have examined mortality from different causes and also the incidence of different malignancies in an historical cohort of workers exposed occupationally to benzene in England and Wales. ANLL rather than acute myeloid leukaemia (AML) was selected as the primary health outcome of interest following exposure to benzene ''to embrace the other specified acute leukaemias that are variably diagnosed in different centres and to avoid exclusion of the rag-bag of acute unspecified leukaemias, the majority of which are likely to be AML or some allied type of disease''.[12]

## METHODS

In 1966/67, at the request of the Medical Research Council, Drs R Whitelaw and T Lloyd-Davies of the (then) Inspectorate of Factories collected, through its regional offices, details from employers of 5514 individuals (5130 men, 384 women) who had been exposed at work to benzene in the recent past in England and Wales.

A total of 233 firms or plants provided details of their benzene exposed workers through their personnel officers. These details included names, date of birth, dates of starting and ending benzene exposed work, and the National Insurance Number. Factory Inspectorate personnel attempted to obtain a single estimate for each facility of the average concentration of benzene in the ambient air to which employees were or had been exposed, but survey correspondence shows that this refers to the time of data collection (1966/67) rather than to earlier years of exposure. Such estimates were available from only 130 of the 233 participating facilities.

The original group of researchers included Professor WM Court Brown and RD, both with the MRC in 1966. Initial unpublished analyses involved a comparison of the study nominal roll with a leukaemia death registry. As the study was one of current or recent employees with very little time having elapsed for any adverse health outcomes to have presented themselves, it was decided to carry out a more informative statistical analysis at a later date. In the early 1980s, all survey materials were passed to LJK who arranged for the study members to be ''flagged'' with the Office for National Statistics (ONS). Details of subjects untraced by ONS were sent to the Department of Health and Social Security (DHSS) for tracing using National Insurance numbers. In these ways, details of subsequent deaths, cancer registrations, and embarkations were obtained. All study materials were transferred recently to the University of Birmingham and study subjects were followed up for mortality and cancer registrations to the end of 2002 and 2001, respectively.

Vital status as recorded in the study computer file was double checked with corresponding computerised data held by the ONS and a few inconsistencies were rectified. On the closing date of the study (31 December 2002), 2543 (46.1%) study subjects were traced alive, 2656 (48.2%) were deceased, 138 (2.5%) had emigrated, and 177 (3.2%) were untraced. Failure to trace subjects was largely a consequence of some factories supplying identifying particulars with initials rather than with full forenames. Of the 670 deaths with cancer as underlying cause in the period 1975–2000, there were 102 for which no cancer registration had been received. A review of these cases by ONS produced registration details for a further

**Abbreviations:** AML, acute myeloid leukaemia; ANLL, acute non-lymphocytic leukaemia; CML, chronic myeloid leukaemia; SRR, standardised cancer registration ratio

**Main messages**

- A large historical cohort of benzene exposed workers indicates that exposure to benzene does not affect risks for lymphohaematopoietic malignancies other than acute non-lymphocytic leukaemia (ANLL).

80 subjects. A corresponding search was not attempted for any of the remaining study subjects.

It was clear from their names, that the companies belonged to many sections of industry, including iron and steel foundries, rubber factories, chemical manufacturers, coking plants, boot and shoe manufacturers, printing plants, electricity generation and transmission facilities, and light engineering companies. For the purpose of this analysis, firms were classified under one of 12 headings using a combination of general knowledge, self-explanatory company names, and a review of contemporaneous Kelly's town directories. All but four factories (with 13 study subjects) could be classified (see table 1). The numbers of plants that, in 1966/67, had estimated benzene exposures ⩾25 ppm are also shown in table 1; these exposure estimates have not been used in the analyses that follow.

Expected numbers of deaths were calculated by applying serial mortality rates for England and Wales, specified by age, sex, and calendar year, to the corresponding person-years-at-risk (p-y) from 1 January 1968 to the closing date of the study (31 December 2002), date of death, date of emigration, or date last known alive, whichever was earliest. Standardised mortality ratios (SMRs) were calculated as the ratio of observed deaths to expected deaths, expressed as a percentage; significance tests were two tailed. The analysis was censored at age 85 years since the age distribution within the ''open ended'' age group ⩾85 years in the cohort might differ appreciably from that of the general population; also, any subjects incorrectly classified as alive at the end of the study would have a disproportionate effect on the expected numbers for the open ended age group. Expected numbers of cancer registrations (cancer incidence data) were calculated similarly for the period 1971–2001.

## RESULTS

Table 2 shows observed and expected numbers of cause specific deaths. Among major causes, the only significant excess was for all malignancies with an SMR of 109 ($p < 0.05$) based on 761 deaths. Overall mortality was close to expectation (SMR 101, based on 2430 deaths). However, significantly reduced SMRs were found for mental disorders (50 based on 8 deaths; $p < 0.05$), digestive disorders (76 based on 51 deaths; $p < 0.05$), and accidents (55 based on 23 deaths; $p < 0.05$). Among specific cancers, significantly increased excesses were found for lung cancer (121 based on 294 deaths; $p < 0.01$), lip cancer (974 based on 2 deaths; $p < 0.05$), and cancers of uncertain origin (140 based on 68 deaths; $p < 0.001$). No significant increase of deaths from leukaemia was observed (137 based on 22 deaths).

Details of deaths from different leukaemia sub-types are shown in table 3 and include a significantly increased SMR for acute non-lymphocytic leukaemia (ANLL) (183 based on 14 deaths; $p < 0.05$). These 14 deaths comprised 12 deaths from AML and two acute leukaemias (unspecified cell type). Mortality from lymphoid leukaemia and chronic myeloid leukaemia (CML) were unexceptional.

Observed and expected numbers of deaths from all causes, all cancers, ANLL, and all other leukaemias are shown by period of death in table 4. The increased mortality shown for ANLL is not limited to earlier periods of follow up. There are no significant trends of SMRs increasing or decreasing with year of death for any of the four sets of findings.

Observed and expected numbers of deaths from lung cancer and from ANLL are shown by industry sector in table 5. Neither set of SMRs is significantly heterogeneous; industry specific findings for ANLL are based on small numbers of deaths. Analyses of deaths from ANLL were also carried out by period of first exposure and by interval from first exposure, and for those leavers with a known date of ceasing exposure, by period of ending exposure and by interval from ending exposure (not shown in table). No clear trends were shown, but the numbers of deaths available for analysis were small.

Table 6 shows standardised cancer registration ratios (SRR) by site. Significant increases are shown for lung cancer (119 based on 293 cases) and pleural cancer (237 based on 15 cases). Deficits are shown for Hodgkin's disease

**Table 1** Study population and available benzene exposure data by type of industry

| Industry | Study subjects (n) | Factories/facilities (n) | | |
|---|---|---|---|---|
| | | Total | With estimated benzene exposure levels | Estimated benzene exposure level ⩾25 ppm* |
| Coking plants, tar refineries, gas production | 700 | 38 | 25 | 9 |
| Manufacture of chemicals and dyes (nec)† | 1692 | 53 | 29 | 6 |
| Manufacture of boots, shoes, and leather goods | 53 | 12 | 11 | 10 |
| Printers and photographic studios | 480 | 26 | 9 | 2 |
| Manufacture of paint, varnish, lacquers, and polish | 464 | 15 | 11 | 7 |
| Manufacture of rubber | 658 | 23 | 12 | 6 |
| Production of carbon black | 23 | 1 | 0 | – |
| Iron and steel foundries, smelters | 123 | 6 | 4 | 0 |
| Oil refineries and petroleum distribution | 339 | 7 | 5 | 2 |
| Electricity generation and transmission | 29 | 6 | 1 | 1 |
| Manufacture of linoleum | 68 | 1 | 1 | 1 |
| Other industries‡ | 872 | 41 | 20 | 10 |
| Not classified | 13 | 4 | 2 | 1 |
| Total | 5514 | 233 | 130 | 55 |

*In 1966/67.
†nec, not elsewhere classified.
‡Principally light engineering, electrical manufacturing, and electronics.

**Table 2** Cause specific findings for mortality of benzene exposed workers (5130 males, 384 females), 1968–2002

| Cause of death | ICD-9 | Obs | Exp | SMR* | (95% CI) |
|---|---|---|---|---|---|
| **Cancers** | | | | | |
| All malignant neoplasms | 140–208 | 761 | 700.9 | 109 | (101 to 117) |
| Lip | 140 | 2 | 0.2 | 974 | (118 to 3519) |
| Tongue | 141 | 2 | 2.2 | 91 | (11 to 330) |
| Salivary gland | 142 | 1 | 0.9 | 109 | (3 to 605) |
| Mouth | 143–145 | 2 | 2.3 | 89 | (11 to 321) |
| Pharynx | 146–149 | 3 | 4.5 | 66 | (14 to 193) |
| Oesophagus | 150 | 20 | 28.5 | 70 | (43 to 108) |
| Stomach | 151 | 57 | 53.9 | 106 | (80 to 137) |
| Small intestine | 152 | 1 | 1.2 | 82 | (2 to 458) |
| Large intestine | 153 | 38 | 47.2 | 81 | (57 to 111) |
| Rectum | 154 | 31 | 29.7 | 105 | (71 to 148) |
| Liver | 155.0, 155.1 | 10 | 6.5 | 154 | (74 to 284) |
| Gallbladder | 156 | 2 | 3.2 | 62 | (8 to 226) |
| Pancreas | 157 | 36 | 29.7 | 121 | (85 to 168) |
| Peritoneum | 158 | 2 | 1.2 | 171 | (21 to 619) |
| Other digestive | 159 | 6 | 4.1 | 146 | (54 to 319) |
| Nose and sinuses | 160 | 1 | 1.1 | 95 | (2 to 527) |
| Larynx | 161 | 2 | 6.3 | 32 | (4 to 115) |
| Lung and bronchus | 162 | 294 | 243.4 | 121 | (107 to 135) |
| Pleura | 163 | 7 | 3.5 | 202 | (81 to 415) |
| Bone | 170 | 0 | 1.2 | 0 | (0 to 299) |
| Connective tissue | 171 | 0 | 2.3 | 0 | (0 to 161) |
| Melanoma | 172 | 4 | 5.0 | 81 | (22 to 206) |
| Skin, other | 173 | 1 | 1.8 | 55 | (1 to 305) |
| Breast | 175 | 6 | 7.8 | 77 | (28 to 167) |
| Cervix | 180 | 1 | 1.1 | 91 | (2 to 510) |
| Uterus | 182 | 1 | 0.6 | 179 | (5 to 999) |
| Ovary | 183 | 3 | 2.4 | 128 | (26 to 373) |
| Other genital | 184, 187 | 0 | 1.1 | 0 | (0 to 230) |
| Prostate | 185 | 50 | 53.2 | 94 | (70 to 124) |
| Testis | 186 | 0 | 1.1 | 0 | (0 to 337) |
| Bladder | 188 | 27 | 26.9 | 100 | (66 to 146) |
| Kidney | 189.0 | 14 | 13.6 | 103 | (56 to 173) |
| Other urinary | 189.1–189.9 | 1 | 0.8 | 127 | (3 to 709) |
| Eye | 190 | 0 | 0.7 | 0 | (0 to 557) |
| Brain | 191–192 | 16 | 15.3 | 105 | (60 to 170) |
| Thyroid | 193 | 0 | 1.1 | 0 | (0 to 322) |
| Other endocrine glands | 194 | 0 | 0.5 | 0 | (0 to 762) |
| Secondary and unspecified | 195–199 | 68 | 48.5 | 140 | (109 to 178) |
| Hodgkin's disease | 201 | 3 | 2.8 | 108 | (22 to 317) |
| Non-Hodgkin's lymphoma | 200, 202 | 15 | 15.9 | 94 | (53 to 156) |
| Multiple myeloma | 203 | 6 | 9.5 | 63 | (23 to 137) |
| Leukaemia | 204–208 | 22 | 16.1 | 137 | (86 to 207) |
| **Non-cancers** | | | | | |
| Diseases of blood | 280–289 | 6 | 6.2 | 97 | (35 to 210) |
| Mental disorders | 290–319 | 8 | 16.1 | 50 | (21 to 98) |
| Diseases of nervous system | 320–389 | 25 | 34.1 | 73 | (48 to 108) |
| Diseases of circulatory system | 390–459 | 1133 | 1148.1 | 99 | (93 to 105) |
| Diseases of respiratory system | 460–519 | 308 | 280.2 | 110 | (98 to 123) |
| Diseases of digestive system | 520–579 | 51 | 67.3 | 76 | (56 to 100) |
| Diseases of genitourinary system | 580–629 | 20 | 24.3 | 82 | (50 to 127) |
| Accidents | 800–949 | 23 | 42.0 | 55 | (35 to 82) |
| Suicide | 950–959 | 13 | 19.3 | 67 | (36 to 115) |
| All causes | | 2430 | 2411.5 | 101 | (97 to 105) |

*SMRs and confidence intervals based on expectations calculated to two places of decimals.

(45) and multiple myeloma (68) based on 2 and 8 cases, respectively. Incidence of non-Hodgkin's lymphoma (100 based on 24 cases) and leukaemia (120 based on 25 cases) was unremarkable. The SRR for ANLL was 165 (based on 12 cases). All 15 employees diagnosed with pleural cancer had died but only six of them had pleural cancer as the underlying cause of death. Of the remaining nine deaths, three deaths from ''mesothelioma of the lung'' were coded to lung cancer, five from ''malignant mesothelioma'' (not further specified) were coded to unspecified cancer, and there was a single suicide. SRRs for pleural cancer were also calculated by industry sector (not shown in table). There was no significant heterogeneity in the set of SRRs, but a significant excess was found for employees engaged in the manufacture of chemicals and dyes (SRR 536, based on 9 cases; $p < 0.001$).

## DISCUSSION

The factories that participated in the study provided details only for their benzene exposed employees. By definition they were all exposed in or before 1966–7; 46.5% of the employees were working with benzene in the 1950s and 11.0% in the 1940s. There was evidence of increased mortality for lung and lip cancers and for ANLL, and increased morbidity for lung and pleural cancers. There is no reason to suspect that benzene is responsible for the increased lung and pleural cancer risks in this study. Benzene was not the only carcinogen to which the subjects were exposed in the course

**Table 3** Mortality by leukaemia sub-type in benzene exposed workers (5130 males, 384 females), 1968–2002

| Type of leukaemia | ICD-9 | Obs | Exp | SMR | (95% CI) |
|---|---|---|---|---|---|
| All leukaemia | 204–208 | 22 | 16.08 | 137 | (86 to 207) |
| Lymphoid leukaemia | 204 | 5 | 5.05 | 99 | (32 to 231) |
| Acute | 204.0 | 0 | 0.83 | 0 | (0 to 444) |
| Chronic | 204.1 | 5 | 4.04 | 124 | (40 to 289) |
| Other and unspecified | 204.2–204.9 | 0 | 0.18 | 0 | – |
| Myeloid leukaemia | 205 | 14 | 9.41 | 149 | (81 to 250) |
| Acute | 205.0 | 12 | 6.60 | 182 | (94 to 318) |
| Chronic | 205.1 | 2 | 2.57 | 78 | (9 to 281) |
| Other and unspecified | 205.2–205.9 | 0 | 0.24 | 0 | – |
| Monocytic leukaemia | 206 | 0 | 0.34 | 0 | – |
| Acute | 206.0 | 0 | 0.25 | 0 | – |
| Chronic | 206.1 | 0 | 0.05 | 0 | – |
| Other and unspecified | 206.2–206.9 | 0 | 0.04 | 0 | – |
| Other and unspecified cell types | 207–208 | 3 | 1.28 | 234 | (48 to 685) |
| Acute | 207.0, 208.0 | 2 | 0.80 | 250 | (30 to 904) |
| Chronic | 207.1, 208.1 | 1 | 0.05 | 1843 | (47 to 10271) |
| Other and unspecified | 207.2–207.9, 208.2–208.9 | 0 | 0.43 | 0 | – |
| ANLL* | 205.0, 206.0, 207.0, 208.0 | 14 | 7.65 | 183 | (100 to 307) |
| All leukaemia excluding ANLL | rem. 204–208 | 8 | 8.43 | 95 | (41 to 187) |

*Acute non-lymphocytic leukaemia is here defined as acute myeloid leukaemia (ICD-9 205.0), acute monocytic leukaemia (ICD-9 206.0), acute erythraemia and erythroleukaemia (207.0), and acute leukaemia of unspecified cell type (208.0). Selected codes in ICD-8 were 205.0, 206.0, 207.0, and 207.2.

**Table 4** Mortality of benzene exposed workers (5130 males, 384 females) by period of death, 1968–2002

| | All causes | | | All neoplasms | | | ANLL* | | | Other leukaemia | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Period | Obs | SMR | (95% CI) | Obs | SMR | (95% CI) | Obs | SMR | (95% CI) | Obs | SMR | (95% CI) |
| 1968–1970 | 95 | 80 | (65 to 98) | 29 | 91 | (61 to 131) | 1 | 263 | (7 to 1465) | 0 | 0† | (0 to 825) |
| 1971–1975 | 274 | 110 | (98 to 124) | 86 | 127 | (102 to 157) | 2 | 266 | (32 to 961) | 1 | 124 | (3 to 688) |
| 1976–1980 | 307 | 96 | (85 to 107) | 92 | 104 | (84 to 128) | 0 | 0‡ | (0 to 405) | 1 | 96 | (2 to 538) |
| 1981–1985 | 384 | 102 | (92 to 112) | 134 | 125 | (104 to 148) | 2 | 183 | (22 to 661) | 1 | 77 | (2 to 428) |
| 1986–1990 | 414 | 102 | (93 to 113) | 129 | 106 | (88 to 126) | 3 | 242 | (50 to 708) | 1 | 70 | (2 to 388) |
| 1991–1995 | 448 | 111 | (101 to 122) | 149 | 119 | (101 to 140) | 1 | 74 | (2 to 410) | 2 | 137 | (17 to 493) |
| 1996–2002 | 508 | 94 | (86 to 103) | 157 | 94 | (80 to 110) | 5 | 260 | (84 to 607) | 2 | 103 | (12 to 371) |
| Total | 2430 | 101 | (97 to 105) | 776 | 110 | (102 to 118) | 14 | 183 | (100 to 307) | 8 | 95 | (41 to 187) |

*Acute non-lymphocytic leukaemia (see footnote to table 3).
†Expected = 0.44.
‡Expected = 0.91.

of their work. Asbestos is known to have been used in some of the factories studied, and the previously established increased lung cancer risks in coking plants, the rubber industry, and iron and steel foundries are believed to be due to polycyclic aromatic hydrocarbons, rubber fume, and foundry fume, respectively.[13–18] The excess mortality for lip cancer was based on two deaths and may well be a chance finding. The increased risk of leukaemia, limited to ANLL,

**Table 5** Mortality from lung cancer and from ANLL among benzene exposed workers by industry sector (5130 males, 384 females), 1968–2002

| | Lung cancer | | | ANLL* | | |
|---|---|---|---|---|---|---|
| Industry | Obs | SMR | (95% CI) | Obs | SMR | (95% CI) |
| Coking plants, tar refineries, gas production | 45 | 130 | (95 to 175) | 3 | 300 | (62 to 877) |
| Manufacture of chemicals and dyes (nec)† | 94 | 139 | (112 to 170) | 3 | 135 | (28 to 393) |
| Manufacture of boots, shoes, and leather goods | 2 | 85 | (10 to 309) | 1 | 1250 | (32 to 6965) |
| Printers and photographic studios | 21 | 104 | (64 to 159) | 1 | 156 | (4 to 871) |
| Manufacture of paint, varnish, lacquers, or polish | 32 | 122 | (83 to 172) | 1 | 135 | (3 to 753) |
| Manufacture of rubber | 40 | 136 | (97 to 185) | 2 | 222 | (27 to 803) |
| Iron and steel foundries, smelters | 2 | 35 | (4 to 127) | 2 | 1176 | (142 to 4250) |
| Oil refineries and petroleum distribution | 18 | 105 | (62 to 166) | 1 | 189 | (5 to 1051) |
| Manufacture of linoleum | 7 | 270 | (109 to 557) | 0 | 0‡ | (0 to 5270) |
| Other industries§ | 33 | 88 | (61 to 123) | 0 | 0¶ | (0 to 286) |
| Total | 294 | 121 | (107 to 135) | 14 | 183 | (100 to 307) |

*Acute non-lymphocytic leukaemia (see footnote to table 3).
†nec, not elsewhere classified.
‡Expected = 0.07.
§Light engineering, electrical manufacturing, electronics, production of carbon black, electricity generation and transmission, and unclassified factories.
¶Expected = 1.29.

**Table 6** Cancer incidence in benzene exposed workers (4740 males, 352 females)*, 1971–2001

| Site of cancer | ICD-9 | Obs | Exp | SRR† | (95% CI) |
|---|---|---|---|---|---|
| All malignant neoplasms‡ | 140–208 | 986 | 923.1 | 107 | (100 to 114) |
| Lip | 140 | 3 | 2.2 | 138 | (28 to 402) |
| Tongue | 141 | 2 | 3.8 | 53 | (6 to 191) |
| Salivary gland | 142 | 0 | 1.9 | 0 | (0 to 190) |
| Mouth | 143–145 | 7 | 4.8 | 145 | (58 to 299) |
| Pharynx | 146–149 | 3 | 6.8 | 44 | (9 to 130) |
| Oesophagus | 150 | 16 | 26.2 | 61 | (35 to 99) |
| Stomach | 151 | 67 | 61.5 | 109 | (84 to 138) |
| Small intestine | 152 | 2 | 2.1 | 97 | (12 to 351) |
| Large intestine | 153 | 60 | 70.0 | 86 | (65 to 110) |
| Rectum | 154 | 61 | 54.0 | 113 | (86 to 145) |
| Liver | 155.0, 155.1 | 8 | 6.1 | 131 | (57 to 259) |
| Gallbladder | 156 | 3 | 4.6 | 66 | (14 to 192) |
| Pancreas | 157 | 36 | 27.9 | 129 | (90 to 179) |
| Peritoneum | 158 | 3 | 1.2 | 246 | (51 to 719 |
| Other digestive | 159 | 3 | 1.6 | 184 | (38 to 538) |
| Nose and sinuses | 160 | 1 | 2.1 | 47 | (1 to 262) |
| Larynx | 161 | 12 | 15.1 | 79 | (41 to 138) |
| Lung and bronchus | 162 | 293 | 245.3 | 119 | (106 to 134) |
| Pleura | 163 | 15 | 6.3 | 237 | (133 to 391) |
| Bone | 170 | 1 | 1.4 | 73 | (2 to 407) |
| Connective tissue | 171 | 2 | 4.0 | 50 | (6 to 182) |
| Melanoma | 172 | 13 | 10.7 | 121 | (64 to 207) |
| Breast | 175 | 15 | 16.7 | 90 | (50 to 149) |
| Cervix | 180 | 1 | 2.0 | 50 | (1 to 279) |
| Uterus | 182 | 2 | 2.2 | 89 | (11 to 323) |
| Ovary | 183 | 3 | 2.8 | 108 | (22 to 317) |
| Other genital | 184, 187 | 7 | 3.5 | 202 | (81 to 416) |
| Prostate | 185 | 121 | 109.9 | 110 | (91 to 132) |
| Testis | 186 | 1 | 3.7 | 27 | (1 to 149) |
| Bladder | 188 | 69 | 66.6 | 104 | (81 to 131) |
| Kidney | 189.0 | 16 | 17.8 | 90 | (51 to 146) |
| Other urinary | 189.1–189.9 | 3 | 3.3 | 92 | (19 to 268) |
| Eye | 190 | 1 | 1.7 | 58 | (1 to 324) |
| Brain | 191–192 | 18 | 15.6 | 116 | (68 to 183) |
| Thyroid | 193 | 0 | 2.1 | 0 | (0 to 174) |
| Other endocrine glands | 194 | 1 | 0.8 | 122 | (3 to 679) |
| Secondary and unspecified | 195–199 | 54 | 49.0 | 110 | (83 to 144) |
| Hodgkin's disease | 201 | 2 | 4.4 | 45 | (5 to 163) |
| Non-Hodgkin's lymphoma | 200, 202 | 24 | 24.0 | 100 | (64 to 149) |
| Multiple myeloma | 203 | 8 | 11.8 | 68 | (29 to 134) |
| Leukaemia | 204–208 | 25 | 20.9 | 120 | (78 to 177) |
| ANLL§ | 205.0, 206.0, 207.0, 208.0 | 12 | 7.3 | 165 | (85 to 288) |
| Other leukaemia | rem. 204–208 | 13 | 13.6 | 96 | (51 to 164) |

*Excludes untraced workers and pre-1971 deaths and embarkations.
†SRRs and confidence intervals based on expectations calculated to two places of decimals.
‡Excluding other skin (ICD-9 173).
§Acute non-lymphocytic leukaemia (see footnote to table 3).

appears to have been small in absolute terms and is attributed to benzene exposure, although it is not possible to exclude some role for other unrecognised leukaemogens.

It seems highly likely that some cancer registrations have been missed, given that the ancillary search carried out by ONS of cancer deaths without cancer registrations produced only an additional 80 cancer registrations. If a similar proportion of under-ascertainment is assumed for other registrations, then some 60 registrations remain untraced. Additional checks on the completeness of cancer registrations for other UK cohort studies might usefully be carried out as a routine. It is also evident that some certifying doctors were probably unaware of how their statements on deaths that were almost certainly pleural mesothelioma would be interpreted by ONS staff for the purpose of national mortality statistics.

The cohort studied is large, all subjects were known to have been exposed to benzene, and a long period of follow up is now available. The cohort, however, is atypical in that it is a ''census'' cohort with a large number of participating companies, and these factors might make comparisons with other studies more difficult to interpret. The study is also limited by the small numbers of leukaemia deaths available in the analyses of industry sectors and the unknown degree of variability in the exposure profiles of subjects from different plants within each sector. Estimates of earlier benzene exposure for individual study subjects were not available and even estimates for 1966/67 were not provided in a standardised manner. Some estimates referred to peak exposures, though most probably referred to average ambient levels when benzene was being used or manufactured. Some employees would, however, have been exposed to benzene throughout the working day, others might only be exposed for a few hours each week; such information was not available to the study. It was also clear from the study correspondence that, at least in some factories, exposures were known to be much higher in earlier time periods than in 1966/67. Assessment of the available exposure data was also hampered by the absence of recorded job titles. It seems likely, however, that in terms of the available benzene literature, this study encompasses a wide range of exposures, including some of the UK workers most heavily exposed to benzene from the 1940s onwards. Study interpretation would also have been assisted if workers employed at the same facilities but without exposure to benzene had been enrolled into the survey. Nevertheless, this study does not support claims that exposure to benzene affects risks for lympho-haematopoietic malignancies other than ANLL.

## ACKNOWLEDGEMENTS

We thank those researchers from the MRC and the Inspectorate of Factories who helped organise this survey in the 1960s. We thank the National Health Service Central Register (NHSCR) of the Office for National Statistics (ONS) for follow up information. We thank Paul Embley (University of Central England) for assistance with the classification of industrial sectors, Jaswant Bal for data consolidation, and Margaret Williams for word processing. LJK thanks Cancer Research UK for earlier financial support. TS thanks The Energy Institute (formerly The Institute of Petroleum) for recent financial support.

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Competing interests: none declared

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# ECHO

## Legacy of blue asbestos lingers, decades on

Please visit the *Occupational and Environmental Medicine* website [www.occenvmed.com] for a link to the full text of this article.

Long term analysis in former workers and residents exposed to blue asbestos in an Australian mining town confirms that lung function has continued to decline nearly four decades after exposure ceased. Furthermore, smoking has not worsened the asbestosis, as once claimed.

Forced expiratory volume in one second ($FEV_1$), forced vital capacity (FVC), and $FEV_1$/FVC were significantly higher for ex-residents of Wittenoom, Western Australia—where blue asbestos was mined from 1943 to 1966—than former workers, according to comparison in a mixed effects linear regression model. Each extra year of exposure reduced $FEV_1$ by 0.9 ml and FVC by 1.5 ml. Younger age at first exposure predicted significantly lower $FEV_1$ and FVC values and so did higher exposures.

Current smokers had significantly lower lung function values than never smokers. $FEV_1$ declined yearly significantly faster in current smokers, but not ex-smokers, versus never smokers. $FEV_1$/FVC declined yearly significantly faster in all smokers versus never smokers. However, there was no statistical interaction between smoking and asbestos exposure on lung function, suggesting each is an independent risk factor.

Subjects were participants in a vitamin A programme, set up in 1990 to offset effects of asbestos exposure. Lung function and its change over time were analysed by occupational and environmental exposure from consolidated annual follow up data from 1979 to 2002 and by self reported smoking history.

The cohorts are unique in having accurate records of known exposures almost exclusively to blue asbestos. They have a greater risk of reduced lung function from fibrosis owing to asbestos exposure and smoking, but independently, it now seems.

▲ Alfonso HS, *et al*. *Thorax* 2004;**59**:1052–1056.