Butadiene and Styrene: Assessment of Health Hazards
IARC Scientific Publications No. 127
Editors M. Sorsa, K. Peltonen, H. Vainio and K. Hemminki
Lyon, International Agency for Research on Cancer, pp. 363–374


# Cancer epidemiology among styrene–butadiene rubber workers

**G. Matanoski, M. Francis, A. Correa-Villaseñor, E. Elliott, C. Santos-Burgoa and L. Schwartz**

*Department of Epidemiology, The Johns Hopkins University, Baltimore, MD, USA*

*Summary*. The standardized mortality ratios for some cancers of the lymphohaematopoietic system were high in an early cohort analysis. Since the presence of large numbers of unexposed workers could conceal risks within a cohort, a case–control study was designed to examine the relationship between estimated exposures and the occurrence of these cancers. The results suggested that the risk for leukaemia was associated with exposure to butadiene and with work in specific areas. Modelling, using rank scores, indicated an increase in the risk for leukaemia with increasing exposure score. Use of cases validated by review of hospital records and selection of a new set of controls did not change the findings. The data indicated that comparison of scores within the same time frame improved the model and increased the estimated odds ratio, suggesting that exposure time or dose rate may prove to be the important variable for risk. Exact measurements from the companies involved showed significant correlations between assigned ranks and level of exposure derived from personal monitoring for butadiene but not for styrene. Thus, use of the measured values might be expected to show an association between leukaemia and exposure to butadiene. The standardized mortality ratio for leukaemia among long-term workers hired before 1960 who had worked in the three plants where the geometric mean butadiene level was three to five times higher than those in the other plants is 1.8 times higher than that of the US population. An appropriate algorithm for comparing cases and controls on the bases of the measured samples is being developed.

## *Introduction*

Several papers have suggested that the manufacture of styrene–butadiene rubber latex is associated with a risk for cancers of the lymphatic and haematopoietic system in workers (McMichael *et al.*, 1976; Meinhardt *et al.*, 1982; Matanoski *et al.*, 1990). The case–control study of McMichael *et al.* (1976) demonstrated that workers in latex manufacturing areas had a risk for developing cancers of these sites that was 6.2 times greater than that of other workers in the industry. The other mortality studies (Meinhardt *et al.*, 1982; Matanoski *et al.*, 1990) were designed to determine whether workers in the industry had higher death rates from any diseases than the US population. Because the rates of lymphohaematopoietic cancers were found to be elevated, a case–control study was undertaken within one worker population (Santos-Burgoa *et al.*, 1992), which was designed to answer the question of whether cases of lymphohaematopoietic cancers occurring in the industry could be explained by differences in exposures among workers. This paper addresses the issues raised in regard to the original papers, discusses the results of some of our recent analyses and, finally, examines the levels of exposure of these workers.

## *Cohort study*

The population studied comprised workers in eight styrene–butadiene rubber manufacturing plants in North America. The plants had been built with approximately the same design. All made several types of rubber, but most of the production was styrene–butadiene rubber. All but one of the plants had begun operation in 1943; one started in 1955. Four plants had complete records from the beginning of operation; for the three plants that had incomplete records, follow-up was begun several years after they opened. For the largest plant, only workers with 10 or more years of employment were included in the cohort, since follow-up was possible only through records of death benefit claims. The missing records for three of the plants and limitations in follow-up in one could lead to underascertainment of the workers' risks.

Our mortality analysis was based on the 12 110 male workers at the plants (Matanoski *et al.*, 1990). The results of that study indicated very low mortality overall but significant excess mortality from cardiovascular disease among the black workers. Furthermore, there was nonsignificant excess mortality from cancers such as those of the oesophagus and kidney, Hodgkin's disease and other lymphatic cancers in white workers and from cancers of the stomach, liver and prostate and leukaemia and other lymphatic cancers in blacks.

A general mortality study like this may mask any effect of exposure among workers because of dilution of the risk in a few people as a result of the addition to the cohort of large numbers of unexposed people. In an attempt to address this possible problem, we classified the cohort of workers by large work areas under the assumption that the group with the highest exposure would be in production. This type of analysis has its own limitations: one is that a worker must be assigned to a single work group even if he has worked in several areas. In addition, the work areas are assumed to be homogeneous. A subsequent review of records indicated that none of the areas was homogeneous with regard to exposure, and in all of them some jobs involved high exposure and some, no exposure. Despite the continued problem of the dilution of possible risks due to exposure to styrene–butadiene rubber chemicals by the presence of both exposed and unexposed workers in any one work area, workers in the production area showed an increased risk for 'other lymphatic cancers' (ICD 202 and 203), and black production workers showed an increased risk for leukaemia, with a standardized mortality ratio (SMR) of 6.6 (three deaths; 95% confidence interval (CI), 1.4–19.1).

These results have been questioned (Cole *et al.*, 1993), because in one plant no records were available for active workers and in another plant race was not designated on all records. In order to address these issues, the information from those two plants was omitted. With this omission, the SMR for leukaemia became 8.3. Addition to the cohort of short-term workers (defined as those who had worked for less than one year) increased the total study population to 18 470 but only served to reduce the risks for lymphohaematopoietic cancers, suggesting that workers with exposures of less than one year contributed little to the excess risk. These additional analyses support the suggestion of the original mortality study that subgroups of the cohort exposed to specific chemicals might be at risk (Matanoski *et al.*, 1990).

### *Case–control study*

In order to elucidate further the possible relationship between exposure to butadiene and cancer, we selected the 59 cases of lymphohaematopoietic cancer (ICD 200–209) and 193 controls and compared the exposures of the two populations (Santos-Burgoa *et al.*, 1992). The cases comprised all cancers of the lymphohaematopoietic group, regardless of where the cancer appeared among the multiple causes listed on the death certificates. This procedure increased the number of cases over that analysed in the cohort study, where only those cancers that were stated to be the underlying cause were included. The controls were similar to the cases with regard to plant, birth date, hire date, duration worked and survival at least until the time of the death of the case.

The entire work history of each subject was abstracted without knowledge of disease status. A group of industrial hygienists and engineers, some of whom had been involved in the manufacture of synthetic rubber since its inception in 1943, reviewed a list of 464 jobs in 93 work subareas, 36 work areas and 10 subdivisions. They classified each job within each work area with regard to possible exposure to butadiene and styrene, ranking each chemical on a scale of 1 to 10. If they considered that there were differences in exposures among the plants, separate ranks were entered by plant. The experts were asked to identify any other exposures that might occur in the jobs. They decided that exposures in particular jobs had not changed greatly over time. The rank assigned to each job was multiplied by the number of months an individual held that job. These job scores were then summed over the total work period for each case and control. Because of marked skewing in the data, the summed score for each individual was transformed into its logarithm (i.e., log score).

The cases and controls were divided into four cancer groups: 26 leukaemias (ICD 204–207) and 84 controls, 18 other lymphatic cancers (ICD 202,203,209) and 56 controls, six lymphosarcomas (ICD 200) and 23 controls and eight Hodgkin's disease (ICD 201) and 29 controls; one case of polycythemia vera with one control were included in the total. For each of the four groups of cases and their controls, an average exposure was calculated on the basis of the log scores. This value was used to divide each group into exposed and unexposed categories for use in logistic regression modelling. The methods have been described recently (Santos-Burgoa *et al.*, 1992).

The results indicated that the geometric mean score for exposure to butadiene is higher for the leukaemia cases than for controls or for any other type of cancer (see Table 1). The score for exposure to styrene followed the same pattern as that for butadiene, probably because the engineers often gave jobs similar ranks for the two exposures.

The analysis of leukaemia cases and controls, using the log mean as a categorical exposure variable as described above, showed an odds ratio of 7.6 (95% CI, 1.6–35.6) for butadiene alone and 2.9 (95% CI, 0.8–10.3) for styrene alone (Table 2). When both variables

**Table 1. Mean exposure scores[a] for all cases and controls and for subsets**

| Case group | Butadiene | | | Styrene | | |
|---|---|---|---|---|---|---|
| | All | Cases | Controls | All | Cases | Controls |
| Total | 85.6 | 127.7 | 75.9 | 59.7 | 90.9 | 59.7 |
| Leukaemia | 97.5 | 225.9 | 75.2 | 77.5 | 181.3 | 59.7 |
| Other lymphatic cancers | 70.8 | 84.8 | 66.7 | 66.7 | 100.5 | 58.0 |
| Hodgkin's disease | 68.7 | 58.6 | 71.5 | 23.8 | 15.0 | 73.7 |
| Lymphosarcoma | 115.6 | 99.5 | 120.3 | 62.8 | 81.4 | 58.6 |

Adapted from Santos-Burgoa *et al.* (1992)
[a]The score for each worker is the rank for each job times the number of months in each job summed for all jobs and transformed into a log score. 'Mean' is the average of the log scores of the individuals reported as the antilog of the mean.

were used in the model, only butadiene was associated with a significantly increased odds ratio. These results indicate that workers with leukaemia are 7.4–7.6 times more likely to have had an exposure to butadiene that was greater than the log mean score than are controls. Since odds ratios are an estimate of relative risk, people with the same characteristics as the cases and controls and who are exposed to butadiene at or above levels represented by this log mean score might have a risk for leukaemia seven times higher than that of individuals exposed to levels below that. No other group had a significant risk, except for the group of 59 combined cancers, where the excess probably reflects the increased risk for leukaemia.

**Table 2. Odds ratios (OR) for leukaemia (26 cases, 84 controls) under the conditional logistic model for categorical exposure variables**

| Model | OR | 95% CI | LRS | df | *p* |
|---|---|---|---|---|---|
| Butadiene | 7.6 | 1.6–35.6 | 9.63 | 1 | 0.002 |
| Styrene | 2.9 | 0.8–10.3 | 3.15 | 1 | 0.076 |
| Butadiene and | 7.4 | 1.3–41.3 | 9.64 | 2 | 0.008 |
| styrene | 1.1 | 0.2–5.0 | | | |

Adapted from Santos-Burgoa *et al.* (1992)
CI, confidence interval; LRS, likelihood ratio statistic; df, degrees of freedom

In order to determine whether any other occupational factor was associated with the risk for leukaemia, data on each work area were examined separately to see if cases were more likely to have been employed longer in that area than controls. Three areas seemed to be overrepresented among the cases: operation services, laboratory and utility. Work in these three areas, as compared with all others, was associated with a 3.8 times greater risk for leukaemia (95% CI, 1.2–11.9) in a conditional logistic regression model. When butadiene was added to the model, there was significant improvement, and both factors appeared to play a role in the risk for leukaemia (see Table 3). This finding may mean that, after correcting for butadiene, (i) some jobs still have not been classified appropriately for exposure to butadiene; (ii) there is another exposure in those jobs related to risk for leukaemia; or (iii) the jobs in which there is exposure to butadiene also involve exposure to another chemical, which is found in all these work areas. The last explanation seems highly unlikely. In fact, a review of the areas suggested that the inclusion of compressor operators in utilities and of truckers in operation services and variation in exposure by type of laboratory job may contribute to misclassification of butadiene exposures in these three work areas. Job titles are often nonspecific and difficult to classify, even in known exposure categories.

**Table 3. Odds ratios (OR) for leukaemia (26 cases, 84 controls) in association with exposure to butadiene and jobs in which such exposure occurs, using butadiene as a categorical variable**

| Model | OR | 95% CI | LRS | df | *p* |
|---|---|---|---|---|---|
| Mixed jobs[a] | 3.8 | 1.2–11.9 | 5.39 | 1 | 0.022 |
| Mixed jobs and | 6.1 | 1.6–23.7 | 17.56 | 2 | < 0.001 |
| butadiene | 13.3 | 2.2–78.5 | | | |

Adapted from Santos-Burgoa *et al.* (1992)
CI, confidence interval; LRS, likelihood ratio statistic; df, degrees of freedom
[a] Operation services, laboratory and utility

Table 4 shows the log score for exposure to butadiene as a continuous variable in a logistic regression model, thus avoiding dichotomization into exposed and unexposed. With the continuous variable, we see a significant increase in estimated risk with increasing exposure score. Again, the model is improved by including the work area category. The importance of this observation is that the significant beta coefficient found when using a continuous variable for butadiene indicates an increasing risk for leukaemia with increasing butadiene score, despite the crude measure of exposure.

**Table 4. Odds ratios (OR) for leukaemia (26 cases, 84 controls) in association with exposure to butadiene and jobs in which such exposure occurs, using butadiene as a continuous variable**

| Model | OR | 95% CI | LRS | df | *p* |
|---|---|---|---|---|---|
| Mixed jobs[a] | 1.3 | 1.1–1.7 | 5.38 | 1 | 0.020 |
| Mixed jobs and | 5.6 | 0.5–18.1 | 13.21 | 2 | 0.001 |
| butadiene | 1.5 | 1.1–2.0 | | | |

CI, confidence interval; LRS, likelihood ratio statistic; df, degrees of freedom
[a] Operation services, laboratory and utility

As jobs within a work area vary widely in rank scores, we found little risk for work in combined areas in the mortality analysis, where the jobs in which exposure occurs are diluted by those with no exposure (Table 5). In every work area (except the pilot plant, which was given an average score), some jobs were classified as involving no exposure, whereas in some areas, some jobs were ranked as high as 10. If exposure in an area is diluted by many jobs with no exposure, the risk for the exposure will disappear. The case–control analysis represents a more specific way of classifying each individual by exposure rank.

**Table 5. Classification of work areas[a]**

| Division rank[b] | Subdivision | Work area | Assigned exposure | |
|---|---|---|---|---|
| | | | Butadiene | Styrene |
| Production | Process | Tank farm<br>Pigment preparation<br>Polymerization<br>Recovery and stripping<br>Finishing<br>Not specified<br>Special plant | 0–10 | 0–8 |
| Auxiliary | Utilities | Water and effluent treatment<br>Refrigeration<br>Steam and electrical generation<br>Pump and boilerhouse<br>Utilities unspecified | 0–6 | 0–1 |
| | Maintenance | Central shops<br>Process unit<br>Nonspecific<br>Plant satellite unit<br>Special plant unit | 0–10 | 0–8 |
| | Services | Services<br>Vehicle driving<br>Operation services | 0–3 | 0–8 |
| | Warehouse | Warehouse, shipping and receiving | 0 | 0 |
| | Administration | Administration<br>Secretarial<br>Medical services<br>Fire and safety<br>Guard security<br>Personnel | 0–5 | 0–6 |
| | Laboratory | Research and development<br>Quality control of operation | 0–10 | 0–10 |
| | Pilot plant | Pilot plant | 3–5 | 4 |
| | Engineering | Process engineering<br>Engineering<br>Plant engineering<br>Non-production engineering | 0–5 | 0–2 |
| | Labour group | Process site-specific<br>General | 0–8 | 0–6 |

Adapted from Santos-Burgoa *et al.* (1992)
[a] Does not include work subareas and job titles
[b] Range of assigned ranks includes those for both Canada and the USA

The case–control study, however, focused only on those men in the population who were like the cases with regard to matching characteristics. All but one case had been hired before 1960, 81% had been employed for 10 or more years in the industry, and 73% had worked in only three of the eight plants. The comparison was made with individually matched controls who were similar in all variables: plant worked, age at hire, year of hire and duration worked. Thus, it would appear that the seven-fold risk applies to only a subset of the cohort and was diluted in the cohort analysis of the whole population. The absence of a risk for workers hired after 1960 may be due to the apparent long latency for this cancer. An average of 24 years was seen between start of employment and death. Few workers who were hired after 1960 had latent periods of this duration by the end of follow-up in 1982. Therefore, with further follow-up of the men hired more recently, a risk may be identified in this group as well.

Because of criticism regarding the use of controls matched for duration of work, all cases of lymphopoietic cancers and their duration-matched controls have been reviewed for additional information and to ensure comparability with the new controls. A new set of three controls per case was selected and matched on all previously matched variables except duration of work. We examined a series of cut points to evaluate sensitivity and consistency of results. On the basis of these evaluations, a log score of 3 was chosen to separate high and low exposure. The results are shown in Table 6. The cases and controls matched for duration of work at this log score had an estimated 8.5-fold (95% CI, 1.1–5.4) increase in risk associated with exposure to butadiene; however, using the same cases with the controls not matched for duration of work, we found a lower odds ratio (6.0; 95% CI, 0.8–47). Addition to the model of a variable to account again for duration of work improved the model and demonstrated a risk for leukaemia associated with exposure to butadiene of 9-fold (95% CI, 1.04–81). Exposure to styrene was not associated with a significant odds ratio. The importance of the duration of work variable suggests that dose per unit time may be the most important exposure variable to investigate. The same dose given over different time periods may not carry the same risk.

**Table 6. Odds ratios (OR) for leukaemia (26 cases, 84 controls) in association with exposure to butadiene, with above log 3 defining exposed: conditional logistic regression with and without matching for duration of employment**

| Model | OR | 95% CI | LRS | df | *p* |
|---|---|---|---|---|---|
| Controls matched for duration of work | 8.5 | 1.1–5.4 | 7.10 | 1 | 0.008 |
| Controls not matched for duration of work | 6.0 | 0.8–47.2 | 4.69 | 1 | 0.030 |
| Controls not matched for duration of work, term to adjust for duration added | 9.2 | 1.04–81.1 | 9.81 | 2 | 0.007 |

CI, confidence interval; LRS, likelihood ratio statistic; df, degrees of freedom

Since verification of specific cancers is important and diagnoses of non-Hodgkin's lymphoma are often coded incorrectly on death certificates, we attempted to retrieve all hospital records on the cases. The records of 55 of the 59 original cases (93%) were retrieved and reviewed, and it was found that 53 of the 55 (96%) had been classified correctly in the lymphohaematopoietic category. One case classified as a lymphoma was found to be a pancreatic cancer at autopsy, and one lymphosarcoma was in fact a rare retroperitoneal fibrosarcoma. Of the other lymphomas (five lymphosarcomas, ICD 200, and seven lymphomas, ICD 202), records were missing for two, and the other 10 were so poorly classified into the 200 and 202 codes on the death certificates as compared with the hospital records that we combined these ICD categories.

Hospital records were available for 25 of 26 leukaemias, and all were confirmed as cases. In comparison with cell types in US national cancer incidence statistics for adults (from the Surveillance, Epidemiology and End Results programme), there was an excess of acute lymphocytic leukaemia: 24% versus 8% in the comparison group. This difference, while interesting, may not be real, either because the number of cases was small or because the comparison was made between mortality data and incidence data. The more interesting observation is that the review of records revealed additional cancers, especially in the lymphohaematopoietic category, in these individuals, to give an average of about 1.4 cancers per patient.

*Exposure measurements*

A recent attempt was made to compare measured exposures in the jobs in these plants with the rank values assigned to those jobs by industrial representatives. Measurements were provided by seven of the eight rubber plants.[1] Values provided by the International Institute of Synthetic Rubber Producers were grouped and proved to be less useful in determining variability by job and plant. The US National Institute for Occupational Safety and Health provided values derived from personal and area monitoring in three plants included in the cohort study. The company data cover the period 1978–83; the data of the US National Institute for Occupational Safety and Health are limited to 1986 and were thus collected three to eight years after those provided by hygienists from the same three plants. A total of 3952 samples for butadiene and 3649 for styrene were reported. A few samples were discarded because they were outliers or appeared to be unusual (such as a value of 2800 ppm). Table 7 presents the results for both styrene and butadiene by plant. As can be seen, the value provided by the US National Institute for Occupational Safety and Health is about one-fourth that of the mean value found in the earlier reports.

Our first thought was simply to apply plant-specific data to the jobs on file (Kauppinen & Partanen, 1988). Even though a large number of samples was available in this study, however, the approach is problematic because some jobs for which samples were available could not be related to the personnel job history file of individuals, partly because the samples correspond more closely to tasks than to jobs and partly because the samples were taken after most of the workers had left the plants. The data on monitoring and the observed exposure levels prompt questions about the specificity of the job titles in relation to the tasks performed. For example, workers indicated that, in least at some plants, pipefitters were actually assigned to attach pipes to tank cars for the unloading of butadiene; that could account for the high exposure levels seen in the job. Different proportions of jobs had been sampled within each plant, and in only one plant were selected jobs sampled randomly throughout each year. For numerous jobs held by cases and controls, no samples had been taken. It may thus be questioned whether workers in those jobs were actually exposed but not tested, received a minimal dose, or had no exposure. For only 18 of the 464 jobs on the original list for ranking were four or more samples taken in more than one plant so that the jobs could be compared across plants. Of course, not all 464 jobs were represented among cases and controls. The

[1]These are the same plants in which the workers constitute the major portion of the cohort investigated within the Chemical Manufacturers' Association Butadiene Panel Research Program.

**Table 7. Mean levels of butadiene and styrene (ppm) by source of information**

| Source | Plant | Butadiene | | | Styrene | | |
|---|---|---|---|---|---|---|---|
| | | Mean | SD | No. | Mean | SD | No. |
| Plants | All | 7.96 | 53.96 | 3952 | 3.53 | 14.32 | 3649 |
| | 1 | 0.96 | 2.85 | 328 | 6.17 | 20.89 | 324 |
| | 2 | 4.47 | 7.47 | 36 | – | – | – |
| | 3 | 2.30 | 6.92 | 89 | – | – | – |
| | 4 | 5.00 | 18.01 | 1091 | 0.86 | 4.67 | 1009 |
| | 5 | 14.93 | 87.11 | 1435 | 6.66 | 19.64 | 1434 |
| | 6 | 2.33 | 5.97 | 165 | 0.29 | 0.48 | 145 |
| | 7 | 6.58 | 17.17 | 407 | 0.57 | 1.04 | 737 |
| NIOSH | 3 | 0.59 | 2.43 | 89 | | | |
| | 6 | 1.31 | 4.36 | 123 | | | |
| | 7 | 3.68 | 11.09 | 119 | | | |
| IISRP | | 2.61 | – | 74 | | | |

NIOSH, US National Institute for Occupational Safety and Health; IISRP, International Institute of Synthetic Rubber Producers

advantage of the original ranking scheme was that every job had an assigned rank which was comparable with that of every other job.

The mean levels of butadiene and styrene differed by plant. The data from plant 1 showed remarkably low levels of butadiene and high levels of styrene; no error was found in the recording of information at this plant through a review of the raw data. For plant 2, measures were available for only a few job titles. In most plants, mean levels by job varied widely (Table 8). Despite the variability, however, there is a significant correlation between log-transformed company data and the rank given for 464 job- and area-specific titles. Unfortunately, the level of correlation was not as high as might have been expected owing to the marked variability in the data from different sources and the number of job titles for which there were few or no data. There was no correlation between styrene levels and the job ranks that were assigned by industry representatives for the case–control study. This suggests that new analyses using real values would avoid the interrelationship between the two chemicals that was seen in previous analyses.

**Table 8. Correlation between ranks and personal measures in jobs (log transformed)**

| Source of data | Butadiene | | Styrene | |
|---|---|---|---|---|
| | No. | Correlation | No. | Correlation |
| Company (seven companies) | 88 | 0.46** | 71 | 0.06 |
| NIOSH (three companies) | 31 | 0.50* | – | – |
| IISRP | 67 | 0.74** | – | – |
| All | 281 | 0.35** | 258 | 0.13 |

NIOSH, US National Institute for Occupational Safety and Health; IISRP, International Institute of Synthetic Rubber Producers; * $p < 0.01$; ** $p < 0.001$

Table 9 presents the data for butadiene as means and geometric means with ranges. These values indicate upper ranges as high as 672 ppm in measurements taken in the 1980s, suggesting that previous exposures of some workers may have been even higher. The high geometric standard deviation in plant 4 is associated with nonspecific job titles, which render most of the data from that plant unusable. In all plants, however, there was marked variation in measurements, as indicated by high geometric standard deviations.

Since the geometric mean values for butadiene levels in three plants are clearly higher than those in the other plants, we reanalysed the cohort data for only those three plants for workers who had the characteristics of the cases: hired before 1960 and 10 or more years of employment. As shown in Table 10, this population of 3429 workers had significantly higher rates of mortality from all lymphohaematopoietic cancers and specifically from leukaemia: the SMRs were 1.6 and 1.8, respectively. The SMRs for other cancers in the group ICD 200–209 were high, although none was significant. The ratios for several cancers of the digestive system were also elevated (oesophagus, 1.8; stomach, 1.2; large intestine, 1.4). The SMR for all causes of death combined was low in these long-term workers and was identical to that of all workers.

**Table 9. Variation in exposure to butadiene (ppm) by plant**

| Plant[a] | No. of samples | Mean | SD | Range | Geometric mean | Geometric SD |
|---|---|---|---|---|---|---|
| 1 | 328 | 0.96 | 2.85 | 0.00–22.0 | 0.58 | 5.19 |
| 2 | 36 | 4.47 | 7.47 | 0.07–39.0 | 1.25 | 6.03 |
| 3 | 89 | 2.30 | 6.92 | 0.05–14.7 | 0.46 | 4.93 |
| 3N | 89 | 0.59 | 2.43 | 0.00–14.4 | 0.09 | 9.07 |
| 4 | 1091 | 5.00 | 18.01 | 0.00–175.8 | 0.18 | 15.48 |
| 5 | 1435 | 14.93 | 87.11 | 0.05–672.0 | 1.90 | 6.74 |
| 6 | 165 | 2.33 | 5.97 | 0.00–48.0 | 0.47 | 7.12 |
| 6N | 123 | 1.31 | 4.36 | 0.01–37.3 | 0.12 | 7.10 |
| 7 | 407 | 6.58 | 17.17 | 0.01–217.0 | 1.55 | 6.10 |
| 7N | 119 | 3.68 | 11.09 | 0.00–99.6 | 0.40 | 8.93 |
| IISRP | 74 | 2.61 | – | – | 1.97 | – |

[a] N, data from the US National Institute for Occupational Safety and Health for same plant; IISRP, International Institute of Synthetic Rubber Producers, data submitted only by numbers in a category

Exposure levels by plants depended on which jobs were sampled. In order to analyse all of the plants together in a cohort, we first assumed that the same exposures occurred in all plants but that exposures within jobs differed between the plants. Differences by plant depend on how many jobs with high exposure were included in the plant sample. In preparation for introducing monitored values in place of scores, we examined job exposure values to determine what differences there were by plant and how they compared with rank scores. The data suggested that the jobs assigned to the high and low ranks (10 and 0–1) were represented in the highest and lowest means or geometric means of the monitored values, but that jobs in the middle ranks (2–8) did not have the same relationship to each other with respect to measurements *versus* ranks. For some jobs, such as tank farm and pipefitters, the geometric standard deviations were 10 or more for the combined plants, which indicates that

**Table 10. Standardized mortality ratios (SMRs) by cause among workers in three plants who had been hired before 1960 and for whom follow-up was started after 10 years of employment**

| Cause of death | Observed | SMR | 95% CI |
|---|---|---|---|
| All | 889 | 0.86 | 0.80–0.92 |
| All diseases of the circulatory system | 459 | 0.85 | 0.77–0.93 |
| Arteriosclerotic heart disease, including coronary heart disease | 349 | 0.90 | 0.81–1.00 |
| All vascular lesions of the central nervous system | 50 | 0.76 | 0.57–1.01 |
| Rheumatic heart disease | 5 | 0.59 | 0.19–1.37 |
| All malignant neoplasms | 215 | 0.96 | 0.83–1.09 |
| Digestive organs and peritoneum | 71 | 1.17 | 0.92–1.48 |
| Oesophagus | 10 | 1.85 | 0.89–3.40 |
| Stomach | 12 | 1.16 | 0.60–2.03 |
| Large intestine | 28 | 1.39 | 0.92–2.01 |
| Rectum | 6 | 0.94 | 0.34–2.04 |
| Liver | 3 | 0.69 | 0.14–2.00 |
| Pancreas | 8 | 0.65 | 0.28–1.29 |
| Respiratory system | 65 | 0.80 | 0.62–1.02 |
| Larynx | 3 | 0.88 | 0.18–2.58 |
| Lung | 60 | 0.78 | 0.59–1.00 |
| Kidney | 6 | 1.06 | 0.39–2.30 |
| All lymphohaematopoietic cancers | 34 | 1.63 | 1.13–2.27 |
| Lymphosarcoma and reticulosarcoma | 5 | 1.16 | 0.37–2.70 |
| Hodgkin's disease | 5 | 2.43 | 0.78–5.68 |
| Leukaemia and aleukaemia | 15 | 1.81 | 1.01–2.99 |
| Other lymphatic tissue | 9 | 1.49 | 0.68–2.82 |

CI, confidence interval

we must improve the specificity of tasks and exposures as related to jobs. Some of the variation might be removed if the job exposure levels were assigned by plant. Thus, in order to use the measured values, we must test the significance of the differences in job levels across plants and across time so that we can extrapolate and apply the data to the cases and controls in the original study.

## Acknowledgements

The authors wish to express their appreciation to the US National Institute for Occupational Safety and Health, who shared their data and contributed their expertise and knowledge of the industry to help in job classification. We also wish to express thanks to the International Institute of Synthetic Rubber Producers and the participating companies, who aided in the work previously.

Funding is furnished under grant RO10H02730 from the US National Institute for Occupational Safety and Health.

## References

Cole, P., Delzell, E. & Acquavella, J. (1993) Exposure to butadiene and lymphatic and hematopoietic cancer. *Epidemiology*, **4**, 96–103

Kauppinen, T. & Partanen, T. (1988) Use of plant and period specific job exposure matrices in studies on occupational cancer. *Scand. J. Work Environ. Health*, **14**, 161–167

Matanoski, G.M., Santos-Burgoa, C. & Schwartz, L. (1990) Mortality of a cohort of workers in the styrene–butadiene polymer manufacturing industry (1943–1982). *Environ. Health Perspectives*, **86**, 107–117

McMichael, A.J., Spirtas, R., Gamble, J.F. & Tousey, P.M. (1976) Mortality among rubber workers: relationship to specific jobs. *J. Occup. Med.*, **18**, 178–185

Meinhardt, T.J., Lemen, R.A., Crandall, M.S. & Young, R.J. (1982) Environmental epidemiologic investigation of the styrene–butadiene rubber industry. Mortality patterns with discussion of the hematopoietic and lymphatic malignancies. *Scand. J. Work Environ. Health*, **8**, 250–259

Santos-Burgoa, C., Matanoski, G.M., Zeger, S. & Schwartz, L. (1992) Lymphohematopoietic cancer in styrene–butadiene polymerization workers. *Am. J. Epidemiol.*, **136**, 843–854

WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

# Butadiene and Styrene: Assessment of Health Hazards

*Edited by*

M. Sorsa, K. Peltonen, H. Vainio and K. Hemminki

IARC Scientific Publications No. 127

International Agency for Research on Cancer
Lyon
1993

Published by the International Agency for Research on Cancer,
150 cours Albert Thomas, 69372 Lyon Cedex 08, France

---



Distributed by Oxford University Press, Walton Street, Oxford OX2 6DP, UK
Distributed in the USA by Oxford University Press, New York



ISBN 92 832 2127 3
ISSN 0300–5085

Printed in the United Kingdom