

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location              | Cohort description  | Exposure assessment   | Organ site (ICD code) | Exposure categories  | No. of cases/deaths | Relative risk (95% CI)                  | Adjustment for potential confounders | Comments   |
|----------------------------------|---|---|-----------------------|--|---------------------|---|--------------------------------------|--|
| McCraw <i>et al.</i> (1985), USA | All white male employees at an oil refinery for at least one day between 1973-1982, and retirees alive as of 1973; total 3976                     | No exposure assessment was performed  | AML 205.0             | None   | 8                   | (SMR)<br>3.9 (1.7-7.9)                  |                                      | Comparison population Surveillance, Epidemiology and End Results, white men. |
| Rushton (1993), United Kingdom   | Cohort of men who worked for at least a year at 8 oil refineries (35569) and 750 distribution centres (23306) in the UK and followed for 39 years | No exposure assessment was performed  | AML 205.0             | Distribution workers<br>Refinery workers   | 25<br>20            | (SMR)<br>1.2 (0.8-1.8)<br>0.7 (0.5-1.2) |                                      |  |
| Wong <i>et al.</i> (1993), USA   | 18135 distribution employees with potential exposure to gasoline for at least 1 year between 1946-1985, followed up to June 1989.                 | 8hr TWA total hydrocarbon exposure in ppm estimated for job categories based on industrial hygiene data and expert judgment. Cumulative exposure defined as the sum of products of TWA exposure and duration of exposure of each job in an employee's work history. | AML 205.0             | Land-based employees exposed to gasoline<br>Marine based employees exposed to gasoline | 13<br>5             | (SMR)<br>1.5 (0.8-2.6)<br>0.7 (0.2-1.7) |                                      | Detailed exposure measurements not applied to analyses of leukaemia subtypes |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location               | Cohort description   | Exposure assessment                                   | Organ site (ICD code) | Exposure categories                   | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders | Comments |
|-----------------------------------|--|---|-----------------------|---------------------------------------|---------------------|------------------------|--------------------------------------|----------|
| Wong (1995), USA                  | Cohort of 1717 workers in two plants manufacturing Pliofilm (rubber hydrochloride)     | Historical records and interviews with former workers | AML 205.0             |                                       |                     |                        | (SMR)                                |          |
|                                   |  |   |                       | Benzene cumulative exposure ppm-years |                     |                        |                                      |          |
|                                   |  |   |                       | <200                                  | 1                   | 0.9 (0.0-5.1)          |                                      |          |
|                                   |  |   |                       | 200-400                               | 2                   | 27.2 (3.3-98.2)        |                                      |          |
|                                   |  |   |                       | >400                                  | 3                   | 98.3 (20.3-287.6)      |                                      |          |
| Total                             | 6  | 5.0 (1.8-11.0)  |                       |                                       |                     |                        |                                      |          |
| Satin <i>et al.</i> , (1996), USA | Cohort of 17,844 petroleum refinery workers, employed 1937-1983, followed through 1987 | No exposure assessment was performed                  | AML 205.0             |                                       | 10                  | (SMR)<br>0.6 (0.3-1.2) |                                      |          |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location   | Cohort description   | Exposure assessment   | Organ site (ICD code)       | Exposure categories             | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders | Comments   |
|---|--|---|-----------------------------|---------------------------------|---------------------|------------------------|--------------------------------------|--|
| Hayes <i>et al.</i> , (1997), PR China                        | 74828 exposed and 35805 unexposed workers employed 1972-1987 in 12 cities in China, followed through 1987                              | Average occupational benzene exposure was estimated by local industrial hygienists and other occupational health personnel, using available ambient benzene exposure measurements and production and related process information for seven calendar periods for study specific job titles in each factory. Work histories were linked to benzene-exposure data to provide individual time-specific benzene-exposure estimates | ANLL<br>205.0, 206.0, 207.0 | Benzene cumulative person-years |                     | (SMR)                  | Age and sex                          | NCI-CAPM cohort  |
|   |  |   |                             | None                            | 4                   | 1.0                    |                                      |  |
|   |  |   |                             | <40                             | 5                   | 1.9 (0.5-7.0)          |                                      |  |
|   |  |   |                             | 40-99                           | 5                   | 4.3 (1.1-16.0)         |                                      |  |
|   |  |   |                             | ≥ 100                           | 11                  | 3.6 (1.1-11.6)         |                                      |  |
| p for trend   | 0.06   |   |                             |                                 |                     |                        |                                      |  |
| Lyng <i>et al.</i> , (1997), Denmark, Norway, Sweden, Finland | Cohort of gasoline service station workers (16524 men, 2445 women), followed through 20 years by linkage to national cancer registries | Service station occupation identified from the 1970 censuses of each country  | AML 205.0                   | Men                             | 13                  | (SIR)<br>1.4 (0.8-2.4) |                                      | Estimated average level of exposure to benzene below 1 mg/m <sup>3</sup> |
|   |  |   |                             | Women                           | 0                   | -                      |                                      |  |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                        | Cohort description                                | Exposure assessment   | Organ site (ICD code)                       | Exposure categories         | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders | Comments  |
|--|---|---|---|-----------------------------|---------------------|------------------------|--------------------------------------|---|
| Rushton & Romaniuk, (1997), United Kingdom | Cohort of petroleum industry distribution workers | Retrospective estimates of workplace exposure for each job reported in the work histories of all the study members were obtained by creating base estimates. Base estimates were estimated based on exposure measurements and adjusted with the use of modifying factors. Modifying factors represented factors that could have affected the exposure levels (e.g. changes in exposure circumstances over time or between two different work-sites) | AML and monocytic leukaemia<br>204.2, 205.0 | Benzene cumulative exposure |                     |                        |                                      | Nested case-control analysis; 4 controls selected per case matched by age. Only 1 case of monocytic leukaemia. Cumulative exposure analysed as a continuous variable showed no association with AML (OR1.0, 95% CI 1.0-1.0) |
|  |   |   |   | <0.26                       | 6                   | 1.0                    |                                      |   |
|  |   |   |   | 0.26-0.59                   | 5                   | 1.9 (0.5-7.2)          |                                      |   |
|  |   |   |   | 0.60-1.64                   | 6                   | 1.7 (0.5-6.1)          |                                      |   |
|  |   |   |   | 1.65-4.78                   | 6                   | 1.6 (0.4-5.8)          |                                      |   |
| ≥4.79                                      | 8   | 2.4 (0.6-8.7)   |   |                             |                     |                        |                                      |   |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                 | Cohort description   | Exposure assessment  | Organ site (ICD code) | Exposure categories                                  | No. of cases/deaths | Relative risk (95% CI)                  | Adjustment for potential confounders | Comments                            |
|-------------------------------------|--|--|-----------------------|--|---------------------|---|--------------------------------------|-------------------------------------|
| Divine <i>et al.</i> (1999b)<br>USA | All (28480) employees who worked at selected refinery, petrochemical, and research establishments at least one day between 1947-1977; employed at these for a cumulative total >5 years; still employed on the end date of the study | Complete work history of all jobs held at the participating factories (Divine <i>et al.</i> , 1999a) | AML 205.0             | Employed: before 1950<br>1950 and after              | 19<br>1             | (SMR)<br>1.5 (0.9-2.4)<br>0.3 (0-1.7)   |                                      | No estimates of exposure to benzene |
| Wong <i>et al.</i> , (2001a)<br>USA | Cohort of 7543 petroleum refinery workers (91% men) employed for at least 1 year, 1945-1996, followed up to 1996   | No exposure assessment performed   | AML 205.0             | Men workers hired before 1950<br>Hired 1950 or later | 11<br>1             | (SMR)<br>1.7 (0.8-3.0)<br>0.6 (0.0-3.6) |                                      | No estimates of exposure to benzene |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                 | Cohort description   | Exposure assessment   | Organ site (ICD code) | Exposure categories                   | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders | Comments  |
|-------------------------------------|--|---|-----------------------|---------------------------------------|---------------------|------------------------|--------------------------------------|---|
| Guénel <i>et al.</i> (2002), France | Cohort of 170000 men employed at an electric utility company for at least one year, 1978-1989                          | Time weighted average exposure to benzene was estimated based on expert judgement (expressed in units of exposure). Estimates were included in a JEM. Cumulative exposure was calculated by summing yearly exposure estimates in a JEM. | AML 205.0             | Benzene unit exposure-years           |                     | (OR)                   |                                      | Nested case-control analysis. Odds ratios were not adjusted for potential confounders |
|                                     |  |   |                       | 0                                     | 20                  | 1.0                    |                                      |   |
|                                     |  |   |                       | <5.5                                  | 1                   | 0.2 (0.1-1.4)          |                                      |   |
|                                     |  |   |                       | ≥5.5                                  | 5                   | 2.4 (0.7-8.5)          |                                      |   |
|                                     |  |   |                       | p for trend                           |                     | 0.14                   |                                      |   |
| Collins <i>et al.</i> (2003), USA   | Hourly workers (4172 men and 245 women) employed at a chemical manufacturing plant from 1940-1977 and followed to 1997 | Work histories, sampling measurements and industrial hygienists assessments   | ANLL 205.0, 206.0     | Benzene cumulative exposure ppm-years |                     | (SMR)                  |                                      | The SMR for peak benzene exposure >40 ppm was 4.1 (95%CI 0.5-14.9) based on 2 deaths. |
|                                     |  |   |                       | 0                                     | 2                   | 0.8 (0.1-2.8)          |                                      |   |
|                                     |  |   |                       | <1                                    | 1                   | 1.4 (0.1-5.1)          |                                      |   |
|                                     |  |   |                       | 1-6                                   | 2                   | 2.7 (0.3-9.9)          |                                      |   |
|                                     |  |   |                       | >6                                    | 2                   | 2.2 (0.3-8.1)          |                                      |   |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                     | Cohort description  | Exposure assessment   | Organ site (ICD code)       | Exposure categories   | No. of cases/deaths | Relative risk (95% CI)                                   | Adjustment for potential confounders | Comments   |
|---|---|---|-----------------------------|---|---------------------|--|--------------------------------------|--|
| Glass <i>et al.</i> , (2003), Australia | Australian petroleum workers cohort   | Benzene exposure based on task-based algorithm involving the subject's occupational history; previously measured exposures for particular tasks in the Australian petroleum industry; and task-, site-, and period-specific data. | ANLL<br>205.0, 208.0        | Cumulative lifetime Benzene exposure (ppm-years)<br>≤ 4<br>>4-8<br>>8 | NA                  | 1.0<br>0.5 (0.1-5.0)<br>7.2 (1.3-40.4)                   |                                      | Nested case-control analysis<br>11 cases, 5 controls per case randomly selected and matched by age and availability at time of diagnosis of the case |
| Lewis <i>et al.</i> , (2003), Canada    | Cohort of 17230 men and 8062 women employed for at least a year of a petroleum company hired between 1964 and 1994 linked to national mortality and cancer incidence databases to 1994. | Estimates of similar exposure groups based upon job title and location by industrial hygienists   | ANLL<br>205.0, 206.0, 207.0 | Men<br>Women  | 4<br>2              | (SIR)<br>[1.0]<br>[1.2]                                  |                                      |  |
| Bloemen <i>et al.</i> , (2004), USA     | Workers exposed to benzene at a chemical plant; 2266 workers (94% men) Followed for up to 30 years.   | Job-titles were assigned to exposure categories by an industrial hygienist, based on industrial hygiene measurements.   | ANLL<br>205.0, 206.0, 207.0 | Benzene cumulative exposure ppm-years<br><28.3<br>28.3-79.1<br>≥79.1  | 2<br>1<br>1         | (SMR)<br>0.9 (0.1-3.1)<br>1.5 (0.0-8.2)<br>1.6 (0.0-9.0) |                                      |  |

**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                            | Cohort description  | Exposure assessment   | Organ site (ICD code)           | Exposure categories         | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders | Comments   |
|--|---|---|---------------------------------|-----------------------------|---------------------|------------------------|--------------------------------------|--|
| Huebner <i>et al.</i> , (2004), USA            | All employees of two refinery/petrochemical plants (Baton Rouge 6941 men, Baytown 6241 men) active in 1970 or hired between 1970-1982 with at least 1 month of employment at the facility and followed through 1997 | No exposure assessment was performed  | ANLL 205.0, 206.0, 207.0, 207.2 | Hired before 1950           |                     | (SMR)                  |                                      |  |
|  |   |   |                                 | Baton Rouge                 | 11                  | 1.9 (1.0-3.5)          |                                      |  |
|  |   |   |                                 | Baytown                     | 9                   | 2.1 (1.0-3.9)          |                                      |  |
|  |   |   |                                 | Hired in 1950 or later      |                     |                        |                                      |  |
| Baton Rouge                                    | 0   | -   |                                 |                             |                     |                        |                                      |  |
| Baytown  | 3   | 2.4 (0.5-6.9)   |                                 |                             |                     |                        |                                      |  |
| Sorahan <i>et al.</i> , (2005), United Kingdom | Cohort of 5130 men and 384 women followed for mortality, 1968-2002  | Occupational exposure to benzene 1966/67 or earlier; as reported by 233 employers | ANLL 205.0, 206.0, 207.0, 208.0 | All benzene exposed workers | 14                  | (SMR)<br>1.8 (1.0-3.1) |                                      | Cohort also followed for incidence by linkage to cancer registries 1971-2001, with similar results |
| Gun <i>et al.</i> (2006), Australia            | Australian petroleum workers cohort, 16547 men and 1356 women, followed 1981-1999   | None  | ANLL 205.0, 208.0               |                             | 11                  | (SIR)<br>1.1 (0.5-1.9) |                                      | Same cases as in Glass <i>et al</i> (2003) 5 of the cases occurred pre-1955                        |



**Table 2.1. Cohort studies of benzene and acute non-lymphocytic leukemia/acute myelogenous leukemia**

| Reference, location                      | Cohort description  | Exposure assessment               | Organ site (ICD code) | Exposure categories               | No. of cases/deaths | Relative risk (95% CI) | Adjustment for potential confounders           | Comments  |
|--|---|-----------------------------------|-----------------------|-----------------------------------|---------------------|------------------------|--|---|
| Kirkeleit <i>et al.</i> (2008)<br>Norway | Cohort of 27919 offshore petroleum workers registered to the Norwegian registry of employers and employees and 366114 matched referents from the general working population | Location of work and job category | AML 205.0             | Exposed upstream offshore workers | 6                   | 2.9 (1.2-6.7)          | Sex, age, year of first exposure and education | Cases identified by linkage to the Norwegian cancer registry. |