# Benzene Exposure in the Petroleum Distribution Industry Associated with Leukemia in the United Kingdom: Overview of the Methodology of a Case-Control Study

Lesley Rushton

Department of Public Health Medicine and Epidemiology, University Hospital, Queen's Medical Centre, Nottingham, UK

This paper describes basic principles underlying the methodology for obtaining quantitative estimates of benzene exposure in the petroleum marketing and distribution industry. Work histories for 91 cases of leukemia and 364 matched controls (4 per case) identified for a cohort of oil distribution workers up to the end of 1992 were obtained, primarily from personnel records. Information on the distribution sites, more than 90% of which were closed at the time of data collection, was obtained from site visits and archive material. Industrial hygiene measurements measured under known conditions were assembled for different tasks. These were adjusted for conditions where measured data were not available using variables known to influence exposure, such as temperature, technology, percentage of benzene in fuel handled, products handled, number of loads, and job activity. A quantitative estimate of dermal contact and peak exposure was also made. — Environ Health Perspect 104(Suppl 6):1371–1374 (1996)

Key words: benzene, petroleum distribution, exposure estimation, methodology

## Introduction

This paper presents a broad overview of the methods employed in a case–control study to investigate the risk of leukemia in oil distribution workers with exposure to low levels of benzene. The retrospective estimation of benzene is also described. Two reports giving the results of the statistical analyses and the full exposure estimation are available from the Institute of Petroleum (IP), London (*1,2*).

Since the mid 1970s, the IP has been sponsoring the follow-up of two large historical cohorts of workers in the oil industry. The cohorts consist of approximately 35,000 men from eight U.K. oil refineries and 23,000 men from U.K. distribution centers. To be eligible for the cohort, the men had to have worked at least 1 year between 1950 and 1975. These cohorts have been followed up for mortality data since 1951, and their records are now flagged at the National Health Service Central Register for both death and cancer registration. Results from two follow-up periods have now been published, the first to 1975 (*3,4*) and the second to 1989 (*5–7*). In the second follow-up of the distribution center cohort, some increased mortality patterns were identified for leukemia, in particular for those whose last job was a driver. Three other cohort studies of oil distribution workers have also been published in recent years, the American Petroleum Institute study (*8*), a Canadian study (*9*), and the Australian Health Watch study (*10*). Table 1 summarizes some of the results from these studies, together with those from the IP study in the UK, for leukemia. It can be seen that the standardized mortality ratios (SMRs) tend to be >1, in particular for acute myeloid leukemia and in drivers although most do not achieve statistical significance at the 5% level.

## Methods

The study was carried out by a research team at Nottingham University. The research team reported to a steering group of the IP. The exposure assessment was carried out by occupational hygienists from the companies involved, who formed a core group of a larger exposure assessment task force. The study benefited from the advice and guidance of a scientific advisory board consisting of independent experts. A quality assurance audit was also carried out by an independent group.

A total of 91 cases of leukemia (*International Classification of Diseases Revision 9*, 204–208) were identified from the 23,000 distribution cohort members up to the end of 1992. Table 2 shows the numbers by type of leukemia. Death certificates were the primary source of identification, with only three cases being identified solely from cancer registration. These three were all deceased but did not have a mention of leukemia on the death certificates. Cancer registrations were also received for 40 of the deaths. Not unexpectedly, the acute leukemias were the underlying cause of death on the certificates. In contrast, 8 of the 31 chronic lymphatic leukemias and 3 of the 11 chronic myeloid leukemias were a contributory cause on the death certificates. Four controls per case were randomly selected from the study population, matched on oil company, with date of birth within 3 years of the case, and alive and under follow-up at the case date of death or diagnosis.

Figure 1 illustrates the exposure assessment process and the data required. The first step was the collection of work histories for the cases and controls. In the cohort study, only last job held had been recorded for those who had left and only current job held for those still employed. The usual source of work history data is personnel records. However, the retention policies of the companies varied, with some retaining all records and some having a policy of discarding records a certain time after an employee had left the company. The quality of the retained records also varied, with few hard-copy files being available and most being on microfiche or microfilm. Medical

This paper was presented at Benzene '95: An International Conference on the Toxicity, Carcinogenesis, and Epidemiology of Benzene held 17–20 June 1995 in Piscataway, New Jersey. Manuscript received 16 January 1996; manuscript accepted 14 June 1996.

This study was funded by the Institute of Petroleum, under the general management of a Steering Group under the chairmanship of C. Roythorne. Other members of the Nottingham University research team were H. Romaniuk and S. Grace. The exposure assessment was carried out by G.H. Bell, N. Cordingley, S.J. Lewis, and E.D. Pearlman with advice and direction of M.F. Claydon, M.K.B. Molyneux, and J.T. Sanderson.

Address correspondence to Dr. L. Rushton, Department of Public Health Medicine and Epidemiology, University Hospital, Queen's Medical Centre, Nottingham, NG7 2UH UK. Telephone: 44 115 970 9303. Fax: 44 115 970 9316. E-mail: lesley.rushton@nottingham.ac.uk

Abbreviations used: BE, base estimate; ICD, International Classification of Diseases; IP, Institute of Petroleum; SMR, standardized mortality ratio; TGWU, Transport and General Workers Union; TWA, time-weighted average; WE, workplace estimate.

**Table 1.** Results for leukemia from petroleum distribution cohort studies.

| Study | Study subgroup | Disease subgroup | Observed deaths | SMR | 95% CI |
|---|---|---|---|---|---|
| United States (*8*) | Total | Total | 27 | 0.89 | 0.59–1.29 |
| | | AML | 13 | 1.51 | 0.80–2.57 |
| | Drivers | Total | 5 | 0.69 | 0.09–1.29 |
| United Kingdom (*6*) | Total | Total | 61 | 1.08 | 0.83–1.40 |
| | | AML | 25 | 1.21 | 0.78–1.79 |
| | Drivers | Total | 28 | 1.25 | 0.83–1.81 |
| | | AML | 13 | 1.55 | 0.82–2.65 |
| Canada (*9*) | Total | Total | 14 | 1.01 | 0.40–2.08 |
| | Drivers | Total | 5 | 3.35 | 1.08–7.81 |
| Australia (*10*) | Total | Total | 5 | 2.20 | 0.70–5.00 |
| | Total | Total plus incidence | 10 | 3.60 | 1.70–6.60 |

Abbreviations: SMR, standardized mortality ratio; AML, acute myeloid leukemia; CI, confidence interval.

**Table 2.** Leukemia cases and source of identification.

| | Cases identified from | | | |
|---|---|---|---|---|
| | Death certificates | | Cancer notification | |
| Leukemia type | Underlying cause | Contributory cause | | Total |
| Acute lymphatic | 7 | — | — | 7 |
| Chronic lymphatic | 22 | 8 | 1 | 31 |
| Other lymphatic | — | 1 | — | 1 |
| Total lymphatic | 29 | 9 | 1 | 39 |
| Acute myeloid | 30 | — | 1 | 31 |
| Chronic myeloid | 8 | 3 | — | 11 |
| Other myeloid | 1 | 1 | — | 2 |
| Total myeloid | 39 | 4 | 1 | 44 |
| All monocytic | 3 | — | — | 3 |
| All other | 4 | — | 1 | 5 |
| All leukemia | 75 | 13 | 3 | 91 |

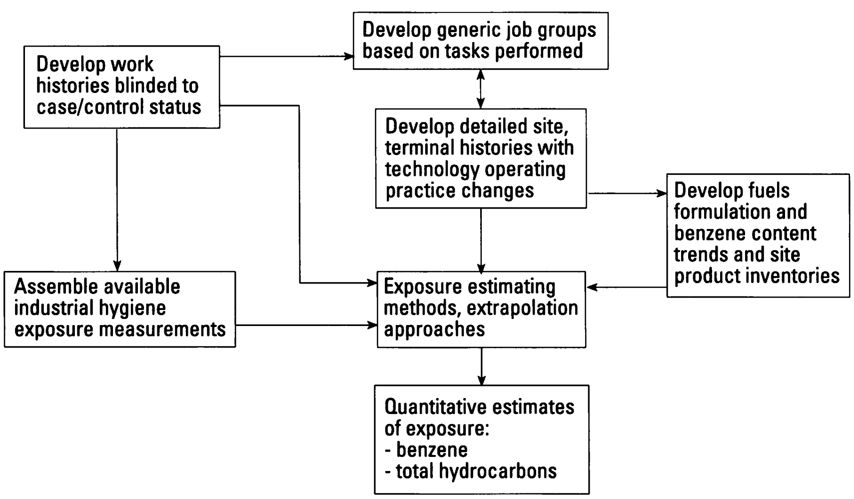


**Figure 1.** Exposure assessment process and data.

and pension records were used to fill some of the gaps in work histories, and interviews were also carried out with long service or retired staff. About 20% of the work histories were incomplete, although many of these had minor omissions, such as an incomplete date. Assumptions were made for these histories; for example, taking a date midway between known dates if there were gaps for either a job or location change. All assumptions were noted on the database to enable analyses to be carried out on the sensitivity of the results to the quality and source of the work histories.

The job titles used in the oil companies did not always closely reflect the tasks that the person actually carried out. There were considerable changes in both titles and tasks; for example, the introduction of a more flexible work schedule, over the years of the study. The titles for the same tasks also differed between companies. To enable the exposure-estimating team to interpret the job titles in the work histories and relate them to the tasks and working practices, a job-task dictionary was developed. This used information from union productivity agreements, historical records from company and other archives, such as Transport and General Workers Union (TGWU) minutes, and a large number of interviews. A history of the process of wages and conditions negotiations and key events that influenced changes in jobs was developed. The job-task dictionary gave a description of the tasks performed under each job title and included both official definitions of tasks and also anecdotal information.

One of the most important pieces of information required for the exposure-estimating process was the percentage of benzene in the fuels. It was discovered, however, that this information was not readily available before the 1980s. The IP therefore developed a model that simulated refinery operations to estimate this percentage. Trade journals were used to obtain the type of crude oil for each of the major refineries in the United Kingdom. The required quality of the final gasolines and the average added lead levels were obtained, and the quality of the average gasoline was determined. The computer model was adjusted to provide the correct volume of gasoline of the appropriate quality. The average pool benzene content was calculated from the finished blend.

There were more than 300 sites involved in the case–control study. These included distribution terminals, lubricating oil plants, and airport terminals. More than 90% of the sites were closed by the time of data collection. A detailed questionnaire was developed to collect data on the sites (including the source and mix of products, methods of storage and distribution, and working practices) and to record changes over time. All open sites were visited. The questionnaire was used to carry out structured interviews with long-term employees or retired staff about closed sites. Other sources of information included photographs, booklets, site plans, company magazines, and other material available from property departments, libraries, and archives records. A major source of archive material on all aspects of the oil industry was the British Petroleum archive held at Warwick University.

The exposure-estimating method was an extension of the methodology developed for the Canadian case–control study (*11*), in which exposure values, measured under known conditions, were adjusted for another set of conditions. This can be expressed as:

$$\mathrm{WE} = \mathrm{BE} \times K_1 \times K_2 \times K_3 \times \ldots K_n$$

where WE represents a workplace estimate; BE represents a base estimate, i.e., exposure data measured under known conditions; and $K_n$ represents adjustment factors to another set of conditions. A workplace estimate was derived for each line of a work history (each job, location, and dates of starting and leaving).

The earliest reports of measurements in the oil industry are from the early 1970s (*12–14*). Since then measurements have been published regularly (*15–18*), although, like many hygiene measurements, these were taken for regulatory compliance purposes and not to characterize exposure for epidemiological studies.

More than 200 sets of measurements were collected relating to petroleum distribution jobs. These were reviewed to establish whether the sampling techniques and analyses were consistent and whether data on variables known to influence exposure were also recorded. Where possible U.K. data were used. The data were standardized where necessary to enable data from different sources to be combined. Sufficient good-quality data were available to derive base estimates from 14 separate tasks. If numbers of data points were large enough, a log-normal distribution was fitted to the data, and the expected arithmetic mean from this distribution was used for the base estimate. For small numbers of data points, the arithmetic mean of the data was used. All the base estimates were expressed as 8-hr time-weighted average (TWA) in parts per million.

There were two job titles for which full-shift measurements were not available. The first of these was drivers using top-submerged loading, for which there were a large number of measurements for loading, which took about 1.5 hr of each shift, but few data on driving and unloading. Additional monitoring was carried out for these activities and combined with the data for loading to give an 8hr TWA measurement.

The other job for which there was few monitoring data available was terminal operators. An operator's job was considered to be made up of up to 12 separate tasks. These were tank draining,* leveling off over- or under-filled tanks,* tanker compartment dipping,* filter cleaning,* storage tank dipping,* dump trolley activities during grade changes and overfilling,* loading, product receipt, spillage cleaning, maintenance, drum filling, and sampling and testing.* (An asterisk indicates that new measurements were taken for those jobs.)

Terminal information obtained from the structured questionnaire established the number of times per month each of the 12 activities was undertaken. The 8-hr TWA was derived from combining the data for the 12 activities for *a*) three terminal sizes, small, medium, and large, based on the number of staff employed, and *b*) five time periods that indicated main changes in oil distribution practice (e.g., the end of splash loading).

The 8-hr TWA values of the base estimates ranged from 0.016 ppm for site background jobs such as office workers and managers, through 0.40 ppm for drivers carrying out top-submerged loading, to 8.2 ppm for drum fillers, an activity that continued until the 1950s.

A large number of factors that could potentially influence exposure were considered and classified into four broad groups relating to the work or task, the products handled, climate conditions, and the technology. Some of these are listed in Table 3. The final choice of factors with which to adjust the base estimates depended to a large extent on the availability of data with which to construct the adjustment factors. It has been shown, for example, that wind speed and the distance at which someone stands from the source of fuel are both important factors affecting exposure measurements. In the latter case, data are never recorded. In the former case, some data were available from the U.K. Meterological Office, but were not suitable for use in adjustment. The six modifying factors used were job activity (to adjust for differences in tasks from those covered in the base estimate), number of loads handled per day, loading technology (in particular to adjust for differences between top-splash and top-submerged loading), percentage of benzene in the fuel, product mix (to adjust for handling products other than motor gasolines, such as diesel, during the same work), and air temperature. A linear relationship was used to adjust number of loads, percentage of benzene, and product mix for the standardized values of the base estimates. Limited exposure data on top-splash loading indicated that a factor of 3 times the base estimate for top-submerged loading was an appropriate adjustment. Air temperature was used as a surrogate for product temperature vapor pressure. The amount of vapor present above liquid gasoline is dependent on a combination of the product and air temperature. An equation was used to relate vapor pressure to air temperature. The modifying factor for air temperature was then the ratio of the vapor pressure of interest to the vapor pressure at the reference temperature of 10°C.

The workplace estimates were derived for each line of a work history, the base estimate being multiplied by the six modifying factors. The adjusted estimate for each job and site for each line was multiplied by the time spent for that job, and these were then summed over each study member's complete work history to give a cumulative exposure (ppm-years).

It was recognized that exposure to benzene by oil distribution workers was not entirely through inhalation, but that there was potential for dermal contact. This was, however, difficult to quantify, especially retrospectively. A ranked grade of dermal contact (none, low, medium, or high) was therefore assigned to each job of the work history.

One of the characteristics of exposure to benzene in distribution sites is that it tends to occur mainly in peaks. This is particularly true for many of the tasks carried out by operators and drivers, such as loading

**Table 3.** Modifying factors considered in exposure estimating.

| Job | Product | Meteorology | Technology |
|---|---|---|---|
| Loading activities | Volume throughput | Air temperature | Loading rate |
| Work practices | Benzene content of gasoline | Wind speed | Vehicle size |
| Worker position | Source of supply | Wind direction | Route of supply |
| Frequency of activities | Product temperature | Seasonal changes | Nature of loading |
| Duration of activities | Vapor pressure | | Number of cargo compartments |
| Splitting of compartments during delivery | Seasonal variations in products | | Type of cargo measurements |
| | Other products | | Gantry construction |
| | | | Site layout |

**Table 4.** Peak codes.

| Code | Frequency | Intensity, ppm | Duration, min |
|---|---|---|---|
| 1 | Daily | 1–3 | 1–15 |
| 2 | Weekly | 1–3 | 1–15 |
| 3 | Monthly | 1–3 | 1–15 |
| 4 | Daily | > 3 | 1–15 |
| 5 | Weekly | > 3 | 1–15 |
| 6 | Monthly | > 3 | 1–15 |
| 7 | Daily | 1–3 | 15–60 |
| 8 | Weekly | 1–3 | 15–60 |
| 9 | Monthly | 1–3 | 15–60 |
| 10 | Daily | > 3 | 15–60 |
| 11 | Weekly | > 3 | 15–60 |
| 12 | Monthly | > 3 | 15–60 |

and unloading road tankers, tank dipping, and sampling. At a workshop on retrospective estimation of benzene exposure, held at Nottingham University in 1991, a large part of the discussion focused on suitable methods of defining peaks and how these related to the current knowledge on the pharmacokinetics of peaked benzene exposure (*19,20*). Each work history job was given a code that characterized the type of peak exposure experienced for that job at that time and site, according to the duration, frequency, and intensity of the peak. These peak codes are listed in Table 4.

## Summary

This paper describes the principles underlying the methodology for obtaining quantitative estimates of benzene exposure for a case–control study in the petroleum marketing and distribution industry. Details of the results of the exposure assessment and comparisons with the values found in similar studies are available in a report from the Institute of Petroleum (*1*). The results of the epidemiological analyses and discussion and interpretation of the results are presented in another report (*2*).

### REFERENCES

1. Bell GM, Cordingley N, Lewis SJ, Pearlman ED. Retrospective estimation of exposure to benzene in a leukaemia case-control study of petroleum marketing and distribution workers in the United Kingdom. London:Institute of Petroleum, 1995.
2. Rushton L, Romaniuk HM. Results of 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. London:Institute of Petroleum, 1995.
3. Rushton L, Alderson MR. An epidemiological survey of eight oil refineries in Britain. Br J Ind Med 38:225–234 (1981).
4. Rushton L, Alderson MR. An epidemiological survey of oil distribution centres in Great Britain. Br J Ind Med 40:330–339 (1983).
5. Rushton L. Further follow-up of mortality in a UK oil refinery cohort. Br J Ind Med 50:549–560 (1993).
6. Rushton L. Further follow-up of mortality in a UK oil distribution centre cohort. Br J Ind Med 50:561–569 (1993).
7. Rushton L. A 39 year follow-up of the UK oil refinery and distribution centre studies: results for kidney cancer and leukaemia. Environ Health Perspect Suppl 101(Suppl 6):77–84 (1993).
8. Wong O, Harris F, Smith TJ. Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States. Environ Health Perspect 101(Suppl 6):63–76 (1993).
9. Schnatter AR, Katz AM, Nicolich MJ, Theriault G. A Retrospective Mortality Study among Canadian Petroleum Marketing and Distribution Workers. Environ Health Perspect 101(Suppl 6):85-99 (1993).
10. Bisby JA. Health Watch, the Australian Institute of Petroleum Health Surveillance Program. Ninth Report. Melbourne: Department of Public Health and Community Medicine, University of Melbourne, 1993.
11. Schnatter AR, Armstrong TW, Nicolich MJ, Huebner WW, Pearlman ED, Thompson FS, Katz AM. The risk of lymphohematopoietic malignancies and quantitative estimates of benzene exposure in Canadian petroleum marketing/distribution workers. Environ Health Perspect 104(Suppl 6):1375–1379 (1996).
12. Parkinson GS. Benzene in motor gasoline—An investigation into possible health hazards in and around filling stations and in normal transport operations. Ann Occup Hyg 14:155–157 (1971).
13. Sherwood RJ. Evaluation of exposure to benzene vapour during the loading of petrol. Br J Ind Med 29:65–69 (1972).
14. Sherwood RJ, Carter FWG. The measurement of occupational exposure to benzene vapour. Ann Occup Hyg 13:125–146 (1970).
15. Christian F Eyres AR. Concawe Rpt 3/86. Review of European oil industry benzene exposure data. The Hague:CONCAWE, 1986;1–26.
16. Rocchi PSJ. CONCAWE Benzene Exposure Study. CONCAWE SIPM-HSE/232, 1991.
17. CONCAWE. Benzene in motor gasoline. An ad hoc review of problems related to benzene reduction of motor gas in Europe. CONCAWE Rpt 1/73, 1973.
18. Tims JM. CONCAWE Rpt 2/81. Exposure to atmospheric benzene vapour associated with motor gasoline. The Hague:Concawe, 1981;1–55.
19. Schnatter AR, Bird MG, Cox A, Herrick RF. Defining optimum exposure assessment methods and metrics for epidemiologic studies of benzene exposure in petroleum distribution workers. Occ Hyg (in press).
20. International Workshop on Petroleum Marketing and Distribution Worker Benzene Estimating, Nottingham 1993. Sponsored by the American Petroleum Institute, CONCAWE, EXXON Chemicals, and the Institute of Petroleum. 1993.